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Drug Class Update with New Drug Evaluation: Targeted Immune Modulators

Date of Review: October 2026

Date of Last Review: October 2025
Dates of Literature Search: 01/01/2025 – 07/08/2026
Brand Name (Manufacturer): ICOTYDE (Johnson & Johnson)
Dossier Received: No

Generic Name: icotrokinra

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:
To evaluate recently published evidence for the safety and efficacy of systemic targeted immune modulators (TIMs) approved for management of autoimmune conditions including rheumatoid arthritis (RA), ankylosing spondylitis (AS), plaque psoriasis (PsO), psoriatic arthritis (PsA), Crohn's disease (CD), and ulcerative colitis (UC). In addition, review the evidence for the safety and efficacy of ICOTYDE (icotrokinra), an interleukin-23 (IL-23) receptor blocker, indicated for the treatment of moderate-to-severe PsO, which recently received Food and Drug Administration (FDA) approval in 2026.

Plain Language Summary:
- Targeted immune modulators are medicines that prevent the body's immune system from attacking the body's own healthy tissues. These medicines are used to treat autoimmune conditions including ankylosing spondylitis, rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis. In these conditions, the immune system attacks healthy tissues, causing inflammation and pain in the area under attack, decreases quality of life, and limits the ability to complete daily activities.
- Rheumatoid arthritis primarily affects the joints, causing pain, swelling, and stiffness.
- Ankylosing spondylitis is a type of arthritis that primarily affects the joints in the spine, causing back pain and stiffness.
- Plaque psoriasis is a skin condition with raised, irritated, and scaly patches of skin that may be flakey, scaly, or itchy and painful.
- Psoriatic arthritis is a condition that causes pain and swelling in the joints of some people with psoriasis.
- Crohn's disease and ulcerative colitis are painful conditions that impact the large intestine and cause diarrhea, abdominal discomfort, and bloody bowel movements.
- This review identified 12 new clinical guidelines that help providers decide the best medicine to treat different autoimmune conditions with targeted immune modulators. The guidelines are in line with current Oregon Health Plan policies. The targeted immune modulators can increase the risk of infections, headache, and feeling tired, so the benefit of the medicine should be considered as well as the possible side effects.
- For all targeted immune modulators, the provider must explain to the Oregon Health Authority why their patient needs the medicine. This process is called prior authorization.

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Research Questions:

1. What is the comparative efficacy of TIMs to treat autoimmune conditions including RA, AS, PsO, PsA, CD, or UC?
2. What are the comparative harms of TIMs to treat RA, AS, PsO, PsA, CD, or UC?
3. Do the included drugs differ in their effectiveness or harms for managing RA, AS, PsO, PsA, CD, or UC based on age, race, ethnicity, gender, patients with comorbidities, patients taking other commonly prescribed drugs, or in patients with early versus established disease?
4. What is the evidence for the safety and efficacy of icotrokinra in treating moderate-to-severe PsO in patients older than 12 years of age?

Conclusions:

- Since the previous Pharmacy and Therapeutics (P & T) Committee review, 3 systematic reviews[1-3] and 12 guidelines have been issued or updated to guide the use of TIMs in treatment of RA,[4] CD,[5-9] UC,[10-14] and hidradenitis suppurativa (HS).[15]

Systematic Reviews

- A 2026 Drug Effectiveness Review Project (DERP) systematic review evaluated the comparative effectiveness of TIMS for management of adults with RA or AS.[1] Two new studies reported that clinical improvement or remission in patients with RA were lower for adalimumab compared with 2 other TIMs (baricitinib, etanercept), although each comparison was limited to a single trial with moderate risk of bias (RoB).[1] Only one new comparative, randomized controlled trial (RCT) with moderate RoB was identified to evaluate treatments for AS.[1] While the study was not designed as a head-to-head comparison of ixekizumab and adalimumab, no statistically significant differences was found in the proportion of ixekizumab- and adalimumab-treated participants who achieved 40% improvement in the Assessment of SpondyloArthritis International Society criteria (ASAS40).[1] In all 3 RCTs, no differences between the TIMs in adverse effects (AEs) and serious adverse events (SAEs) were found.[1]
- A 2025 Cochrane systematic review assessed the benefits and harms of tumor necrosis factor inhibitors (TNFis) in adults with PsA.[2] Most studies comparing TNFis to other TIMs in methotrexate (MTX)-inadequate responders used adalimumab as the TNFi.[2] These studies were mostly pivotal trials sponsored by pharmaceutical companies, comparing a new TIM to a placebo, and using adalimumab as an active comparator.[2] Point estimates suggest no major difference in the benefits and harms of adalimumab compared to bimekizumab, ixekizumab, secukinumab, and ustekinumab.[2] However, the certainty of evidence (CoE) was low or very low.[2]
- A 2025 systematic review and network meta-analysis (NMA) informed the 2025 American Gastrological Association (AGA) Clinical Guidelines on the management of moderate-to-severe CD.[3] To induce remission in TIMs-naïve patients, moderate-to-high CoE support treatment of adalimumab and ustekinumab compared with certolizumab pegol and upadacitinib.[3] In patients with prior exposure to TIMs, moderate-to-high CoE support treatment with risankizumab and guselkumab compared with vedolizumab and ustekinumab.[3] For maintenance of clinical remission in patients with prior TIMs exposure, risankizumab and guselkumab is more effective than ustekinumab, and mirikizumab may be more effective than ustekinumab. However, no differences in efficacy between TIMs have been found in biologic-naïve patients with moderate-to-severe CD.[3] No differences in risk of serious infections were found across different agents.[3]

Clinical Guidelines

- The European Alliance of Associations for Rheumatology (EULAR) updated guidance for treatment of RA with TIMs in 2026. [4] Initially, MTX in combination with short-term glucocorticoid treatment is recommended; upon insufficient response after 3 to 6 months, a biologic disease-modifying anti-rheumatic drug (bDMARD) should be added; after careful consideration of risks, including major adverse cardiovascular events (MACEs), malignancies and thromboembolic events, a Janus Kinase inhibitor (JAKi) may also be considered. If the first bDMARD (or JAKi) fails, any other bDMARD (from another or the same class) or JAKi (considering risks) is recommended.[4] With sustained remission, DMARDs may be tapered, but caution is required as stopping often leads to a flare.[4] The CoE was high for most recommendations.[4] The specific recommendations are summarized in the narrative below.

- The American College of Gastroenterology (ACG) published updated guidance for management of adults with CD in 2025.[5] Recommendations include the following statements:
  - Tumor necrosis factor inhibitors (infliximab, adalimumab, certolizumab pegol) are recommended for induction and maintenance of remission for moderately to severely active CD (strong recommendation, moderate CoE).[5]
  - Combination therapy with infliximab and an immunomodulator (thiopurine) is recommended compared with treatment with either immunomodulators alone or infliximab alone in patients with CD who are naive to those agents (strong recommendation, moderate CoE).[5]
  - Intravenous (IV) vedolizumab is recommended for induction and maintenance of symptomatic remission in patients with moderately to severe CD (strong recommendation, moderate CoE).[5]
  - Subcutaneous (SC) vedolizumab is recommended as an option for maintenance of remission in patients with moderately to severely active CD who respond to 2 IV induction doses of vedolizumab (strong recommendation, moderate CoE).[5]
  - Ustekinumab and risankizumab are recommended in patients with moderate-to-severe CD for induction and maintenance of remission (strong recommendation, moderate CoE).[5]
  - Risankizumab is recommended over ustekinumab in patients with moderate-to-severe CD and prior exposure to TNFi therapy (conditional recommendation, low CoE).[5]
  - Mirikizumab is recommended for induction and maintenance of remission in patients with moderate to severe CD (strong recommendation, moderate CoE).
  - Intravenous guselkumab is recommended for induction followed by SC guselkumab for maintenance of remission in patients with moderate to severe CD (strong recommendation, moderate CoE).
  - Subcutaneous guselkumab is recommended for induction and maintenance of remission in patients with moderate to severe CD (strong recommendation, moderate CoE).[5]
  - Upadacitinib is recommended for induction and maintenance of remission for patients with moderately to severe CD who have previously been exposed to TNFi agents (strong recommendation, moderate CoE).[5]
- The AGA updated guidance for treatment of CD in 2025.[6] The AGA guidance is similar to the ACG guidance, but the AGA grades TIMs with higher efficacy and lower efficacy in their recommendations based on the NMA that supports this guidance.[3,6]
  - In adult outpatients with moderate-to-severe CD who are naïve to TIMs, the AGA suggests using a HIGHER efficacy medication (infliximab, adalimumab, vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab), rather than a LOWER efficacy medication (certolizumab pegol, upadacitinib) (conditional recommendation, low to high CoE).[6]
  - In adult outpatients with moderate-to-severe CD who have previously been exposed to at least one TIM, particularly TNFi therapies, the AGA suggests using a HIGHER efficacy medication (adalimumab, risankizumab, guselkumab, upadacitinib) OR an INTERMEDIATE efficacy medication (ustekinumab, mirikizumab), rather than a LOWER efficacy medication (vedolizumab, certolizumab pegol) (conditional recommendation, low to moderate CoE).[6]
  - In adult outpatients with moderate-to-severe CD who are NAÏVE to thiopurines and starting infliximab, the AGA suggests using infliximab in combination with thiopurines rather than infliximab monotherapy (conditional recommendation, low CoE).[6]
- In 2025 ACG updated guidance for the management of UC in adults.[10] Recommendations for induction therapy with TIMs in moderate or severe UC include:
  - Infliximab (IV) or upadacitinib (strong recommendation, high CoE).[10] When infliximab is used, combine therapy with a thiopurine (strong recommendation, moderate CoE for azathioprine).[10]

- Sphingosine 1-phosphate (S1P) receptor modulator, ozanimod, etrasimod, ustekinumab, guselkumab, mirikizumab, risankizumab, vedolizumab, adalimumab, golimumab, or tofacitinib (strong recommendation, moderate CoE).[10]

Recommendations for maintenance of remission include:

- Ozanimod, etrasimod, ustekinumab, guselkumab, mirikizumab, risankizumab, vedolizumab (IV or SC), adalimumab, golimumab, infliximab (IV or SC), tofacitinib or upadacitinib (strong recommendation, moderate CoE).[10]
- Vedolizumab is recommended over adalimumab for induction and maintenance of remission (strong recommendation, moderate CoE).[10]

- Canada's Drug Agency (CDA) published TIM recommendations for CD and UC and a recommendation for management of hidradenitis suppurativa (HS).
  - Mirikizumab or guselkumab is recommended for adults with moderate to severe CD in which conventional treatment or biologic therapies have led to an inadequate response, a loss of response, or intolerable side effects.[7,8]
  - Guselkumab is recommended for moderate to severe UC in cases in which conventional treatment or biologic therapies have led to an inadequate response, a loss of response, or intolerable side effects.[11]
  - Risankizumab is recommended for adults with moderate to severe UC who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a JAKi.[12]
  - Bimekizumab is recommended in adults with moderate to severe HS with an inadequate response to conventional systemic therapy.[15]
- The National Institute for Health and Care Excellence (NICE) issued recommendations for treatment of CD and UC with TIMs in 2025.
  - Guselkumab can be used for previously treated moderate to severe CD or UC in adults, when conventional or biological treatment has not worked or cannot be tolerated, and a TNFi has not worked or cannot be tolerated or is not suitable.[13,14]
  - Mirikizumab can be used to treat moderate to severe CD in adults, only if the disease has not responded well enough or stopped responding to a previous biological treatment, or a previous biological treatment was not tolerated, or TNFi are not suitable.[9]

New Indications

- June 2026: Subcutaneous risankizumab received FDA approval for pediatric patients down to 6 years of age with PsO or PsA.[16] Subcutaneous risankizumab was previously only approved for adults with PsO or PsA (in addition to adults with CD or UC).[16]
- April 2026: Ustekinumab received FDA approval for pediatric patients 2 years of age and older with moderate or severe CD.[17] Ustekinumab was previously only approved for adults with CD.[17]
- March-April 2026: Subcutaneous secukinumab injection received FDA approval for pediatric patients 12 years of age and older with AS or HS.[18] Subcutaneous secukinumab was previously approved only for adults with AS or HS.
- March 2026: Deucravacitinib oral tablets received FDA approval for adults with PsA.[19] Efficacy and safety for the indication were assessed in 2 multicentered, double-blind, placebo-controlled RCTs in adults with active PsA.[19] In both trials, treatment with deucravacitinib resulted in statistically significant improvement in disease activity, as measured by American College of Rheumatology (ACR) 20, ACR 50, and ACR 70 response, compared to placebo at Week 16 (see **Table 3**).[19]
- October 2025: Tofacitinib oral tablets and oral solution received FDA approval for pediatric patients 2 years of age and older with PsA who have an inadequate response or intolerance to at least one TNFi.[20] Tofacitinib was previously approved only for adults with PsA.

New Formulations

- May 2026: An Interchangable biosimilar formulation of golimumab-sldi (IMMGOLIS) received FDA approval for treatment of adults with RA in combination with MTX and for adults with moderate-to-severe UC.[21]

- January 2025: An Interchangable biosimilar formulation of tocilizumab (AVTOZMA) received FDA approval for treatment of adults with RA, hospitalized with Coronavirus Disease-19 (COVID-19), and adults with giant cell arteritis; and patients aged 2 years of age and older with polyarticular juvenile idiopathic arthritis (JIA) and systemic JIA.[22]
- August 2025: The FDA approved a new extended release oral tablet of the phosphodiesterase-4 inhibitor (PDE-4i) apremilast, OTEZLA XR.[23] This medication is indicated for treatment of adults with active PsA, PsO who are candidates for phototherapy or systemic therapy, and oral ulcers associated with Behçets' Disease.[23] In pediatric patients aged 6 years and older weighing at least 20 kg, extended-release apremilast is also indicated for treatment of active PsA and moderate-to-severe PsO.[23]
- There is insufficient evidence of clinical differences between TIMs for groups of patients based on specific demographic characteristics (e.g., age, race, ethnicity, comorbidities, disease duration, or severity) in treatment of AS, RA, PsO, CD, or UC.

New Drug Evaluation: Icotrokinra

- Icotrokinra, an orally administered interuleukin-23 (IL-23) receptor antagonist, received FDA approval in 2026 for the treatment of moderate-to-severe PsO in patients aged 12 years and older, who weigh more than 40 kg and are candidates for systemic therapy or phototherapy.[24]
- Four placebo-controlled, phase 3 RCTs (ICONIC-LEAD, ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and ICONIC-TOTAL) evaluated the efficacy of icotrokinra 200 mg once daily for the treatment of patients (2367 adults and 72 adolescents) with moderate-to-severe PsO.[25] The co-primary endpoints for 3 of the trials (ICONIC-LEAD and ICONIC ADVANCE 1 and 2) were the Investigators Global Assessment (IGA) score of 0 or 1 and 2 or greater grade improvement from baseline on a 5-point scale, and achievement of 90% or greater reduction in the Psoriasis Area and Severity Index (PASI-90) score at week 16.[25] The ICONIC-TOTAL RCT evaluated patients with PsO in specific site areas including the scalp, genitals, and hands/feet, so the PASI-90 was not assessed as a co-primary endpoint in this trial.[25] Deucravacitinib was used as an active comparator in the ICONIC-ADVANCE 1 and 2 studies.[25]
- In all 4 RCTs for the primary endpoint of percentage of patients who achieved IGA 0/1 response at Week 16, icotrokinra was statistically superior to placebo (ICONIC-LEAD: 65% vs. 8%; risk difference [RD] 57%; 95% confidence interval [CI], 50 to 62; p<0.001; ICONIC ADVANCE 1: 69% vs 11%; RD 58%; 95% CI, 45 to 58; p<0.001; ICONIC ADVANCE 2: 71% vs. 9%; RD 62%; 95% CI, 53 to 69; p<0.001; ICONIC-TOTAL; 57% vs 6%; RD 51%; 85% CI, 42 to 59; p,0.001; moderate-quality evidence).[25] Icotrokinra was statistically superior to deucravacitinib across all prespecified key primary and secondary endpoints in both the ICONIC-ADVANCE 1 & 2 studies.[26] More complete study details are presented in **Table 6**.
- The most frequently reported AEs with icotrokinra were headache, nausea, cough, fungal infections, and fatigue (see **Table 5**).[24] Infections other than mycoses were reported in 0.2% of icotrokinra-treated patients compared with 0.4% in placebo-treated patients.[24]

Recommendations:

- Update TIMs prior authorization (PA) criteria (**Appendix 8**) to include expanded indications for recent FDA approvals and icotrokinra for treatment of moderate-to-severe PsO.
- Based on review of recently published systematic reviews and guidelines, no other preferred drug list (PDL) changes are warranted.
- After reviewing drug costs in executive session, the following changes to the PDL were accepted:
- **Adalimumab**
  -Make HADLIMA syringe & autoinjector preferred, Tier 1.
  -Make adalimumab-fkjp (non-branded), and adalimumab-aaty non-preferred Tier 2
  -Make all other forms of adalimumab products non-preferred Tier 3 including HUMIRA, SIMLANDI, and AMJEVITA.
- **Ustekinumab**
  -Make ustekinumab-hmny (STARJEMZA) vial and syringe preferred Tier 1

-Make ustekinumab–kfce (YESINTEK), and ustekinumab–srif (IMULDORSA) non-preferred Tier 2.
-Make all other forms of ustekinumab non-preferred Tier 3

- **Infliximab**
  -Make infliximab-abda (RENFLEXIS) vial preferred Tier 1;
  -Make infliximab (REMICADE) vial and infliximab-axxq (AVSOLA) vial non-preferred tier 2.
- Make rituximab-pvvr (RUXIENCE) vial preferred Tier 1.
- Make tocilizumab biosimilar (TYENNE) vial, autoinjector, and syringe preferred, Tier 2.
- Make Otezla, Taltz, and Tremfya non-preferred, Tier 3

Summary of Prior Reviews and Current Policy

- The systemic TIMs used in autoimmune conditions were last reviewed by the P & T Committee at the October 2025 meeting. All TIMs require PA to evaluate disease severity and to implement step therapy for common diagnoses. At the October 2025 meeting, the following PDL recommendations were implemented for TIMs and related biosimilar products:
  - Make infliximab preferred, Tier 1
  - Make ustekinumab biosimilar (PYCHEVIA) syringes and vials preferred, Tier 2 and make guselkumab (TREMFYA) preferred, Tier 2.
  - All other TIMs and their biosimilar products were designated as non-preferred.
- FDA-approved TIMs and PDL status for selected autoimmune conditions are summarized in **Appendix 1.**
- Frequently used assessment outcomes for assessing disease improvement in AS, RA, PsO, PsA, CD, and UC are presented in **Appendix 2**.
- A table of FDA-approved TIMs, their molecular target, and approved indications is presented in **Appendix 3**.
- The PA criteria for systemic TIMs approved for use in autoimmune conditions are presented in **Appendix 8.**

OHP FFS Utilization:

- In the second quarter of 2026 (April 1 to June 30), there were 79 pharmacy claims for TIMs in the fee-for-service (FFS) population. Sixty percent of the claims were for preferred formulations of adalimumab, apremilast, etanercept, guselkumab, ixekizumab, and tofacitinib. For the non-preferred agents, 40% of claims were for adalimumab biosimilar (HADLIMA), secukinumab, risankizumab and upadacitinib. In the first quarter of 2026 (January 1 to March 30), the most frequently utilized physician-administered TIMs included abatacept, infliximab, infliximab biosimilars (AVSOLA, INFLECTRA, RENFLEXIS) rituximab, rituximab biosimilar (TRUXIMA), and vedolizumab.

Background:

Targeted immune modulators include bDMARDs and targeted synthetic DMARDs (tsDMARDs). Biologic DMARDs are large, complex, proteins that must be administered parentally. The bDMARDs include TNFi, integrin inhibitors, IL-antagonists, and lymphocyte antagonists. The FDA has approved biosimilars for some bDMARDs including adalimumab, etanercept, golimumab, infliximab, natalizumab, rituximab, tocilizumab, and ustekinumab.[27] Targeted synthetic DMARDs are small chemical molecules that can be taken orally. The JAKi, S1P receptor modulators, PDE-c, and tyrosine-kinase-2 inhibitors (TYK2i) are classified as tsDMARDs.

Axial Spondyloarthritis

Axial spondyloarthritis (axSpA) is a chronic rheumatic disorder that primarily affects the sacroiliac joints and spine.[28] Patients with axSpA can be classified as having either of 2 subtypes of axSpA: radiographic axSpA (r-axSpA, also termed ankylosing spondylitis [AS]) or nonradiographic axSpA (nr-axSpA).[29] Diagnosis of AS is based on radiologic confirmation of sacroiliitis and the presence of at least one clinical symptom: low back pain for at least 3 months, limited lumbar spine motion, or decreased chest expansion.[30] The goals of treatment for patients with AS are to reduce symptoms, maintain spinal flexibility, reduce functional limitations, maintain work ability, and decrease disease complications.[31] The prevalence of AS in the United States (US) is approximately 1% among adults and is more common in men than women (3:1 ratio).[32] It tends to have a gradual onset, usually before age 45, and is often underdiagnosed, which can lead to more severe damage to the spine, resulting in physical disability and worsened quality of life.[33]

All FDA-approved TIMs to manage AS reduce disease activity as assessed by ASAS scores, which is a composite score of 4-6 domains.[34] Percentage of responders in each improvement criteria are reported as ASAS20 (20% improvement) and ASAS40 (40% improvement).[34] Additional outcomes used to assess the efficacy of TIMs to manage AS disease activity in clinical trials are summarized in **Appendix 2**.

The 2022 Assessment of Spondyloarthritis International Society-European Alliance of Associations for Rheumatology (ASAS-EULAR) 2022 recommendations for management of AS include the following statements:

- Patients suffering from pain and stiffness should use a nonsteroidal anti-inflammatory drug (NSAID) as first-line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs, continuous use is preferred if needed to control symptoms (Strong Recommendation; High-Quality Evidence).[35]

- Patients with purely axial disease should normally not be treated with conventional synthetic DMARDs (csDMARDs) (e.g., leflunomide, sulfasalazine, MTX), due to lack of efficacy; however, sulfasalazine may be considered in patients with peripheral arthritis (Strong Recommendation; High-Quality Evidence).[35]
- Tumor necrosis factor inhibitors, interleukin-17 inhibitors (IL-17i), or JAKi should be considered in patients with persistently high disease activity (Ankylosing Spondylitis Disease Activity Score [ASDAS] $\geq$ 2.1) despite conventional treatments; current practice is to start with a TNFi or IL-17i (Strong Recommendation; High-Quality Evidence).[35]
- If there is a history of recurrent uveitis or active inflammatory bowel disease (IBD), preference should be given to a TNFi (Strong Recommendation; High-Quality Evidence). In patients with significant psoriasis, an IL-17i may be preferred (Strong Recommendation; Moderate-Quality Evidence).[35]

Rheumatoid Arthritis

The hallmark symptoms of RA are inflammation of the synovial tissues with progressive erosion of bone leading to malalignment of the joint and, in most cases, disability.[36] Typically, RA involves the small joints of the hands and feet, however as the disease progresses, any synovial joint can be involved.[37] The most prominent risk factor for the development of RA is genetic inheritance, as family history is associated with an increased risk for RA.[37] Rheumatoid arthritis has an annual incidence in the US and Western and Northern Europe of about 40 per 100,000 people.[32] Rheumatoid arthritis can occur at any age, but the incidence peaks in the third through fifth decades of life, and the disease is 2 to 3 times as common among women as it is among men.[37] Tumor necrosis factor plays a central role in the pathophysiology of RA.[36]

The severity of RA is usually measured by the number and size of involved joints.[38] Primary endpoints used in RA clinical trials are the ACR response, the Health Assessment Questionnaire Disability Index (HAQ-DI), and the Disease Activity Score-28 (DAS-28). The ACR response is considered a measure of treatment efficacy and evaluates tender joint count, swollen joint count, patient's assessment of pain, patient's and physician's global assessments of disease activity, patient's assessment of physical function, and laboratory evaluation of an acute-phase reactant (erythrocyte sedimentation rate [ESR] or C-reactive protein

[CRP] level).[39] The HAQ-DI is a self-reported measure of functional capacity (total score 0 to 3).[40] Scores of 0 to 1 are generally considered mild to moderate disability, 1 to 2 moderate to severe disability, and 2 to 3 severe to very severe disability.[40] The DAS-28 is another index of disease activity (similar to the ACR response) which assesses 28 joints in swelling, tenderness, ESR or CRP levels, and patient global assessment of health.[40] A DAS-28 score greater than 5.1 corresponds to high disease activity and less than 3.2 corresponds to low disease activity.[40] A DAS-28 score of 2.6 corresponds with remission.[40] Outcomes used to assess RA in clinical trials are summarized in **Appendix 2**.

The primary treatment goal in all patients with RA is sustained remission or low disease activity.[41] The 2022 EULAR recommendations for RA management suggest treatment begin with a csDMARD such as MTX as soon as diagnosis of RA is established.[41] Other csDMARDs recommended to treat RA include hydroxychloroquine, leflunomide and sulfasalazine.[41] If the treatment target is not achieved with the first csDMARD strategy and when poor prognostic factors are present, a bDMARD (i.e. TNFi, IL inhibitor) should be added; tsDMARDs such as JAKi may be considered, but risk factors for cardiovascular events and malignancies associated with JAKi must be considered (Efficacy: Strong Recommendation; High-Quality Evidence and Safety: Strong Recommendation; Moderate-Quality Evidence).[41]

Plaque Psoriasis and Psoriatic Arthritis

Plaque psoriasis is a chronic, immune-mediated inflammatory disorder of the skin, scalp and joints that affects about 2 to 3% of the population.[42] The development of the disease is driven by multiple pathways of immune mediators, including TNF, IL-23, and IL-17 cytokines. Plaque psoriasis is characterized by itchy, red, scaly, raised lesions on the skin, especially on the scalp, elbows, knees, and trunk. Typically, PsO is classified as mild, moderate, or severe. Mild disease involves less than 5% of the body surface area and has little to no impact on quality of life or function. Per 2021 American Academy of Dermatology-National Psoriasis Foundation (AAD-NPF) guidance, first-line agents for PsO include topical medications such as: corticosteroids, vitamin D analogs (e.g., calcipotriene), retinoids (e.g., tazarotene) or calcineurin inhibitors (e.g., tacrolimus or pimecrolimus).[43] Phototherapy is an option for patients with moderate-to-severe PsO who have not responded to topical therapy.[44] Systemic csDMARDs are recommended for patients with moderate-to-severe PsO unresponsive to topical treatments or phototherapy and include MTX, cyclosporine, or acitretin.[44] Biologics including TNFi, IL-12/22i, IL-23i, or IL-17 may be added for patients with moderate-to-severe PsO not controlled by other therapies.[45] Targeted synthetic DMARDs approved to manage PsO include the PDE-4 inhibitor, apremilast and the TYK2 inhibitor, deucravacitinib.

Several tools have been developed to evaluate symptom improvement and quality of life in patients with PsO. In clinical trials, symptom improvement is often evaluated using the PASI, the static Physician's Global Assessment scale (sPGA), or the Psoriasis Symptom Inventory (PSI). There is no consensus on the most reliable scale, but the PASI is used most often in clinical trials and is considered the most validated scale.[46] The PASI ranges from 0 to 72 points and evaluates body surface area involvement, induration, scaling, and erythema.[46] Because the PASI only evaluates skin involvement on the trunk, head, arms and legs, the PASI has limited sensitivity in patients with mild to moderate disease or limited BSA involvement.[46,47] The PASI scoring does not consider symptoms affecting hands, feet, face or genitals. Because the PASI scale is not linear, small changes in BSA involvement can result in a significant improvement of the overall score without change in other symptoms.[46] In addition, though the PASI evaluates symptoms on a range of 0 to 72 points, in clinical practice, patients often do not have scores greater than 40.[47] The most commonly reported outcome in clinical trials is improvement of greater than 75% in the PASI score (PASI-75). However, an improvement of 100%, indicating complete disease clearance, is considered more clinically significant.[47] Additional outcomes used to assess PsO and PsA in clinical trials are summarized in **Appendix 2.**

Psoriatic arthritis is a disease with heterogeneous manifestations in patients who have psoriasis.[48] It comprises both musculoskeletal as well as non-musculoskeletal manifestations; the latter particularly include the skin and the nails, but also potentially the gut (IBD) or the eyes (uveitis).[48] Active chronic PsA is

associated with cardiovascular, psychological and metabolic comorbidities, which, together with the musculoskeletal manifestations, impose a significant impact on quality of life and increased risk of mortality.[48] The 2023 EULAR recommendations for pharmacologic management of PsA include the following statements:

- In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD (TNFi, IL-17i, IL-23i, interleukin 12/23 inhibitor [IL12/23i], or JAKi) should be commenced (Strong Recommendation; High-Quality Evidence).[49]
- In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate, a JAKi (tofacitinib, upadacitinib) may be considered, taking safety considerations (patients aged 65 years or above, those who are current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors, and with known risk factors for venous thromboembolism) into account (Strong Recommendation; Moderate Quality Evidence).[49]
- In patients with mild disease (oligoarticular or entheseal disease without poor prognostic factors and limited skin involvement) and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi is appropriate, a PDE-4i may be considered. (Strong Recommendation; Moderate Quality Evidence).[49]
- The choice of mode of action should reflect non-musculoskeletal manifestations related to PSA; with clinically relevant skin involvement, preference should be given to an IL-17i, IL-23i, or IL-12/23i; with uveitis to a TNFi, and with IBD to a TNFi, IL-23i IL-12/23i or JAKi. (Strong Recommendation; Moderate Quality Evidence).[49]

Hidradenitis Suppurativa

Hidradenitis suppurativa is a chronic inflammatory skin disease which has a prevalence of 1-4% worldwide and is 3 times more common in women than men.[50,51] The mean age of onset is 22 years.[50] It is characterized by inflamed nodules which occur most frequently in the axillary, inguinal, and anogenital regions of the body.[50,51] These nodules are painful, recurrent, and can result in abscesses, chronic draining sinus tracts, scarring, disfigurement, and disability.[50] Genetic predisposition, hormonal factors, immune factors, medications such as lithium and medroxyprogesterone acetate, obesity, and smoking all are potential contributors to the etiology.[50]

The Hurley clinical staging system describes disease severity by 3 stages: stage 1 indicates abscess formation, single or multiple, without sinus tracts and cicatrization (scar formation); stage 2 indicates recurrent abscesses with tract formation and cicatrization, single or multiple, widely separated lesions; and stage 3 indicates diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area.[52] About 69% of patients have stage 1 disease, while approximately 28% and 4% of patients have more severe stage 2 and 3 disease.[52] The minimum clinically significant change in Hurley staging is unclear.[53]

Nonpharmacological treatments for HS include local hygiene and cleansing, reducing heat, humidity, and friction in the area, weight loss to ideal weight, and smoking cessation.[50] Surgical treatment may also be an option for Hurley stage 2 and 3 patients.[50] Pharmacological treatments for HS include antibiotics, retinoids, corticosteroids, and TNFi.[50,52] However, the most commonly used treatments are topical and oral antibiotics.[54] The most commonly used oral antibiotic treatments are tetracyclines.[54]

Crohn's Disease and Ulcerative Colitis

Crohn's disease and UC are classified as IBDs. Crohn's disease is characterized by inflammation involving the full thickness of the bowel wall at any point from mouth to anus, whereas UC is characterized by mucosal ulceration limited to the colon and rectum.[55] Symptoms of both conditions include blood and/or mucus

in the stool, urgency, tenesmus, incontinence, increased frequency of bowel movements, and abdominal discomfort.[55] Systemic symptoms include fatigue, weight loss, loss of appetite, anemia, inflammatory eye disease, sclerosing cholangitis, and arthritis.[55] Clinical diagnosis of both conditions is most accurately made with colonoscopy.[55]

Two scoring tools are used to assess disease activity in CD and UC. The Crohn's Disease Activity Score (CDAI) is an evaluation of 8 clinical factors involved in CD assessment, including number of soft stools per day, abdominal pain, general well-being, use of medications for diarrhea, presence of abdominal mass, hematocrit, and percentage deviation from standard weight.[55] A total score of 450 or greater indicates extremely severe disease, a score of 150 or greater indicates active disease, and a score less than 150 indicates minimal disease.[55] The Mayo Clinic Score is used to evaluate UC symptoms.[56] Four subscores evaluate rectal bleeding, stool frequency, patient-reported outcomes, and endoscopy results. Each domain is scored from 0 to 3 points, with a higher score indicating more severe disease.[56] The total score can range from 0-12 with higher scores indicating worse severity.[56] A critical component of this score is the endoscopic findings.[56] Patients with lower scores but with an endoscopic score of 2 or greater are considered more severe regardless of the final score.[56] The domains for the CDAI and Mayo Clinic Score are presented in more depth in **Appendix 2**.

Practice guidelines for CD recommend considering the disease location, severity, complications, and extra intestinal manifestations when choosing a treatment strategy.[55] Treatment is largely directed at symptom relief rather than cure, and active treatment of acute disease (inducing remission) should be distinguished from preventing relapse (maintaining remission).[55] NICE guidance recommends TNFi for induction, but only after failure of conventional therapy with corticosteroids, aminosalicylates (i.e., sulfasalazine, mesalamine), azathioprine or mercaptopurine, and should only be used for maintenance if there is clear evidence of active disease.[57] The ACG strongly recommends induction with a TNFi to maintain remission in patients who have moderate-to-severe CD despite treatment with conventional therapy.[55] Cyclosporine, mycophenolate mofetil, and tacrolimus should not be used to treat CD due to insufficient evidence demonstrating efficacy.[55]

The choice of therapy for UC considers the level of disease activity (mild, moderate, or severe), the extent of the disease (proctitis, left-sided disease, extensive disease, or pancolitis), and patient preferences.[58] In 2024, the AGA published updated guidance for the management of UC.[59] AGA recommendations include the following statements:

- In adult outpatients with moderate-to-severe UC, the use of infliximab, golimumab, vedolizumab, tofacitinib, upadacitinib, ustekinumab, ozanimod, etrasimod, risankizumab and guselkumab are recommended over no treatment (Strong Recommendation, Moderate to High Certainty of Evidence).[59]
- In adult outpatients with moderate-to-severe UC, the use of adalimumab, filgotinib or mirikizumab is suggested over no treatment (Conditional Recommendation, Moderate Certainty of Evidence).[59]
- In adult outpatients with moderate-to-severe UC who are *naïve to advanced therapies*, using a HIGHER efficacy medication (infliximab, vedolizumab, ozanimod, etrasimod, upadacitinib, risankizumab, guselkumab) OR an INTERMEDIATE efficacy medication (golimumab, ustekinumab, tofacitinib, filgotinib, mirikizumab), is suggested rather than a LOWER efficacy medication (adalimumab) (Conditional Recommendation, Low Certainty of Evidence).[59]
- In adult outpatients with moderate-to-severe UC who have previously been exposed to 1 or more advanced therapies (particularly a TNFi), using a HIGHER efficacy medication (tofacitinib, upadacitinib, ustekinumab) OR an INTERMEDIATE efficacy medication (filgotinib, mirikizumab, risankizumab, guselkumab), is suggested rather than a LOWER efficacy medication (adalimumab, vedolizumab, ozanimod, etrasimod) (Conditional Recommendation, Low Certainty of Evidence).[59]

Methods:

A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canada's Drug Agency (CDA-AMA), the Oregon Mental Health Clinical Advisory Group (MHCAG), and the Scottish Intercollegiate Guidelines Network (SIGN) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high-quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:

Drug Effectiveness Review Project: Targeted Immune Modulators for Rheumatoid Arthritis and Axial Spondyloarthritis (2026)

A 2026 DERP systematic review evaluated the comparative effectiveness of TIMs for management of adults with RA or axSpA.[1] This report updates a previously published 2022 report.[1] Literature was searched through November 2025 for comparative RCTs with a minimum of 12 weeks follow-up.[1] Placebo-controlled trials and comparisons of a biosimilar to its reference drug were excluded.[1] Three new studies met inclusion criteria.[1] Two studies compared different TIMs for treatment of RA, while the third compared adalimumab and ixekizumab for treatment of AS.[1] Sixteen RCTs focused on RA treatment with TIMs and one RCT that evaluated treatment of AS were carried forward from the from the previous DERP report, which was previously shared with the P & T Committee.[1] Only results from the 3 new RCTs will be summarized in this class update.

One high RoB RCT compared adalimumab 40 mg SC every other week to baricitinib 4 mg orally once daily over 24 weeks in adults with moderate-to-severe RA who had inadequate response to csDMARDs.[1,60] All participants received background therapy with MTX.[60] The study did not have any industry funding. No differences were found between the groups in the co-primary endpoints of mean change from baseline in DAS28-CRP and the proportion of participants achieving clinical remission (DAS28-CRP < 2.6) at week 24.[60] Mean change from baseline for DAS28-CRP did not differ significantly for the adalimumab group (−2.9) and the baricitinib group (−3.3) at 12 weeks (P = 0.05).[60] Similarly, no difference was found between groups in remission rates for DAS28-CRP < 2.6 (45% vs. 50%; P = 0.30).[60] No differences between groups in overall adverse effects (AEs) were found.[1]

Another high RoB study compared adalimumab 40 mg SC every other week to etanercept 50 mg SC every week over 24 weeks in adults with RA receiving stable MTX doses.[1,61] Remission rates (DAS28-CRP < 2.6) did not differ between groups at 12 weeks (28% adalimumab vs. 23% etanercept; P = 0.70) or 24 weeks (22% adalimumab vs. 35% etanercept; P = 0.36).[1] Similarly, no differences between groups in ACR20, ACR50, or ACR70 response at 12 or 24 weeks were found.[1] No differences between groups in overall AEs were found.[1]

The only trial that evaluated AS treatment was a moderate RoB phase 3 randomized, double-blind, placebo-controlled superiority study that compared ixekizumab (80 mg SC every 2 weeks or every 4 weeks) to adalimumab 40 mg SC every 2 weeks, or placebo in 341 adult participants.[1,62] Patients previously had inadequate response or intolerance to NSAIDs and an established diagnosis of AS.[1] The primary endpoint was the proportion of participants achieving an ASAS 40 response at week 16.[1] Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (defined as ASDAS < 1.3) was a secondary endpoint.[1] The study was not designed as a head-to-head comparison of ixekizumab and adalimumab; instead, the adalimumab reference group was included as an in-study active

reference for comparison with placebo to provide additional context for interpretation of the ixekizumab study results.[1] The study was funded by the manufacturer of ixekizumab.[1] The DERP report excluded results for the study arm that received unapproved bi-weekly dosing.[1]

At 16 weeks, 48% of ixekizumab-treated participants and 36% of adalimumab-treated participants achieved an ASAS40 response which were higher than placebo (18%).[1] Mean difference between ixekizumab and placebo was 29.8% (95% CI, 16.2 to 43.3; P < 0.001), while the mean difference between adalimumab and placebo was 17.2% (95% CI, 4.4 to 30.0; P = 0.005).[1] Both TIMs-treated participants were more likely than placebo-treated participants to have low disease activity (ASDAS < 1.3; 43% ixekizumab, 38% adalimumab, 13% placebo; P < .001 for both comparisons to placebo).[1] In addition, both TIMs-treated participants were more likely than placebo-treated participants to be in remission (ASDAS < 2.1) at week 16 (16% ixekizumab, 16% adalimumab, 2% placebo; P <.01 for both comparisons to placebo).[1] While the study was not designed as a head-to-head comparison of ixekizumab and adalimumab, endpoint estimates were similar between them, with no differences found in ASAS40 response (P = 0.11), achieving low disease activity (P = 0.50) or achieving remission (P ≥ .05).[1] No differences between the groups in overall AEs and SAEs were found.[1]

In summary, 2 recently published studies reported that clinical improvement or remission were lower for adalimumab compared with 2 other TIMs (baricitinib, etanercept) in patients with RA, although each comparison was limited to a single trial with moderate RoB.[1] Only one new comparative, randomized controlled trial (RCT) with moderate RoB was identified to evaluate treatments for AS.[1] While the study was not designed as a head-to-head comparison of ixekizumab and adalimumab, no statistically significant differences was found in the proportion of ixekizumab- and adalimumab-treated participants who achieved 40% improvement in the ASAS40.[1] In the 3 new RCTs the incidence of adverse events AEs and SAEs did not differ across comparisons of TIMs.[1]

Tumor Necrosis Factor Inhibitors For Psoriatic Arthritis (2025)

A 2025 Cochrane systematic review assessed the benefits and harms of TNFi therapies in adults with PsA.[2] Literature was searched comparative RCTs that evaluated TNFis to placebo, NSAIDs, corticosteroids, and TIMs[2] Major outcomes included clinical improvement, minimal disease activity, physical function, health-related quality of life, radiographic progression, SAEs, and withdrawals due to AEs.[2] The primary time point was 12 weeks for clinical improvement; 24 weeks for minimal disease activity, function, quality of life, and radiographic progression; and the end of the trial period for SAEs and withdrawals due to AEs.[2]

Twenty-five RCTS (n=7857) met inclusion criteria.[2] Four studies compared TNFi to MTX and one study compared a TNFi to ustekinumab in DMARD-naïve participants. In csDMARD-inadequate responders, 11 studies compared TNFi to placebo; 4 studies compared TNFi to placebo and ixekizumab, bimekizumab, tofacitinib, or upadacitinib; and 3 studies compared TNFi to ixekizumab, secukinumab, and ustekinumab.[2] Performance (32%), detection (56%) and reporting (80%) biases were at high or unclear risk across studies.[2] Only one study had a low RoB in all domains.[2] Most studies were funded by pharmaceutical companies and most authors declared extensive conflicts of interest.[2] Most of the included participants had polyarticular PsA.[2] Most csDMARD-inadequate responders had a long disease duration.[2] To maintain brevity in this report, only the evidence for the primary outcome of clinical improvement at 12 weeks (efficacy) and safety results will be summarized for head-to-head TIMs comparisons.

TNFi vs. other bDMARDs

No conclusions could be drawn about the effect of TNFis versus other bDMARDs in DMARD-naïve participants as only one high ROB RCT with a small number of participants was identified.[2] Five trials were identified that compared TNFis with other bDMARDs in csDMARD-inadequate responders.[2] Comparisons were as follows: TNFi (the specific TNFi was not described) compared to ustekinumab; adalimumab versus secukinumab; a 3 parallel-arm trial, where bimekizumab was tested against a placebo, and adalimumab was used as an active comparator; a 4 parallel-arm trial investigating ixekizumab 80 mg every other week, ixekizumab

80 mg every four weeks against placebo, and using adalimumab as an active comparator; and adalimumab versus ixekizumab.[2] Different bDMARDs were not pooled in the same meta-analysis.[2]

Two trials did not show a statistically significant difference in ACR50 at 12 weeks between adalimumab (41%) and ixekizumab (39%) (RR 1.05, 95% CI 0.89 to 1.25; I^2 = 0%; n=774; low CoE).[2] Two trials did not show a statistically significant difference in ACR50 at 24 weeks either (adalimumab 44% vs. ixekizumab 48%; RR 0.93, 95% CI 0.80 to 1.08; n=774; low CoE).[2] One trial did not show a statistically significant difference in ACR50 at 12 weeks between adalimumab (34%) and secukinumab (32%) (RR 1.06, 95% CI 0.88 to 1.29; n=853; low CoE).[2] One study did not show a statistically significant difference in ACR50 at 24 weeks either (adalimumab 40% vs. secukinumab 43%; RR 0.93, 95% CI 0.79 to 1.09; n=853; low CoE).[2] One trial did not show a statistically significant difference in ACR50 at 12 weeks between that adalimumab (46%) and bimekizumab (44%) (RR 1.04, 95% CI 0.85 to 1.29; n=571; low CoE).[2] One study did not show a statistically significant difference in ACR50 at 24 weeks either (adalimumab 47% vs. bimekizumab 45%; RR 1.04, 95% CI 0.85 to 1.27; n=571; moderate CoE).[2]

The difference in SAEs between TNFis (7%) and ixekizumab (4%) is uncertain (RR 1.62, 95% CI 0.62 to 4.22; I^2 = 52%; n=774; very low CoE).[2] The differences in SAEs between TNFis and secukinumab or bimekizumab is also uncertain.[2] Among participants randomized to secukinumab, 8% experienced SAEs versus 7% on adalimumab (RR 0.85, 95% CI 0.52 to 1.38; n=853; very low CoE).[2] Among participants randomized to bimekizumab, 4% experienced SAEs versus 4% on adalimumab (RR 0.91, 95% CI 0.34 to 2.41; n=571; very low CoE).[2]

The difference in early treatment withdrawal due to AE between TNFis and ixekizumab is uncertain. In one study, 4% on adalimumab withdrew due to AE versus 2% on ixekizumab (RR 1.68, 95% CI 0.74 to 3.81; I^2 = 0%; n=774; very low CoE).[2] In another study, 7% percent given a TNFi withdrew due to AEs versus 4% on secukinumab (RR 1.88, 95% CI 1.06 to 3.33; n=853).[2] In another study, no participants given TNFi withdrew due to AEs versus 4% on ustekinumab (RR 0.32, 95% CI 0.01 to 7.48; n=47; very low CoE).[2] In another study, 5% given a TNFi withdrew due to AE versus 3% on bimekizumab (RR 1.80, 95% CI 0.72 to 4.47; n= 571; very low CoE).[2]

TNFi vs. tsDMARDs

Two studies compared TNFis with tsDMARDs in csDMARD-inadequate responders.[2] One study investigated upadacitinib 15 mg and 30 mg daily against placebo and used adalimumab as an active comparator. Another study investigated tofacitinib 5 mg and 10 mg twice a day against placebo and used adalimumab as an active comparator.[2] Clinical improvement, as measured by ACR50 response at 12 weeks, was achieved by 28% on tofacitinib and 33% on adalimumab (RR 1.18, 95% CI 0.78 to 1.77; n=213; low CoE).[2] In the other study, both upadacitinib and adalimumab groups achieved 37% ACR50 response rates (RR 1.00, 95% CI 0.84 to 1.19; n=858; moderate CoE).[2]

Comparisons of SAEs and early treatment withdrawal due to AE with TNFis compared to tofacitinib or upadacitinib did not show differences although the evidence is uncertain.[2] At 52 weeks, 8% on adalimumab and 7% on tofacitinib experienced a SAE (RR 1.14, 95% CI 0.46 to 2.83; n=213; very low CoE).[2] At 24 weeks, 4% on adalimumab and 3% on upadacitinib experienced a SAE (RR 1.14, 95% CI 0.56 to 2.31; n=858).[2] One study reported that 4% on TNFi and 6% on tofacitinib withdrew from the trial due to AEs (RR 0.67, 95% CI 0.20 to 2.32; n=213; very low CoE). Another study reported that 5% on upadacitinib and 5% on adalimumab withdrew due to AEs (RR 1.10, 95% CI 0.62 to 1.95; n=858; very low CoE).[2]

Conclusions for Comparative TNFi Data

Most studies comparing TNFis to other bDMARDs and tsDMARDs in csDMARD-inadequate responders used adalimumab as the TNFi.[2] These studies were mostly pivotal trials sponsored by pharmaceutical companies, comparing a new tsDMARD or bDMARD to a placebo, and using adalimumab as an active comparator.[2]

Point estimates suggest no major difference in the benefits and harms of adalimumab compared to bimekizumab, ixekizumab, secukinumab, and ustekinumab.[2] However, the CoE was low or very low. Data were more exhaustive for adalimumab treatment against bimekizumab, ixekizumab, and secukinumab, although data on radiographic progression at a meaningful time point were available only for the comparison of adalimumab versus bimekizumab, which showed likely no or little difference between the two treatments (moderate CoE).[2] TNFi may have similar clinical, functional, and radiographic outcomes compared to tofacitinib and upadacitinib (low to moderate CoE).[2] The effects on health-related quality of life and the safety of these comparisons are uncertain due to very low CoE.[2]

Comparative Efficacy of Advanced Therapies for Management of Moderate-to-Severe Crohn's Disease (2025)

A 2025 systematic review and NMA informed the 2025 AGA Clinical Guidelines on the management of moderate-to-severe CD.[3] There are a limited number of head-to-head trials of active interventions, which can inform stakeholders regarding the comparative effectiveness of these interventions.[3] To overcome limitations to limited comparative data, NMA or indirect treatment comparison meta-analyses, are another assessment tool.[3]

Literature was searched through August 14, 2024, to identify RCTs in adults with moderate-to-severe CD, comparing advanced therapies (e.g., TNFis, vedolizumab, IL-12/23i, or IL-23p19i and/or JAKi) with placebo or another active comparator.[3] Primary outcomes were induction and maintenance of clinical remission (CDAI < 150) and analyses were stratified by biologic therapy exposure status.[3] Clinically meaningful difference (CMD) was defined as 50 per 1000 patients treated between 2 agents to define important versus trivial differences, consistent with previous AGA guidelines on the management of moderate-to-severe UC.[3] The timing of outcome assessment with induction trials was up to 14 weeks; when outcomes at multiple time points were reported, outcomes at week 8 or 6 were used.[3] For trials of maintenance therapy, efficacy outcomes were maintenance of clinical remission and clinical response.[3] For maintenance trials, outcomes were assessed at last point of follow-up, usually week 52.[3] Recognizing limitations of trials in evaluating treatment safety, the authors qualitatively and quantitatively synthesized the overall safety of all agents, regardless of biologic exposure status, and presented these estimates as proportions of patients with SAEs and serious infections.[3] Twenty-eight trials of induction therapy and 22 trials of maintenance therapy met inclusion criteria.[3]

- *Induction Trials*

Eight placebo-controlled trials assessed TNFi (2 = infliximab, 4 = adalimumab, and 2 = certolizumab pegol); 3 trials assessed vedolizumab; 3 trials evaluated ustekinumab, 9 trials included the IL-23p19i, (3 = risankizumab, 2 = mirikizumab, and 4 = guselkumab),and 3 trials assessed upadacitinib.[3] Two head-to-head trials, comparing ustekinumab versus adalimumab and comparing risankizumab to ustekinumab were identified.[3] Five placebo-controlled trials of IL23-p19i therapies included ustekinumab as an active comparator.[3]

The mean age of included participants was 37 years and 52% were male.[3] The mean of disease duration was 8.3 years.[3] A median of 34% of patients were concomitantly on immunomodulators and 35% were concomitantly on corticosteroids at randomization.[3] Patient characteristics were generally comparable across clinical trials.[3] Prior advanced therapy use was composed predominantly of TNFi exposure in the earlier RCTs, and subsequent biologic and small molecule trials included patients with exposure to other advanced therapies.[3] Trials of infliximab and certolizumab pegol trials did not include patients with prior biologic exposure.[3] Clinical remission in most trials was defined based on CDAI < 150 and was reported between weeks 4 and 8 in trials of TNFi, vedolizumab and ustekinumab, and between weeks 12 and 16 in trials of IL-23p19i and upadacitinib.[3] The pooled placebo rate for induction of clinical remission for biologic-naïve and biologic-exposed patients was 19% (95% CI, 15%–24%) and 14% (95% CI, 12%–18%), respectively.[3] Most trials were deemed to be at low ROB.[3]

Induction of Remission in Biologic-Naïve Patients

Evidence for induction of clinical remission was available for infliximab, adalimumab, certolizumab pegol, vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab, and upadacitinib.[3] On examination of direct evidence, moderate-to-high certainty evidence supported the use of infliximab, adalimumab,

vedolizumab, ustekinumab, risankizumab, mirikizumab, and guselkumab, and low certainty evidence supported the use of certolizumab pegol and upadacitinib for inducing remission in biologic-naïve patients.[3]

On comparing active interventions, adalimumab and ustekinumab were associated with an important benefit in inducing remission compared with certolizumab pegol in biologic-naïve patients with moderate-to-severe CD (moderate-to-high certainty evidence), and adalimumab and ustekinumab were likely associated with important benefit in inducing remission compared with upadacitinib (moderate certainty of evidence).[3] Vedolizumab, risankizumab, mirikizumab, and guselkumab may be associated with important benefit compared with certolizumab pegol (low certainty of evidence).[3] Adalimumab, mirikizumab, and guselkumab may be associated with an important benefit compared with upadacitinib in biologic-naïve patients with moderate-to-severe CD (low certainty of evidence).[3]

The NMA used a p-score to rank the probability of being ranking the best therapy in the network.[3] Among biologic-naïve patients with moderately-to-severely active CD, adalimumab (P score, 0.83) and ustekinumab (P score, 0.70) were ranked highest for induction of clinical remission.[3] With an estimated placebo rate of inducing remission of 19% in biologic-naïve patients with moderate-to-severe CD, the authors estimated that 48% of adalimumab-treated, 43% of ustekinumab-treated or vedolizumab-treated, 42% of infliximab-treated, 41% of guselkumab-treated, 40% of mirikizumab-treated, and 38% of risankizumab-treated patients would achieve remission with induction therapy.[3] Overall results were largely unchanged when varying baseline risk for induction of clinical remission with placebo (15% and 25%).[3]

Induction of Clinical Response in Biologic-Naïve Patients

The evidence supporting the efficacy of different treatments for achieving clinical response in biologic-naïve patients at the end of induction was broadly consistent with induction of clinical remission data.[3] Compared with placebo, all agents except certolizumab pegol and mirikizumab were more effective than placebo in inducing clinical response. Overall, infliximab (P score, 0.98), adalimumab (P score, 0.78) and ustekinumab (P score, 0.75) were ranked highest.[3]

Induction of Remission in Biologic-Exposed Patients

Evidence for induction of clinical remission was available for adalimumab, vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab, and upadacitinib.[3] Adalimumab was studied in a subset of biologic-exposed patients who had previously been treated with infliximab and then discontinued therapy either due to intolerance or secondary loss of response (after initial clinical improvement); patients with prior primary nonresponse to infliximab were excluded.[3] On examination of direct evidence, moderate-to-high certainty evidence supported the use of adalimumab, ustekinumab, risankizumab, guselkumab, and upadacitinib, and low certainty evidence supported the use of vedolizumab and mirikizumab for inducing remission.[3]

On comparing active interventions, adalimumab, risankizumab, and guselkumab were likely associated with an important benefit compared with vedolizumab in biologic-exposed patients with moderate-to-severe CD (moderate certainty of evidence).[3] Risankizumab and guselkumab were likely associated with an important benefit compared with ustekinumab (moderate certainty of evidence).[3] Adalimumab, risankizumab, and upadacitinib may be associated with an important benefit compared with mirikizumab in biologic-exposed patients with moderate-to-severely CD (low certainty of evidence).[3]

Results from the NMA showed that among biologic-exposed patients with moderately-to-severely active CD, adalimumab (P score, 0.87), guselkumab (P score, 0.82), and risankizumab (P score, 0.71) were ranked highest for induction of clinical remission.[3] With an estimated placebo rate of inducing remission of 14% in biologic-exposed patients with moderate-to-severe CD, the authors predicted that 42% of adalimumab-treated, 36% of guselkumab-treated, 33% of risankizumab-treated, 30% of upadacitinib-treated, and 27% of ustekinumab-treated patients would achieve remission with induction therapy.[3] Overall results were largely unchanged when varying baseline risk for induction of clinical remission with placebo (15% and 25%).[3]

Induction of Clinical Response in Biologic-Exposed Patients

The evidence supporting efficacy of different treatments for achieving clinical response in biologic-exposed patients at the end of induction was broadly consistent with induction of clinical remission data.[3] Compared with placebo, all agents were more effective than placebo in inducing clinical response. Overall, guselkumab (P score, 0.95) and risankizumab (P score, 0.81) were ranked highest.[3]

- *Maintenance Trials*

Seven treat-through studies were identified, in which patients were randomized to active interventions or placebo and continued follow-up through 48–52 weeks (1 head-to-head trial comparing ustekinumab with adalimumab,1 head-to-head trial comparing risankizumab with ustekinumab, and 5 trials of IL-23p19i with both placebo and ustekinumab as active comparators (1 = mirikizumab, 4 = guselkumab).[3] Fifteen trials were included in which responders to induction therapy were re-randomized to active drug vs placebo (8 trials of TNFi [3 infliximab including 1 trial of subcutaneous infliximab, 4 adalimumab, and 1 certolizumab pegol], 3 trials of vedolizumab, 2 trials of ustekinumab, 1 trial of risankizumab, and 1 trial of upadacitinib).[3] Patient characteristics were generally comparable across these maintenance trials.[3] Clinical remission was defined based on CDAI <150 and was reported between 22 and 56 weeks after randomization. The pooled placebo rate for maintenance of clinical remission in trials of re-randomization of responders to induction therapy was 19% (95% CI, 15%–24%).[3] Most trials were deemed to be at low risk of bias.[3]

Four trials of adalimumab, ustekinumab, guselkumab, and mirikizumab informed evidence on achieving clinical remission at 1 year using a treat-through design in biologic-naïve patients with moderate-to-severe CD.[3] On NMA, the benefit of any intervention over another was uncertain.[3] Guselkumab 200 mg every 4 weeks (P score, 0.74), mirikizumab (P score, 0.72), and ustekinumab (P score, 0.68) were ranked highest for achieving clinical remission.[3]

Four trials of risankizumab, ustekinumab, guselkumab, and mirikizumab informed evidence on achieving clinical remission at 1 year using a treat-through design in biologic-exposed patients with moderate-to-severe CD.[3] On NMA, risankizumab and guselkumab were associated with an important benefit compared with ustekinumab in biologic-exposed patients with moderate-to-severe CD (moderate-to-high certainty evidence).[3] Mirikizumab may be associated with important benefit over ustekinumab in these patients (low certainty evidence).[3]Risankizumab (P score, 0.96) and guselkumab 200 mg every 4 weeks (P score, 0.74) were ranked highest for achieving clinical remission.[3]

Data were available from trials of all agents, except mirikizumab and guselkumab, where responders to induction therapy were re-randomized to active agent vs placebo.[3] Moderate-to-high certainty evidence supported the use infliximab, adalimumab, certolizumab pegol, vedolizumab, ustekinumab, and upadacitinib for maintenance of remission in patients with initial response to induction therapy, whereas low certainty evidence supported the use of risankizumab.[3] Of note, maintenance of remission rates with placebo in one trial of risankizumab were higher compared with trials of other agents.[3]

On comparing active interventions, adalimumab was associated with higher rates of maintenance of remission compared with vedolizumab and risankizumab, although trials of the vedolizumab and risankizumab included both biologic-naïve and biologic-exposed patients (moderate-to-high certainty evidence).[3] Upadacitinib 30 mg daily was also associated with higher rates of maintaining remission compared with certolizumab pegol, vedolizumab, ustekinumab, and risankizumab (moderate-to-high certainty evidence).[3] Upadacitinib 30 mg daily (P score, 0.94) and adalimumab (P score, 0.85) were ranked highest for maintenance of clinical remission among patients with clinical response to induction therapy.[3]

- *Safety*

Serious adverse events were defined using the trial-specific definitions and included worsening of underlying CD.[3] On NMA of trials of maintenance therapy, risk of SAEs was lower in patients treated with guselkumab 200 mg every 4 weeks compared with infliximab, vedolizumab, ustekinumab, and guselkumab 100 mg every 8 weeks.[3] In trials of maintenance therapy, risk of serious infections between active interventions and placebo was comparable.[3] In comparing active interventions also, there was no difference between advanced therapies included in this analysis.[3]

- *Conclusions*

In summary, for biologic-naïve patients, moderate-to-high certainty evidence supported the use of infliximab, adalimumab, vedolizumab, ustekinumab, risankizumab, mirikizumab, and guselkumab, and low certainty evidence supported the use of certolizumab pegol and upadacitinib over no treatment for inducing remission.[3] Among active comparators, moderate-to-high certainty evidence supported the use of adalimumab and ustekinumab compared with certolizumab pegol and upadacitinib.[3]

Among patients with prior exposure to biologics, moderate-to-high certainty evidence supported the use of adalimumab, ustekinumab, risankizumab, guselkumab, and upadacitinib, and low certainty evidence supported the use of vedolizumab and mirikizumab, over no treatment, for inducing remission.[3] Among active comparators, moderate certainty evidence supported the use of risankizumab and guselkumab compared with vedolizumab and ustekinumab in patients with prior biologic exposure.[3]

In trials assessing maintenance of response, risankizumab and guselkumab are more effective than ustekinumab, and mirikizumab may be more effective than ustekinumab, in biologic-exposed patients in maintaining clinical remission, but without any important differences in efficacy in biologic-naïve patients.[3]
No significant differences were observed in the risk of serious infections across different agents, although it is important to recognize that regulatory trials are not powered to detect differences in safety end points.[3] This systematic review and NMA highlights the importance of prior treatment exposure on subsequent therapy selection in moderate-to-severe CD.[3] Vedolizumab may be more efficacious in biologic-naïve patients, whereas upadacitinib may be more efficacious in patients with prior TNFi exposure for induction of remission. IL-23p19i were also more effective than ustekinumab, primarily in patients with prior exposure to TNFi but not in TNFi-naïve patients.[3]

After review, 52 systematic reviews were excluded due to poor quality (e.g., indirect network-meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

New Guidelines:
High-Quality Guidelines:

European Alliance of Associations for Rheumatology*: *Guidelines for Management of Rheumatoid Arthritis with Disease-Modifying Anti-Rheumatic Drugs (2026)
The EULAR updated guidance for treatment of RA with TIMs in 2026.[4] As no new drugs have been approved since 2022 in the European Union, and also no new RCTs on the cardiovascular or malignancy risks of JAKi have been published over the last 3 years, the focus of the task force was on the evaluation of the previous recommendations and incorporation of recent insights from strategic trials and safety data.[4] Consequently, most of the previous recommendations remained unchanged from 2022.[4] The recommendations and levels of evidence were drafted using the EULAR standardized operating procedures described in **Table 1**.[63]

Table 1. EULAR Category of Evidence and Strength of Recommendations[63]

Level of Evidence	
Category	Evidence
1a	From meta-analysis of randomized controlled trials
1b	From at least one randomized controlled trial
2a	From at least one controlled study without randomization
2b	From at least one type of quasi-experimental study
3	From descriptive studies, such as comparative studies, correlation studies, or case–control studies
4	From expert committee reports or opinions and/or clinical experience of respected authorities
Strength of Recommendation	
A	Category I evidence
B	Category II evidence or extrapolated recommendations from category I evidence
C	Category III evidence or extrapolated recommendation from category I or II evidence
D	Category IV evidence or extrapolated recommendation from category II or III evidence
Abbreviations: EULAR: European Alliance of Associations for Rheumatology	

EULAR recommendations for pharmacologic management of RA include the following statements:

- Therapy with DMARDs should be started as soon as the diagnosis of RA is made (Level of Evidence: 1a; Strength of Recommendation: A).[4]
- Methotrexate should be part of the first treatment strategy; in patients with a contraindication to MTX (or early intolerance), leflunomide or sulfasalazine should be considered. (Level of Evidence: 1a; Strength of Recommendation: A).[4]
- Short-term glucocorticoids should be considered when initiating or changing csDMARDs, in different dose regimens and routes of administration, but should be tapered and discontinued as rapidly as clinically feasible. (Level of Evidence: 1a; Strength of Recommendation: A).[4]
- If the treatment target is not achieved with the csDMARD strategy, a bDMARD should be added; JAKi may be considered, but pertinent risk factors* must be considered. (EFFICACY - Level of Evidence: 1a; Strength of Recommendation: A and SAFETY - Level of Evidence: 2a; Strength of Recommendation: B).[4]
  *The following risk factors for cardiovascular events and malignancies must be considered when intending to prescribe a JAKi: Age over 65 years, history of current or past smoking, other cardiovascular risk factors (such as diabetes, obesity, hypertension), other risk factors for malignancy (current or previous history of malignancy other than successfully treated non-melanoma skin cancer), risk factors for thromboembolic events (history of myocardial infarction or heart failure, cancer, inherited blood clotting disorders or a history of blood clots, as well as patients taking combined hormonal contraceptives or hormone replacement therapy, undergoing major surgery or immobile).[4]
- For RA treatment bDMARDs/tsDMARDs should be combined with a csDMARD; in patients who cannot use csDMARDs as co-medication, IL-6 pathway inhibitors and JAKi may have some advantages compared with other bDMARDs. (Level of Evidence: 1a; Strength of Recommendation: A).[4]
- If a bDMARD or tsDMARD has failed, treatment with another bDMARD or a tsDMARD should be considered; if one TNF or IL-6 receptor inhibitor therapy has failed, patients may receive an agent with another mode of action or a second TNF-/IL-6R-inhibitor. (EFFICACY for bDMARD/tsDMARD: Level of Evidence: 1a; Strength of Recommendation: A and EFFICACY for second TNF-/IL-6R-inhibitor: Level of Evidence: 4; Strength of Recommendation: D and SAFETY for bDMARD/tsDMARD: Level of Evidence: 1b; Strength of Recommendation: B and SAFETY for second TNF-/IL-6R-inhibitor: Level of Evidence: 1b; Strength of Recommendation: C).[4]
- After glucocorticoids have been discontinued and a patient is in sustained remission, continuation of DMARDs (bDMARDs/tsDMARDs and/or csDMARDs) is recommended, but dose reduction may be considered. (Level of Evidence: 1b; Strength of Recommendation: A).[4]

American College of Gastroenterology: Management of Crohn's Disease in Adults (2025)

The ACG published updated guidance for management of adults with CD in 2025.[5] Management recommendations for patients with CD are based on disease location, severity, presence of disease-associated complications including extraintestinal manifestations, and factors affecting future prognosis.[5] The anatomic distribution of disease is important primarily for medications with targeted delivery systems, such as enteric-coated budesonide. For all other agents (i.e., systemic corticosteroids, thiopurines, MTX, biologics, and oral small molecules), therapeutic activity against CD is believed to occur throughout the entire gastrointestinal (GI) tract.[5]

Recommendations for management of moderate-to-severe CD with TIMs include:

- AGA suggests against requiring failure of conventional therapy before initiation of advanced therapy for the management of CD (conditional recommendation, low level of evidence).[5]
- TNFis (IV infliximab, SC adalimumab, SC certolizumab pegol) are recommended for induction and maintenance of remission for moderately to severely active CD (strong recommendation, moderate level of evidence).[5]
- Combination therapy of IV infliximab with immunomodulators (thiopurines) is recommended compared with treatment with either immunomodulators alone or IV infliximab alone in patients with CD who are naive to those agents (strong recommendation, moderate level of evidence).[5]
- Subcutaneous infliximab is recommended as an option for maintenance of remission in patients with moderately to severely active CD who respond to IV induction with infliximab (strong recommendation, moderate level of evidence).[5]
- Intravenous vedolizumab is recommended for induction and maintenance of symptomatic remission in patients with moderately to severely active CD (strong recommendation, moderate level of evidence).[5]
- Subcutaneous vedolizumab is recommended as an option for maintenance of remission in patients with moderately to severely active CD who respond to 2 IV induction doses of vedolizumab (strong recommendation, moderate level of evidence).[5]
- Ustekinumab and risankizumab are recommended in patients with moderate-to-severe CD for induction and maintenance of remission (strong recommendation, moderate level of evidence).[5]
- Risankizumab is recommended as compared with ustekinumab in patients with moderate-to-severe CD and prior exposure to TNFi therapy (conditional recommendation, low level of evidence).[5]
- Mirikizumab is recommended for induction and maintenance of remission in patients with moderate to severely active CD (strong recommendation, moderate level of evidence).
- Intravenous guselkumab is recommended for induction followed by SC guselkumab for maintenance of remission in patients with moderate to severely active Crohn's disease (strong recommendation, moderate level of evidence).
- Subcutaneous guselkumab is recommended for induction and maintenance of remission in patients with moderate to severely active Crohn's disease (strong recommendation, moderate level of evidence).[5]
- Upadacitinib is recommended for induction and maintenance of remission for patients with moderately to severely active CD who have previously been exposed to TNFi agents (strong recommendation, moderate level of evidence).[5]
- Infliximab is recommended for induction of remission of perianal fistulizing CD (strong recommendation, moderate level of evidence).[5]
- Adalimumab is recommended for induction of remission of perianal fistulizing CD (conditional recommendation, low level of evidence).[5]
- Vedolizumab, ustekinumab or upadacitinib are recommended for induction of remission of perianal fistulizing CD (conditional recommendation, very low level of evidence).[5]

American Gastroenterological Association: Pharmacologic Management of Moderate-to-Severe Crohn's Disease (2025)

The AGA guideline panel agreed on 15 pharmacologic recommendations in the 2025 guideline update for treatment of CD.[6] Since the publication of the previous AGA guidelines for moderate-to-severely active CD in 2021, two additional classes of advanced therapies with 5 novel agents have been approved for treating moderate-to-severely active CD.[6] These therapies were followed by the introduction of biosimilars for infliximab, adalimumab, and ustekinumab over the past decade, as well as SC delivery options for infliximab and vedolizumab.[6] The guidance is similar to the ACG guidance, but the AGA grades TIMs with higher efficacy and lower efficacy in their recommendations based on the NMA that supports this guidance.[3,6] In some patients with partial response to FDA-approved dosing, particularly those with more severe disease, extended induction regimens or dose escalation may be beneficial for most advanced therapies.[6] There are 2 dosing options available for maintenance therapy for risankizumab, guselkumab, and upadacitinib.[6] Higher maintenance doses may be preferred in patients with a high burden of inflammation and/or more severe disease, and those who have previously failed TNFi therapies.[6] There are limited data on the safety of JAKi in pregnancy.[6] These drugs should generally be avoided in women contemplating pregnancy in the near future.[6]

Recommendations for use of TIMs to manage moderate-to-severe CD include:

- In adult outpatients with moderate-to-severely active CD, the use of infliximab, adalimumab, ustekinumab, risankizumab, mirikizumab, guselkumab, or upadacitinib is recommended, over no treatment (strong recommendation, moderate to high certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD, the use of certolizumab pegol or vedolizumab is suggested, over no treatment (conditional recommendation, moderate certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD who are naïve to advanced therapies, the AGA suggests using a HIGHER efficacy medication (infliximab, adalimumab, vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab), rather than a LOWER efficacy medication (certolizumab pegol, upadacitinib). (Conditional recommendation, low to high certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD who have previously been exposed to 1 or more advanced therapies, particularly TNF antagonists, the AGA suggests using a HIGHER efficacy medication (adalimumab, risankizumab, guselkumab, upadacitinib) OR an INTERMEDIATE efficacy medication (ustekinumab, mirikizumab), rather than a LOWER efficacy medication (vedolizumab, certolizumab pegol). (Conditional recommendation, low to moderate certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD who are in corticosteroid-free clinical remission for at least 6 months on combination therapy with TNF antagonists and an immunomodulator, the AGA suggests withdrawing the immunomodulator. (Conditional recommendation, low certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD who are in corticosteroid-free clinical remission for at least 6 months on combination therapy of TNFi and an immunomodulator, the AGA suggests AGAINST withdrawal of the TNFi. (Conditional recommendation, low certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD, the AGA suggests upfront use of advanced therapy compared with step-up therapy with initial use of corticosteroids and/or immunomodulator monotherapy. (Conditional recommendation, very low certainty of evidence).[6]

In addition, ACG provides guidance regarding combination therapy of biologics and immunomodulators, although the benefit of routinely combining immunomodulators with TNFi in patients who have previously failed immunomodulator monotherapy is uncertain.[6] In patients who previously failed immunomodulator monotherapy, there may be benefits of adding immunomodulators when starting TNFi in specific situations where patients may be at a higher risk for immunogenicity.[6] These situations include patients with history of immunogenicity with a TNFi, patients being re-exposed to TNFi after a

prolonged lapse in therapy, patients carrying HLA-DQ-A1∗05 variants and patients with high drug clearance, such as those with more severe disease, high burden of inflammation, or low albumin.[6]

Recommendations for combination biologic and immunomodulator therapy:

- In adult outpatients with moderate-to-severely active CD who are NAÏVE to thiopurines and starting infliximab, the AGA SUGGESTS using infliximab in combination with thiopurines rather than infliximab monotherapy (conditional recommendation, low certainty of evidence).[6]
- In adult outpatients with moderate-to-severely active CD, the AGA makes NO RECOMMENDATION on using infliximab in combination with methotrexate over infliximab monotherapy. (No recommendation, knowledge gap).[6]
- In adult outpatients with moderate-to-severely active CD, the AGA makes NO RECOMMENDATION on using adalimumab in combination with thiopurines or methotrexate over adalimumab monotherapy. (No recommendation, knowledge gap).[6]
- In adult outpatients with moderate-to-severely active CD, the AGA makes NO RECOMMENDATION in favor of, or against, using non–TNF-targeting biologics (vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab) in combination with thiopurines or methotrexate or corresponding biologic monotherapy. (No recommendation, knowledge gap)

American College of Gastroenterology: Ulcerative Colitis in Adults (2025)

Since the 2019 publication of the last guideline from the ACG on UC, the management of UC has grown increasingly complex with availability of additional treatments and therapeutic classes.[10] In addition, approaches to initiate, optimize, and monitor response to existing therapies have undergone considerable evolution.[10] Therapeutic management in UC should be guided by the extent of bowel involvement, an assessment of disease activity (i.e., quiescent, mild, moderate, or severe), and disease prognosis.[10] This updated guideline emphasizes that patients with moderately to severely active UC or those who have UC with high risk of hospitalization or colectomy should be treated with therapies that have evidence for their efficacy in this degree of active disease or with this specific prognosis, based on evidence in clinical trials and real world observational studies.[10] Much of the data for comparative effectiveness in naive and biologic-exposed patients with UC are post hoc from the registry clinical trials or from indirect sources such as NMA.[10]

Infliximab is the preferred TNFi therapy for patients with moderately to severely active UC.[10] The strong effect of infliximab for outcomes including short-term and long-term clinical response, clinical remission and prevention of colectomy in UC has been demonstrated consistently across studies.[10] The magnitude of the effect provides evidence of the effectiveness of this agent in UC.[10] Additional observational data support the benefit of infliximab over adalimumab in UC when considering adverse events such as hospitalization or serious infection.[10]

Some patients with moderately to severely active UC who are at higher risk for infectious complications may benefit from vedolizumab or an anti-IL-23 strategy over more systemically immunosuppressive medical option.[10] A head-to-head prospective RCT of vedolizumab compared with adalimumab in patients with moderately to severely active UC demonstrated superiority of vedolizumab at achieving clinical remission and endoscopic improvement at 52 weeks (31.3% vs 22.5%; P = 0.006; 39.7% vs 27.7%; P < 0.001, respectively).[10] These results would support the use of vedolizumab over adalimumab in patients with moderately to severely active UC.[10] A post hoc analysis demonstrated that patients who were anti–TNF-naive were more likely to respond to vedolizumab compared with those who had received anti-TNF therapy previously.[10] These data further support a strategy of considering vedolizumab early in the treatment algorithm for patients with moderately to severely active UC.[10]

There is great interest in understanding whether the IL-23p19 inhibitors (guselkumab, mirikizumab, and risankizumab) are more effective than the IL-12/23p40 inhibitor (ustekinumab).[10] There are prospective comparative trials demonstrating superiority of 2 of the p19 therapies (guselkumab and risankizumab) in patients with moderately to severely active CD, but no such data exist for moderately to severely active UC.[10] Patients with concomitant inflammatory arthritis (not necessarily arthralgias) may benefit from use of anti-TNF or JAKi therapies, and patients with concomitant inflammatory skin conditions such as psoriasis and in particular those who develop inflammatory skin conditions while receiving anti-TNF therapy may benefit from IL-23 based strategies.[10]

Recommendations for the management of mild-to-moderate UC include 5-ASA therapies (mesalamine, olsalazine, sulfasalazine), oral and topical corticosteroids, and oral budesonide.[10] Strength of recommendation and evidence for the use of TIMs in induction and maintenance of moderate-to-severe UC are summarized below.

Recommendations for Induction of Remission:

- In patients with moderately to severely active UC, S1P receptor modulators, ozanimod and etrasimod, are recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, ustekinumab is recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, guselkumab, mirikizumab, or risankizumab are recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, vedolizumab is recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, infliximab is recommended for induction of remission (strong recommendation, high quality of evidence).[10]
- In patients with moderately to severely active UC, adalimumab or golimumab are recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, tofacitinib is recommended for induction of remission (strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC, upadacitinib is recommended for induction of remission (strong recommendation, high quality of evidence).[10]
- In patients with moderately to severely active UC who have failed 5-ASA therapy and in whom advanced therapies with biologics or JAKi are used for induction of remission, it is not suggested to use 5-ASA for added clinical efficacy (conditional recommendation, very low quality of evidence).[10]
- When infliximab is used as induction therapy for patients with moderately to severely active UC, combination therapy with a thiopurine is recommended (strong recommendation, moderate quality of evidence for azathioprine).[10]

Recommendations for Maintenance of Remission:

- In patients with prior moderately to severely active UC who have achieved remission but previously failed 5-ASA therapy and are now on anti-TNF therapy, it is suggested to not use concomitant 5-ASA for efficacy of maintenance of remission. (conditional recommendation, low quality of evidence).[10]
- In patients with prior moderately to severely active UC, systemic corticosteroids are not recommended for maintenance of remission (strong recommendation, moderate quality of evidence).[10]

- For patients with prior moderately to severely active UC now in remission because of corticosteroid induction, thiopurines are suggested for maintenance of remission as compared with no treatment or corticosteroids (conditional recommendation, low quality of evidence).[10]
- In patients with prior moderately to severely active UC now in remission, it is suggested to not use MTX for maintenance of remission (conditional recommendation, low quality of evidence).[10]
- Continuing ozanimod or etrasimod, ustekinumab, guselkumab, mirikizumab or risankizumab, is recommended for maintenance of remission as compared with no treatment after induction of remission with these agents (Strong recommendation, moderate quality of evidence).[10]
- Continuing vedolizumab is recommended as compared with no treatment for maintenance of remission (IV or SC dosing) in patients with prior moderately to severely active UC now in remission after vedolizumab induction (Strong recommendation, moderate quality of evidence).[10]
- Continuing anti-TNF therapy is recommended using adalimumab, golimumab, or infliximab (IV or SC dosing) for maintenance of remission after anti-TNF induction in patients with prior moderately to severely active UC (Strong recommendation, moderate quality of evidence).[10]
- Continuing tofacitinib or upadacitinib is recommended as compared with no treatment for maintenance of remission in patients with prior moderately to severely active UC now in remission after induction with tofacitinib or upadacitinib (Strong recommendation, moderate quality of evidence).[10]
- In patients with moderately to severely active UC who are responders to anti-TNF therapy and now losing response, it is suggested to measure serum drug levels and antidrug antibodies (if there is not sufficient drug present) to assess reason for loss of response (Conditional recommendation, very low quality of evidence).[10]
- In patients with moderately to severely active UC, vedolizumab is recommended as compared with adalimumab for induction and maintenance of remission (Strong recommendation, moderate quality of evidence).

Canada's Drug Agency

The CDA published 4 reimbursement recommendations focused on management of CD and UC with TIMs in 2025 and 2026. One additional publication focused on the use of bimekizumab for treatment of hidradenitis suppurativa (HS). The 5 recommendations and evidence supporting the decisions are summarized below.

CDA: Mirikizumab for Treatment of Crohn's Disease (2025)

One phase 3, double-blind, placebo- and active-controlled (versus ustekinumab) trial (VIVID-1; N = 1,152) demonstrated that treatment with mirikizumab, administered over a 12-week induction and a 40-week maintenance period, results in added clinical benefit compared to placebo and similar benefit compared to ustekinumab in patients with moderately to severely active CD and prior inadequate response, loss of response, or intolerance to 1 or more biologic or conventional therapies.[7] The safety profile of mirikizumab in the VIVID-1 trial appeared generally consistent with other IL-23i therapies used to treat CD, with no new safety concerns identified.[7]

- CDA recommends that mirikizumab be reimbursed by public drug plans for the treatment of moderately to severely active CD in cases in which conventional treatment or biologic therapies have led to an inadequate response, a loss of response, or intolerable side effects.[7]

CDA: Guselkumab for Treatment of Crohn's Disease

Evidence from 3 clinical trials demonstrated that at week 48, treatment with guselkumab (IV or SC induction followed by SC maintenance) resulted in improvements in clinical remission and response as well as endoscopic remission and response, when compared with placebo or ustekinumab.[8] These outcomes were observed in patients with moderately to severely active CD who had either an inadequate response or were intolerant to prior conventional or biologic therapies.[8] In all 3 RCTs serious TEAEs, TEAEs leading to discontinuation of treatment, notable harms (i.e., infections), and deaths were infrequent and similar

across the treatment groups.[8] There were no new safety signals identified and that the safety of guselkumab was consistent with the known safety profile of the drug class.[8]

- CDA recommends that guselkumab be reimbursed by public drug plans for the treatment of adult patients with moderately to severely active CD who have disease that failed conventional therapy and previous biologic treatments.[8]

CDA: Guselkumab for Treatment of Ulcerative Colitis

Evidence from 2 clinical trials demonstrated that more patients with UC who were treated with guselkumab showed clinical remission and response and endoscopic improvement than patients who received placebo, and this benefit was maintained for up to 44 weeks.[11] In both trials, TEAEs, TEAEs leading to discontinuation of treatment, notable harms (i.e., infections), and deaths were infrequent and similar across the treatment groups.[11] There were no new safety signals identified and that the safety of guselkumab was consistent with the known safety profile of the drug class.[11]

- Guselkumab should only be covered for a patient population similar to that eligible for other advanced therapies for UC (e.g., biologics, SP-1 receptor modulators, or JAKi) for treatment of moderately to severely active UC in adults who have had an inadequate response or loss of response to other treatment options (conventional therapy [6-mercaptopurine, azathioprine, or corticosteroids] or advanced therapies [TNFi, vedolizumab, or tofacitinib]).[11]

CDA: Risankizumab for Treatment of Ulcerative Colitis (2025)

Two phase 3, double-blind, placebo-controlled trials (INSPIRE induction trial: N = 977; COMMAND maintenance trial: N = 584) demonstrated that risankizumab, administered as a 1,200 mg IV infusion for induction and as either 180 mg or 360 mg SC injections for maintenance, provided added clinical benefit compared to placebo in adults with moderately to severely active UC who had inadequate response or were unable to tolerate conventional or advanced therapy.[12] Evidence from these 2 clinical trials demonstrated that more patients treated with risankizumab showed clinical remission and endoscopic improvement than patients treated with placebo, both during the first 12 weeks of treatment and at longer-term follow-up.[12] There were no new safety signals identified in clinical trials, and the safety of risankizumab was consistent with the known safety profile of the drug class.[12]

- CDA recommends that risankizumab be reimbursed by public drug plans for the treatment of adult patients with moderately to severely active UC who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a JAKi.[12]

CDA: Bimekizumab for Treatment of Hidradenitis Suppurativa (2026)

Evidence from 2 clinical trials demonstrated that treatment with bimekizumab reduced HS severity and improved HS symptoms after 16 weeks of treatment compared with placebo.[15] The committee also noted limited comparative evidence beyond 16 weeks and uncertainty about whether bimekizumab would address loss of response seen with existing advanced therapies (adalimumab and secukinumab).[15] The proportion of SAEs reported in the pooled bimekizumab 320 mg every 2 weeks group was 2.8% in the BE HEARD I trial and 3.1% in the BE HEARD II trial.[15] No SAEs were reported in the placebo group in either study.[15] In the initial treatment period (safety set) of the BE HEARD I and II trials, oral candidiasis was reported in 5.9% and 8.3% of patients in the pooled bimekizumab 320 mg every 2 weeks groups, respectively.[15] No oral candidiasis was reported in the placebo groups of either trial.[15]

- CDA recommends that bimekizumab be reimbursed by public drug plans for the treatment of adult patients with moderate to severe HS with an inadequate response to conventional systemic therapy.[15] Bimekizumab should only be covered to treat patients who have moderate to severe HS (Hurley stage II or III), a total abscess and nodule count of 5 or greater, lesions in at least 2 separate areas of the body, and whose HS did not adequately respond to conventional therapy (systemic antibiotics).[15]

National Institute for Health and Care Excellence
NICE issued 3 recommendations for treatment of CD and UC with TIMs in 2025.

NICE: Guselkumab for Treatment of Crohn's Disease (2025)
Usual treatment for moderately to severely active CD when conventional treatments stop working or are unsuitable is biological treatment, which can include TNFi or ustekinumab.[13] If these do not work well enough, stop working or are not tolerated, or if TNFi are unsuitable, people can then have risankizumab or vedolizumab.[13] Guselkumab would be offered to the same population as risankizumab and vedolizumab.[13] Clinical trial evidence shows that guselkumab increases the likelihood of disease remission and endoscopic response compared with placebo.[13] It has not been directly compared in a clinical trial with risankizumab or vedolizumab.[13]

- Guselkumab can be used as an option for previously treated moderately to severely active CD in adults, when conventional or biological treatment has not worked (that is, the condition has not responded well enough or lost response to treatment), or cannot be tolerated, and a TNFi has not worked, cannot be tolerated or is not suitable.[13]

NICE: Guselkumab for Treatment of Ulcerative Colitis (2025)
Tumor necrosis factor inhibitors are the most used biological treatments for moderately to severely active UC when a conventional treatment has not worked or cannot be tolerated.[14] When a TNF-alpha inhibitor has not worked, or is not tolerated or suitable, potential treatment options include mirikizumab or vedolizumab.[14] Guselkumab is another biological treatment that would be offered to the same population.[14] Clinical trial evidence shows that guselkumab is more effective than placebo.[14] Guselkumab has not been directly compared in a clinical trial with mirikizumab or vedolizumab.[14]

- Guselkumab can be used as an option for treating moderately to severely active UC in adults when a conventional treatment, biological treatment or JAKi has not worked (that is, the condition has not responded well enough or lost response to treatment), or cannot be tolerated, and a TNFi has not worked, cannot be tolerated or is not suitable.[14]

NICE: Mirikizumab for Treatment of Crohn's Disease (2025)
Usual treatment for moderately to severely active CD includes biological treatments such as TNFi, risankizumab, ustekinumab and vedolizumab.[9] Mirikizumab is another biological treatment option.[9] Clinical trial evidence shows that mirikizumab works as well as ustekinumab in reducing symptoms and achieving disease remission.[9] Although there are no head-to-head studies of mirikizumab with risankizumab, clinical expert opinion also suggests that mirikizumab would be used at the same point in the treatment pathway as risankizumab.[9]

- Mirikizumab can be used as an option to treat moderately to severely active CD in adults, only if the disease has not responded well enough or stopped responding to a previous biological treatment, or a previous biological treatment was not tolerated, or TNFi are not suitable.[9]

After review, 7 guidelines were excluded due to poor quality.

New Indications or Formulations:
New Indications

- **Risankizumab** (SKYRIZI) injection received expanded approval for SC use in pediatric patients aged 6 years and older with PsO and PsA in June 2026.[16] Prior to this approval, risankizumab was only approved for use in adults with PsO and PsA, in addition to treatment of CD and UC in adults.[16] Use of risankizumab for pediatric PsA is supported by evidence from studies of risankizumab in adults with psoriatic PsA, pharmacokinetic data from adult patients with PsA or PsO, and pharmacokinetic, safety, and immunogenicity data from pediatric patients with moderate-to-severe PsO.[16] Risankizumab exposures in pediatric

patients with PsA at the recommended dosage are predicted to be comparable to those observed in adults with PsA based on population pharmacokinetic modeling and simulation.[16]

Use of risankizumab for pediatric PsO is supported by evidence from a four-part trial in a total of 137 pediatric subjects 6 years of age and older with moderate-to-severe PsO.[16] In addition to two lead-in pharmacokinetic cohorts, the trial also included a randomized, efficacy assessor-blinded, active treatment-controlled cohort that enrolled 82 pediatric subjects 12 years of age and older with moderate-to-severe PsO.[16] Subjects were randomized 2:1 to receive risankizumab (n=54) or ustekinumab (n=28).[16] The co-primary endpoints were sPGA score of 0 ("clear") or 1 ("almost clear") and at least a 2-point improvement from baseline, and PASI 75 at Week 16.[16] At week 16, response rates were similar between arms for a PASI75 response, it was achieved in 85.2% of patients treated with risankizumab vs 85.7% of those treated with ustekinumab.[64] In addition, clear or almost clear (sPGA0/1) at week 16 was achieved in 79.6% vs 75.0% of the cohorts, respectively, whereas an sPGA 0/1 with at least a 2-grade improvement was achieved in 68.5% vs 67.9%, respectively.[64] Results are only reported in abstract form, confidence intervals and p-values not reported. In another part of the study, children (6 to <12 years old) received open label risankizumab for 1 year; risankizumab improved skin symptoms as soon as 16 weeks with improvements maintained for 1 year (specific outcome data not reported).[64]

- **Ustekinumab** (STELARA) received expanded approval for use in pediatric patients aged 2 years and older with moderately-to-severely active CD as of April 2026.[17] Prior to this expanded approval, ustekinumab was approved for adults with CD.[17] Use of ustekinumab in pediatric CD is supported by evidence from studies in adults with additional safety, efficacy, and pharmacokinetic data from a 52-week study in 101 pediatric subjects aged 2 to 17 years of age in a multi-center trial consisting of an open-label IV 8-week induction phase followed by randomization to one of 2 SC dosage regimens in a 44-week double-blind maintenance phase.[17] The primary endpoint of the study was clinical remission at Week 52 (from initiation of induction) which was evaluated in the subset of patients who achieved clinical response at Week 8.[17] At Week 8, the proportion of patients who achieved clinical remission (defined as Pediatric Crohn's Disease Activity [PCDAI] score of ≤10) was 46% (43/93).[17]

- **Secukinumab** (COSYNTEX) injection recently received 2 expanded indications in March and April of 2026. The first approval was to extend the use of SC secukinumab in pediatric patients aged 12 years and older with hidradenitis suppurativa (HS) in March 2026.[18] The second approval was to extend the use of SC secukinumab in pediatric patients aged 12 years and older with active AS in April 2026.[18] The previous approval was for treatment of adults with AS or HS.[18] Because both of these conditions are very rare in pediatric patients, the FDA approved the extended pediatric age range based upon clinical efficacy studies conducted in adults in addition to pharmacokinetic (PK) modeling and simulation data based on adult subjects.[18]

- **Deucravacitinib** (SOTYKTU) oral tablets received an expanded indication for treatment of active PsA in adults in March 2026.[19] The efficacy and safety of deucravacitinib for this new indication were assessed in 2 multicenter, double-blind, placebo-controlled RCTs (Trial PsA-1 and Trial PsA-2) in subjects 18 years and older with active PsA defined as 3 or more swollen joints, 3 or more tender joints, and a C-reactive protein (CRP) level of ≥3 mg/L.[19] In Trial PsA-1, subjects also had presence of at least one bone erosion on X-ray of hands and/or feet.[19] Trial PsA-1 evaluated 670 subjects who were randomized to placebo or deucravacitinib 6 mg once daily.[19] Trial PsA-2 evaluated 624 subjects who were randomized to placebo or deucravacitinib 6 mg once daily; in addition, 105 subjects were randomized to apremilast 30 mg twice daily.[19] In both trials, subjects randomized to placebo were switched to deucravacitinib at Week 16.[19] The primary endpoint in both trials was the percentage of subjects (n=1294) who achieved an ACR 20 response at Week 16.[19] Secondary endpoints were ACR 50 and ACR70 response at Week 16.[19]

In the 2 RCTs, the majority of subjects were naïve to biologic treatment and had experienced an inadequate response, intolerance, or loss of response to

NSAIDs, csDMARDs, or apremilast.[19] In addition, Trial PsA2 included TNFi-experienced subjects.[19] In the 2 RCTs, 56% of subjects were taking concomitant MTX, 10% were taking other concomitant csDMARDs, and 34% were not taking csDMARDs.[19] In both trials, treatment with deucravacitinib resulted in statistically significant improvement in disease activity, as measured by ACR 20, ACR 50, and ACR 70 response, compared to placebo at Week 16 (see **Table 2**).[19] The overall safety profile of deucravacitinib observed in subjects with active PsA was generally consistent with the safety profile observed in subjects with PsO.[19]

Table 2. Efficacy Results for Deucravacitinib in Adults with Active Psoriatic Arthritis[19]

	Trial PsA-1			**Trial PsA-2**		
Endpoint	Deucravacitinib n=336	Placebo n=334	Difference from Placebo	Deucravacitinib n=312	Placebo n=312	Difference from Placebo
ACR20 Response						
Week 16	54%	34%	20% 95% CI, 13 to 27	54%	39%	15% 95% CI, 7 to 23
ACR 50 Response						
Week 16	25%	14%	11% 95% CI, 5 to 17	29%	16%	13% 95% CI, 6 to 19
ACR 70 Response						
Week 16	12%	5%	6% 95% CI, 2 to 10	11%	5%	5% 95% CI, 1 to 9
Abbreviations: ACR = American College of Rheumatology; CI = confidence interval						

- **Tofacitinib** (XELJANZ) oral tablets and solution received an expanded indication in October 2025 for use in pediatric patients aged 2 years of age and older with PsA who have an inadequate response or intolerance to one or more TNFi therapies.[20] Prior to this approval, tofacitinib was only approved to treat adults with PsA. Use of tofacitinib for pediatric patients with PsA is supported by evidence from studies of tofacitinib in adults with RA, PK data from adult patients with RA, and with additional safety, efficacy, and PK data from a clinical trial of tofacitinib in pediatric patients 2 years and older with active polyarticular course JIA.[20]

New Formulations:

- An interchangeable biosimilar formulation of **golimumab-sldi** (IMMGOLIS) received FDA approval for treat of adults with RA in combination with MTX and moderate-to-severe UC in May 2026.[21]

- An Interchangeable biosimilar formulation of **tocilizumab** (AVTOZMA) received FDA approval in January 2025 for treatment of adults with RA, hospitalized with COVID-19, and giant cell arteritis; and patients aged 2 years of age and older with polyarticular JIA and systemic JIA.[22]

- The FDA approved a new extended release oral tablet of the PDE-4i **apremilast**, OTEZLA XR in August 2025.[23] This medication is indicated for treatment of adults with active PsA, PsO who are candidates for phototherapy or systemic therapy, and oral ulcers associated with Behçets' Disease.[23] In pediatric patients aged 6 years and older weighing at least 20 kg, extended-release apremilast is indicated for treatment of active PsA and moderate-to-severe PsO.[23] Recommended dosing of extended-release apremilast in adults and pediatric patients 6 years and older who weigh at least 20 kg is 75 mg once a

day after a 5-day titration with the immediate-release formulation.[23] Extended-release apremilast is not recommended for patients with severe renal impairment, as the dose must be reduced to 20 or 30 mg once daily (depending on patient's weight) with the immediate release tablets.[23] The safety and effectiveness of extended-release apremilast was supported by PK data from healthy adults demonstrating comparable PK exposure between OTEZLA XR 75 mg once daily and apremilast immediate release 30 mg twice daily.[23]

New FDA Safety Alerts:

Table 3. Description of New FDA Safety Alerts[65]

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
Anakinra	KINERET	10/2025	Warnings and Precautions	**Amyloidosis** Post-marketing cases of injection site amyloid deposits have been reported in NOMID patients after receiving high doses of KINERET injected subcutaneously into the same area of skin over long periods of time. Systemic AIL1RAP (IL-1 receptor antagonist protein) amyloidosis occurred in some of these patients with injection site amyloid deposits; these patients presented with proteinuria. Recommend patients to rotate their injection sites. In patients with confirmed injection site amyloid deposits, monitor proteinuria for systemic amyloidosis.
Adalimumab	HUMIRA	7/2025	Warnings and Precautions	**Autoimmunity** Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome or autoimmune hepatitis . If a patient develops symptoms and findings suggestive of a lupus-like syndrome or autoimmune hepatitis following treatment with HUMIRA, discontinue treatment and evaluate the patient.

Randomized Controlled Trials:

A total of 357 citations were manually reviewed from the initial literature search. After further review, 356 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). The remaining trial is summarized in the table below. The full abstract is included in **Appendix 4**.

Table 4. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Outcomes	Results	Notes/Limitations

Mysler, E. et al.[66] SELECT-SWITCH MC, DB, RCT	1. Upadacitinib 15 mg po once a day (n=245) Vs. 2. Adalimumab 40 mg SC every other week (n=246)	Adults with RA unresponsive to TNFi therapy (certolizumab, etanercept, golimumab, infliximab) + MTX for > 3 months Randomized 1:1 to 1 or 2 x 12 weeks N=492	Primary Outcome: DAS28-CRP ≤ 3.2 at week 12 Secondary Outcome: ACR50 at week 12	DAS28-CRP ≤ 3.2 at week 12 1. n=106 (43.3%) 2. n=55 (22.4%) Difference: 21% 95% CI 12.9 to 29.1 P<0.0001 ACR50 at week 12 1. 38.2% 2. 26.8% Difference: 11.4% 95% CI 3.1 to 19.6 P=0.0068 Safety was comparable between 2 treatment arms	-Upadacitinib demonstrated superiority over adalimumab at 12 weeks in DAS28-CRP and ACR50 in patients who were unresponsive to TNFi therapy -Short term trial was not long enough to identify adverse cardiovascular or venous thromboembolic events with upadacitinib -Patients had long mean disease duration, high inflammatory burden, and functional impairment, which may not be representative of all patients with RA in clinical practice following first TNFi failure -Patients who were adalimumab intolerant/resistant were excluded from SELECT-SWITCH, resulting in almost 70% of patients having experienced first TNFi failure with etanercept -Trial was sponsored by Abbvie, the manufacturer of upadacitnib -Authors reported substantial support and conflict of interest from various manufacturers
Abbreviations: ACR50 = 50% improvement in American College of Rheumatology response criteria; CI = Confidence Interval; DAS28-CRP = Disease Activity Score 28-C-reactive protein; DB = double-blind; MC = multi-center; po = oral; MTX = methotrexate; RA = rheumatoid arthritis; RCT= randomized clinical trial; SC = subcutaneous; TNFi = tumor necrosis factor inhibitor					

NEW DRUG EVALUATION: ICOTYDE (icotrokinra)

See **Appendix 4** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and pharmacokinetic properties are listed in **Appendix 6**.

Clinical Efficacy:

Icotrokinra is an orally administered IL-23 receptor antagonist.[24] It is FDA-approved for the treatment of moderate-to-severe PsO in patients aged 12 years and older, who weigh more than 40 kg, and are candidates for systemic therapy or phototherapy.[24] Four placebo-controlled, phase 3 RCTs (ICONIC-LEAD, ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and ICONIC-TOTAL) evaluated the efficacy of icotrokinra 200 mg once daily for the treatment of patients (2367 adults and 72 adolescents) with moderate-to-severe PsO.[25] The co-primary endpoints were the Investigators Global Assessment (IGA) score of 0 or 1 and ≥ 2 grade improvement from baseline on a 5-point scale, and achievement of PASI-90 at week 16.[25] Demographics and baseline disease characteristics were well-balanced in all 4 trials, although more subjects 65 years of age or older were randomized to icotrokinra (9.6%) than to placebo (4.9%) in the ICONIC-TOTAL trial.[25] All 4 RCTs enrolled more male subjects than female subjects.[25] The clinical trials that contribute to the efficacy data for this indication are described and evaluated below in **Table 6.**

The ICONIC-LEAD trial randomized 684 adults and adolescents aged 12 years and older in a 2:1 ratio to icotrokinra 200 mg once daily or placebo.[25] Randomization was performed separately for adult (n=618) and adolescent participants (n=66).[25] Randomization of the adult group was further stratified by baseline weight category (≤ 90 kg and > 90 kg) and geographic region (North and South America, Europe or Asia-Pacific).[25] Randomization of the adolescent group was stratified by geographic region.[25]

The ICONIC-ADVANCE 1 & 2 trials were identically designed except for the randomization ratio.[25] Once-daily oral icotrokinra was compared to placebo and deucravacitinib in adults with moderate-to-severe PsO.[25] ICONIC-ADVANCE 1 randomized 750 participants in a 2:1:2 ratio to icotrokinra 200 mg once daily, placebo, or deucravacitinib 6 mg once daily.[25] ICONIC-ADVANCE 2 randomized 675 participants in a 4:1:4 ratio to icotrokinra 200 mg once daily, placebo, or deucravacitinib 6 mg once daily.[25] Randomization in both trials was stratified by baseline weight category (≤ 90 kg or >90 kg) and geographic region.[25] In both trials, placebo-treated participants switched to icotrokinra 200 mg once daily at Week 16, while participants in the deucravacitinib arm switched to icotrokinra 200 mg once daily at Week 24.[25] Demographic and baseline disease characteristics were well-balanced across the 3 treatment arms in both trials.[25]
The ICONIC-TOTAL trial was conducted in adults and adolescents aged 12 years and older with moderate-to-severe PsO involving special areas (scalp, genital, and/or palmoplantar).[25] In this trial PSAI-90 was not evaluated because this study focused on improvement of psoriasis symptoms in the scalp, genitals, hands, and feet.[25] The single primary efficacy endpoint was IGA 0/1 response, and at least a 2-grade improvement from baseline at Week 16.[25] ICONIC-TOTAL randomized approximately 300 participants in a 2:1 ratio to icotrokinra 200 mg once daily or placebo.[25] Randomization was stratified by special area involvement (baseline Physicians Global Assessment of hands and feet [hf-PGA] ≥ 3, Static Physician's Global Assessment of Genitalia [sPGA-G] ≥ 3, and Scalp-Specific Investigator Global Assessment [ss-IGA] ≥3), geographic region, and body surface area [BSA] category (< 10% or ≥ 10%).[25] These site-specific assessments are described in **Appendix 2**. Notable demographic imbalances were observed, with a higher proportion of subjects ≥ 65 years of age randomized to icotrokinra compared to placebo (9.6% versus 4.9%). Imbalances were present in severe hf-PGA scores (8.2% icotrokinra versus 3.9% placebo) and in > 90 kg (34.1% icotrokinra versus 40.8% placebo).[25]

In all 4 RCTs for the primary endpoint of IGA 0/1 response, icotrokinra was statistically superior to placebo (p-values <0.001).[25] Icotrokinra efficacy versus placebo on the coprimary endpoints of IGA 0/1 response and PASI-90 response at Week 16 was demonstrated in ICONIC-LEAD, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2; efficacy on the primary endpoint of IGA 0/1 response at Week 16 was demonstrated in ICONIC-TOTAL.[25] The risk-difference estimate for icotrokinra versus placebo for IGA 0/1 response was 56% in ICONIC-LEAD, 58% in ICONIC-ADVANCE 1, 51% in ICONIC-TOTAL, and 62% in ICONIC-ADVANCE 2.[25] The risk-difference estimate for PASI-90 response was 45% in ICONIC-LEAD, 51% in ICONIC-ADVANCE 1, and 56% in ICONIC-ADVANCE 2.[25]

The secondary endpoint results were supportive of the primary endpoint results, with icotrokinra being statistically superior to placebo across multiple clinical measures including skin clearance assessments (IGA 0, PASI-75, PASI-100) and scalp-specific assessments (ss-IGA 0/1).[25] Icotrokinra was statistically superior to placebo in all but one key secondary endpoint across all 4 trials.[25] In ICONIC-TOTAL, the key secondary efficacy endpoint of hf-PGA 0/1 (p=0.1441) was not statistically significant for the hands and feet assessment; however, it did not affect the statistical significance of the other key secondary efficacy endpoints per the prespecified multiplicity adjustment procedure.[25] Icotrokinra was statistically superior to deucravacitinib across all prespecified key secondary endpoints in both the ICONIC-ADVANCE 1 & 2 studies with risk differences consistently being around or above 15%.[25]

Trial Limitations
All 4 RCTs excluded patients previously treated with an IL-23 inhibitor, which may have introduced selection bias. A small proportion of adolescents were enrolled in the ICONIC-LEAD (10%) and ICONIC-TOTAL (2%) trials. Most of the participants in the 4 RCTs had moderate PsO (73-80%). Investigators in the ICONIC-LEAD trial did not select an active comparator, although 2 oral agents are FDA-approved to treat PsO (apremilast and deucravacitinib). Apremilast is approved for children aged 6 years and older with PsO, while deucravacitinib is only approved for use in adults. People enrolled in the ICONIC trials were predominantly White and other races and ethnicities were under-represented. The results from the ICONIC series of RCTs are limited by the duration of the reporting period (up to week 16); longer-term data from ongoing 3-year studies will provide more data to assess the magnitude and durability of responses and long-term safety.[26]

Clinical Safety:

Adverse effect data was pooled from the 4 RCTs that compared icotrokinra to placebo over 16 weeks and is presented in **Table 5**.[24] The most frequently reported AEs were headache, nausea, cough, fungal infections, and fatigue.[24] Serious infections other than mycoses were reported in 0.2% of icotrokinra-treated patients compared with 0.4% in placebo-treated patients over the 16-week treatment period.[24]

Table 5. Adverse Effects Reported in Four Clinical Trials of Icotrokinra versus Placebo over 16 Weeks[24]

Adverse Effect	**Icotrokinra N = 1296**	**Placebo N = 568**
Headache	51 (4.1%)	19 (3.3%)
Nausea	15 (1.2%)	3 (0.5%)
Cough	15 (1.2%)	1 (0.2%)
Fungal Infections	14 (1.1%)	0 (0%)
Fatigue	15 (1.0%)	3 (0.5%)

Medications that interact with the immune system may increase the risk of infection while taking icotrokinra.[24] The manufacturer recommends evaluating patients for tuberculosis (TB) infection prior to initiating treatment with icotrokinra based on clinical judgement.[24] Consider anti-TB therapy prior to initiating icotrokinra in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.[24] Monitor patients for signs and symptoms of active TB during and after icotrokinra treatment.[24] Avoid use of live vaccines in patients during treatment with icotrokinra.[24] Prior to initiating therapy with icotrokinra, complete immunizations according to current immunization guidelines.[24] No data are available on the response to live or inactive vaccines.[24] The available data on the use of icotrokinra during pregnancy or lactation are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.[24] Must be taken on an empty stomach with water and patients should wait 30 minutes before eating food.[24]

Look-alike / Sound-alike Error Risk Potential: No results available

Comparative Endpoints:

Clinically Meaningful Endpoints:

1) Improvement in PsO symptoms as evaluated by IGA score of 0/1, PASI-75, PASI-90, or PASI-100
2) Improved quality of life
3) Serious adverse events
4) Study withdrawal due to an adverse event

Primary Study Endpoints:

1) Percentage of patients who achieved IGA score 0 or 1 and 2 grade or greater improvement from baseline to Week 16
2) Percentage of patients who achieved PASI-90 at Week 16

Table 6. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1.Bissonnette RS, et al.[67] ICONIC-LEAD MC, DB, PC, Phase 3 RCT	1. Icotrokinra 200 mg po once daily through Week 24 2. Placebo po once daily through Week 16 Duration: 156 weeks Placebo-treated patients transitioned to icotrokinra after Week 16 and continued through Week 24. After Week 24, all patients with a treatment response were randomized to a withdrawal and active-treatment period through Week 52. Open-label active-treatment period conducted from Week 52 to Week 156.	<u>Demographics</u>: -Mean age: 42.6 yo -Male: 65% -Ethnicity Hispanic or Latino: 13% Not Hispanic or Latino: 86% -Race White: 72% Asian: 24% Black: 1% Unknown: 2% -Duration of PsO: 17 years -Moderate baseline IGA score (3): 75% -Severe baseline IGA score (4): 25% -Mean baseline PASI score: 20 -Mean percent of affected BSA: 26% -Previous treatment --Conventional systemic therapy: 48% --Biologic therapy: 34% --Phototherapy: 30% -Number of adolescents: 66 (10%) <u>Key Inclusion Criteria</u>: -Adults and adolescents aged 12 yo and older -Diagnosis of PsO at least 26 weeks prior to study enrollment -Total BSA ≥ 10% -PASI ≥ 12 -IGA ≥ 3 -Candidate for phototherapy or systematic therapy	<u>ITT</u>: 1. 456 2. 228 <u>PP</u>: 1. 437 2. 214 <u>Attrition</u>: 1. 19 (4%) 2. 14 (6%)	<u>Co-Primary Endpoints</u>: -Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 1. 65% 2. 8% Risk Difference: 57% 95% CI 50 to 62; P<0.001 -Percentage of patients who achieved PASI-90 response at Week 16 1. 50% 2. 4% Risk Difference: 46% 95% CI 40 to 50; P<0.001 <u>Secondary Endpoints</u>: -Percentage of patients who achieved IGA score of 0 at Week 16 1. 33% 2. 1% Risk Difference: 32% 95% CI 27 to 37; P<0.001 -Percentage of patients who achieved PASI-100 at Week 16 1. 27% 2. 1% Risk Difference: 26% 95% CI 22 to 31; P<0.001 -Percentage of patients who achieved PASI-75 at Week 16 1. 69% 2. 11% Risk Difference: 58% 95% CI 52 to 64; P<0.001	57%/2 46%/3 32%/3 26%/4	<u>Safety to Week 16</u> <u>AEs</u> 1. 49% 2. 49% <u>AE leading to discontinuation</u> 1. 1% 2. <1% <u>SAEs</u> 1. 1% 2. 3% <u>Nasopharyngitis</u> 1. 7% 2. 7% <u>Upper respiratory tract infection</u> 1. 7% 2. 7% <u>Headache</u> 1. 4% 2. <1% p-value and CI's NR	NA for all	**Risk of Bias (low/high/unclear)**: <u>Selection Bias</u>: Unclear. Randomized 2:1 to icotrokinra or placebo via a computer-generated schedule. Patients were stratified according to age (12 to <18 yo or 18 yo and older), weight (≤ 90 kg or > 90 kg), and geographic region (North and South America, Europe, or Asia-Pacific). Baseline demographics were balanced between groups. Excluded patients previously treated with an IL-23 inhibitor, which may have introduced selection bias. <u>Performance Bias</u>: Low. Participants and investigators blinded to treatment assignment. Placebo matched icotrokinra tablets in size and color. <u>Detection Bias</u>: Low. Outcomes assessors were blinded to treatment assignment. <u>Attrition Bias</u>: Low. Attrition rates were low and due to lack of efficacy in the placebo group and study withdrawal in the icotrokinra arm. <u>Reporting Bias</u>: Low. Protocol available online. All pre-specified endpoints reported as outlined in the protocol. <u>Other Bias:</u> Unclear. Trial was funded by manufacturer. Fifteen investigators reported conflicts of interest due to financial support from various manufacturers. **Applicability**: <u>Patient</u>: Most patients had moderate PsO (IGA score =3) and were White. Only 10% of enrolled patients were adolescents. <u>Intervention</u>: Dosing determined in a Phase 2 RCT, where doses ranging from 25 mg to 100 mg were taken once or twice daily. The 100 mg dose given twice daily showed the highest treatment difference from placebo with minimal

		-Patients aged 12 to 17 yo must weigh at least 40 kg at baseline Key Exclusion Criteria: -Non-plaque form of psoriasis (e.g., pustular, guttate, erythrodermic) -Drug-induced psoriasis -Severe or uncontrolled organ damage (renal, liver, cardiac, pulmonary, neurologic, etc.) -Previous treatment failure with at least one biologic targeting IL-23			58%/2			AEs. The 200 mg once daily dosing was first evaluated in the phase 3 RCTs, as it was assumed to be equivalent to 100 mg twice a day. Once daily dosing was selected to increase adherence to treatment. Comparator: Placebo is an appropriate comparator. Investigators did not opt to include an active oral comparator (either a PDE-4i or TYK-2i). Outcomes: Skin clearance as assessed by IGA and PASI-90 are appropriate endpoints. Setting: 138 study sites in North America, South America, Asia, Australia, and Europe
2. Gold LS et al.[26] ICONIC-ADVANCE 1 & ICONIC-ADVANCE 2 PC, AC, MC, DB, Phase 3 RCTs	1. Icotrokinra 200 mg po once daily x 16 weeks 2. Deucravacitinib 6 mg po once daily x 24 weeks 3. Placebo po once daily x 16 weeks Duration: 156 weeks. Patients assigned to placebo or deucravacitinib transitioned to icotrokinra beginning at Week 16 or 24, respectively. Open-label, long-term extension period from	Demographics: ICONIC-ADVANCE 1 -Mean age: 46.7 yo -Male: 68% -Ethnicity Hispanic or Latino: 17% Not Hispanic or Latino: 82% -Race Asian: 23% Black: 1% White: 74% -Moderate baseline IGA score (3): 80% -Severe baseline IGA score (4): 20% -Mean baseline PASI score: 20.1 ICONIC-ADVANCE 2 -Age: 46.1 yo -Male: 68% Ethnicity Hispanic or Latino: 14% Not Hispanic or Latino: 86% -Race Asian: 12% Black: 3% White: 83%	ICONIC-ADVANCE 1 ITT: 1. 311 2. 307 3. 156 PP: 1. 297 2. 286 3. 141 Attrition: 1. 14 (5%) 2. 21 (7%) 3. 15 (10%) ICONIC-ADVANCE 2 ITT: 1. 322 2. 327 3. 82 PP:	ICONIC-ADVANCE 1 Co-Primary Endpoints: -Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (PP analysis of icotrokinra vs. placebo) 1. 69% 3. 11% Risk Difference: 58% 95% CI 50 to 65; P<0.001 -Percentage of patients who achieved PASI-90 at Week 16 (icotrokinra vs. placebo) 1. 56% 3. 4% Risk Difference: 52% 95% CI 45 to 58; P<0.001 Secondary Endpoints: -Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (icotrokinra vs. deucravacitinib) 1. 68% 2. 50% Risk Difference: 18% 95% CI 11 to 26; P<0.0001	58%/2 52%/2 18%/6	Safety to Week 16: ICONIC-ADVANCE 1 AEs 1. 46% 2. 56% 3. 59% AE leading to discontinuation 1. 2% 2. 3% 3. 6% SAEs 1. 2% 2. 2% 3. 3% Serious Infection 1. 0 2. 1% 3. 1% Nasopharyngitis 1. 6% 2. 8% 3. 5%	NA for all	**Risk of Bias (low/high/unclear)**: Selection Bias: Low. Randomized 2:2:1 in Trial 1 and 4:4:1 in Trial 2 via centralized randomization using an IWRS. Stratified by weight (≤ 90 kg and > 90 kg) and geographical region (Europe, North and South America, and Asia-Pacific). Baseline demographics were balanced between groups. Excluded patients previously treated with an IL-23 inhibitor, which may have introduced selection bias. Performance Bias: Low. Participants and investigators blinded to treatment assignment. Placebo matched icotrokinra tablets in size and color. Detection Bias: Low. Outcomes assessors were blinded to treatment assignment. Attrition Bias: Low. Attrition rates were low and due to lack of efficacy in the placebo group and study withdrawal in the icotrokinra arm. Reporting Bias: Low. Protocol available online. All pre-specified endpoints reported as outlined in the protocol. Other Bias: Unclear. Manufacturer funded study and had a role in study design, data collection, data analysis, and writing of reports. Sixteen investigators reported conflicts of interest due to

	Week 16 (placebo group) or Week 24 (deucravacitinib group) through Week 156	-Baseline IGA score of 3 (moderate): 80% -Baseline IGA score of 4 (severe): 20% -Mean baseline PASI score: 19.8 Key Inclusion Criteria: -Adults aged 18 yo and older for both RCTs -see #1 for additional criteria Key Exclusion Criteria: see #1	1. 307 2. 309 3. 74 Attrition: 1. 15 (5%) 2. 18 (6%) 3. 8 (10%)	-Percentage of patients who achieved PASI-90 at Week 16 (icotrokinra vs. deucravacitinib) 1. 55% 2. 30% Risk Difference: 25% 95% CI 18 to 33; P<0.0001 -Percentage of patients who achieved ss-IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (icotrokinra vs. placebo) 1. 72% 3. 15% Risk Difference: 57% 95% CI 50 to 63; P<0.0001 ICONIC-ADVANCE 2 Co-Primary Endpoints: -Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (PP analysis: icotrokinra vs. placebo) 1. 71% 3. 9% Risk Difference: 62% 95% CI 53 to 69; P<0.001 -Percentage of patients who achieved PASI-90 at Week 16 (icotrokinra vs. placebo) 1. 58% 3. 0% Risk Difference: 58% 95% CI 50 to 64; P<0.001 Secondary Endpoints: Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (icotrokinra vs. deucravacitinib) 1. 70% 2. 54% Risk Difference: 16% 95% CI 9 to 24; P<0.0001	25%/4 57%/2 62%/2 58%/2 16%/7	Upper respiratory tract infection 1. 5% 2. 4% 3. 3% Headache 1. 5% 2. 3% 3. 6% ICONIC-ADVANCE 2 AEs 1. 49% 2. 57% 3. 54% AE leading to discontinuation 1. 2% 2. 2% 3. 2% SAEs 1. 3% 2. 2% 3. 0% Serious Infection 1. <1% 2. 1% 3. 0% Nasopharyngitis 1. 6% 2. 10% 3. 7% Upper respiratory tract infection 1. 2% 2. 6% 3. 4%		financial support from various manufacturers. **Applicability**: Patient: 80% of patients had moderate PsO and 20% of patients had severe PsO. Most patients were White and all patients were adults. Baseline demographics were balanced between groups. Excluded patients previously treated with an IL-23 inhibitor, which may have introduced selection bias. Intervention: Dosing determined in a Phase 2 RCT, where doses ranging from 25 mg to 100 mg were taken once or twice daily. Comparator: Most approved treatments for PsO are injectable. One oral agent, a TYK2i, was selected as an active comparator. Outcomes: Skin clearance as assessed by IGA and PASI-90 are appropriate endpoints. Setting: ICONIC-ADVANCE 1: 149 study sites across 13 countries North America, South America, Asia, Australia, and Europe ICONIC-ADVANCE 2: 114 sites across 11 countries

				-Percentage of patients who achieved PASI-90 at Week 16 (icotrokinra vs. deucravacitinib) 1. 57% 2. 34% Risk Difference: 23% 95% CI 16 to 30; P<0.0001 Percentage of patients who achieved ss-IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 (icotrokinra vs. placebo) 1. 74% 3. 18% Risk Difference: 56% 95% CI 44 to 68; P<0.0001	23%/5 56%/2	p-value and CI's NR		
3.Gooderham M, et al.[68] ICONIC-TOTAL PC, DB, Phase 3 RCT	1. Icotrokinra 200 mg po once daily through Week 16 2. Placebo po once daily through Week 16 Duration of trial: 156 weeks. After Week 16, placebo-treated participants crossed over to receive icotrokinra 200 mg once daily through Week 156 and icotrokinra-treated patients continued icotrokinra through Week 156.	<u>Demographics</u>: Mean age: 44.7 yo -Male: 64% -Ethnicity Hispanic or Latino: 7% Not Hispanic or Latino: 93% -Race Asian: 20% Black: 1% White: 78% -Moderate baseline IGA (3): 73% -Severe baseline IGA score (4): 27% -Mean baseline PASI score: 14.4 - Mean percent of affected BSA: 16% - Baseline ss-IGA score: Absent: 6% Mild: 11% Moderate: 64% Severe: 17% -Baseline sPGA-G score: Clear: 46.3% Mild: 1% Moderate: 33% Severe: 11% -Baseline hf-PGA score: Clear: 65%	<u>ITT</u>: 1. 208 2. 103 <u>PP</u>: 1. 199 2. 92 <u>Attrition</u>: 1. 9 (4%) 2. 11 (11%)	<u>Primary Endpoint</u>: Percentage of patients who achieved IGA score of 0 or 1 and ≥ 2-grade improvement from baseline at Week 16 1. 57% 2. 6% Difference: 51% 95% CI 42 to 59; P<0.001 <u>Secondary Endpoints</u>: -Percentage of patients who achieved ss-IGA score of 0/1 at Week 16 1. 66% 2. 11% Risk Difference: 55% 95% CI 45 to 64; P<0.0001 -Percentage of patients who achieved PSSI-90 at Week 16 1. 58% 2. 6% Risk Difference: 52% 95% CI 42 to 60; P<0.001 -Percentage of patients who achieved hf-PGA score of 0/1 at Week 16 1. 42% 2. 26% Risk Difference: 17% 95% CI -6.2 to 37; P=0.1441	51%/2 55%/2 52%/2 NS	<u>AES</u> 1. 50% 2. 42% <u>SAEs</u> 1. 0.5% 2. 1.9% <u>Serious Infection</u> 1. 0% 2. 1% <u>Nasopharyngitis</u> 1. 13% 2. 11% <u>Upper respiratory tract infection</u> 1. 4.3% 2. 4.9% p-value and CI's NR		**Risk of Bias (low/high/unclear)**: <u>Selection Bias</u>: Low. Randomized 2:1 to icotrokinra or placebo using a computer-generated schedule. Permuted block randomization stratified participants by high-impact site involvement (scalp, genital, hand/foot), geographic region (North and South America, Europe, Asia-Pacific) and BSA category (<10% or ≥ 10%). More subjects 65 years of age or older were randomized to icotrokinra (9.6%) than to placebo (4.9%). Imbalances were present in severe hf-PGA scores (8.2% icotrokinra versus 3.9% placebo) and in > 90 kg (34.1% icotrokinra versus 40.8% placebo). Excluded patients previously treated with an IL-23 inhibitor, which may have introduced selection bias. <u>Performance Bias</u>: Low. Participants and investigators blinded to treatment assignment. Placebo matched icotrokinra tablets in size and color. <u>Detection Bias</u>: Low. Outcomes assessors were blinded to treatment assignment. <u>Attrition Bias</u>: Low. Attrition rates were low and due to lack of efficacy in the placebo group and study withdrawal in the icotrokinra arm.

		Mild: 8% Moderate: 33% Severe: 11% -Number of adolescents: 6 (2%) -Number with scalp Pso = 252 (81%) -Number with genital PsO = 140 (45%) -Number with hand/foot PsO: 71 (23%) <u>Key Inclusion Criteria</u>: -Adults and adolescents aged 12 yo and older -Diagnosis of PsO at least 26 weeks prior to study enrollment -Total BSA ≥ 1% -IGA ≥ 2 -ss-IGA ≥ 3, and/or SPGA-G ≥ 3, and/or hf-PGA ≥ 3 -Confirmation of PsO in a special area (including scalp, genital, palmoplantar) -Failure to respond to at least 1 topical therapy (corticosteroids, calcineurin inhibitors, and/or Vitamin D analogs) <u>Key Exclusion Criteria</u>: -Dermatoses other than PsO (such as contact dermatitis) or palmoplantar pustulosis of the palmoplantar area (if hf-PGA ≥ 3 at baseline) -See # 1 for additional criteria		Percentage of patients who achieved s-PGA-G score of 0/1 at Week 16 1. 77% 2. 21% Risk Difference: 55% 95% CI 39 to 68; P<0.001 -Percentage of patients who achieved IGA score of 0 at Week 16 1. 26% 2. 1% Risk Difference: 25% 95% CI 18 to 32; P<0.001	55%/2 25%/4			<u>Reporting Bias</u>: Low. Protocol available online. All pre-specified endpoints reported as outlined in the protocol. <u>Other Bias:</u> Unclear. Manufacturer funded study and had a role in study design, data collection, data analysis, and writing of reports. Sixteen investigators reported conflicts of interest due to financial support from various manufacturers. **Applicability**: <u>Patient</u>: Most of the participants had moderate PsO (73%) with scalp involvement (81%). Most of the participants were White (78%) and only 2% were adolescents. <u>Intervention</u>: Dosing determined in a Phase 2 RCT, where doses ranging from 25 mg to 100 mg were taken once or twice daily. <u>Comparator</u>: Placebo is an appropriate comparator. Investigators did not opt to include an active oral comparator (either a PDE-4i or TYK-2i). <u>Outcomes</u>: IGA score was the primary endpoint and site-specific assessments (scalp, genital, hands/feet) were used as secondary endpoints. <u>Setting</u>: 69 study sites in 10 countries: Argentina, Canada, Germany, Hungary, Poland, South Korea, Spain, Taiwan, United Kingdom, and United States.

<u>Abbreviations</u>: AC = active comparator; AE = adverse effects; ARR = absolute risk reduction; BSA = body surface area; CI = confidence interval; DB = double-blind; hf-PGA = Physicians Global Assessment of Hands and Feet; IGA = Investigators Global Assessment; IL-23 = interleukin-23; ITT = intention to treat; IWRS = interactive web response system; kg = kilograms; MC = multi-center; mITT = modified intention to treat; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; PASI = Psoriasis Area and Severity Index; PC = placebo-controlled; PDE-4i = phosphodiesterase inhibitor; po = oral; PP = per protocol; PsO = plaque psoriasis; PSSI = Psoriasis Scalp Severity Index; SAEs = serious adverse effects; ss-IGA = scalp-specific Investigators Global Assessment; sPGA-G = Static Physician's Global Assessment of Genitalia; TYK-2i = tyrosine-kinase-2 inhibitor; yo = years old

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Appendix 1: Current Preferred Drug List

Generic	Brand	Route	Form	PDL
adalimumab	HUMIRA PEN	SUBCUT	PEN IJ KIT	Y
adalimumab	HUMIRA(CF) PEN	SUBCUT	PEN IJ KIT	Y
adalimumab	HUMIRA(CF) PEN CROHN'S-UC-HS	SUBCUT	PEN IJ KIT	Y
adalimumab	HUMIRA(CF) PEN PSOR-UV-ADOL HS	SUBCUT	PEN IJ KIT	Y
adalimumab	HUMIRA	SUBCUT	SYRINGEKIT	Y
adalimumab	HUMIRA(CF)	SUBCUT	SYRINGEKIT	Y
adalimumab-atto	AMJEVITA(CF) AUTOINJECTOR	SUBCUT	AUTO INJCT	Y
adalimumab-atto	AMJEVITA(CF)	SUBCUT	SYRINGE	Y
adalimumab-fkjp	ADALIMUMAB-FKJP(CF) PEN	SUBCUT	PEN IJ KIT	Y
adalimumab-fkjp	ADALIMUMAB-FKJP(CF) PEN	SUBCUT	PEN INJCTR	Y
adalimumab-fkjp	ADALIMUMAB-FKJP(CF)	SUBCUT	SYRINGE	Y
adalimumab-fkjp	ADALIMUMAB-FKJP(CF)	SUBCUT	SYRINGEKIT	Y
adalimumab-ryvk	SIMLANDI(CF) AUTOINJECTOR	SUBCUT	AUTOINJKIT	Y
adalimumab-ryvk	SIMLANDI(CF)	SUBCUT	SYRINGEKIT	Y
apremilast	OTEZLA	ORAL	TAB DS PK	Y
apremilast	OTEZLA	ORAL	TABLET	Y
etanercept	ENBREL MINI	SUBCUT	CARTRIDGE	Y
etanercept	ENBREL SURECLICK	SUBCUT	PEN INJCTR	Y
etanercept	ENBREL	SUBCUT	SYRINGE	Y
etanercept	ENBREL	SUBCUT	VIAL	Y
guselkumab	TREMFYA	INTRAVEN	VIAL	Y
guselkumab	TREMFYA ONE-PRESS	SUBCUT	AUTO INJCT	Y
guselkumab	TREMFYA PEN	SUBCUT	PEN INJCTR	Y
guselkumab	TREMFYA PEN INDUCTION (2 PEN)	SUBCUT	PEN INJCTR	Y
guselkumab	TREMFYA	SUBCUT	SYRINGE	Y
infliximab	INFLIXIMAB	INTRAVEN	VIAL	Y
infliximab	REMICADE	INTRAVEN	VIAL	Y
infliximab-axxq	AVSOLA	INTRAVEN	VIAL	Y
ixekizumab	TALTZ AUTOINJECTOR	SUBCUT	AUTO INJCT	Y
ixekizumab	TALTZ AUTOINJECTOR (2 PACK)	SUBCUT	AUTO INJCT	Y
ixekizumab	TALTZ AUTOINJECTOR (3 PACK)	SUBCUT	AUTO INJCT	Y
ixekizumab	TALTZ SYRINGE	SUBCUT	SYRINGE	Y
tofacitinib citrate	TOFACITINIB CITRATE	ORAL	SOLUTION	Y
tofacitinib citrate	XELJANZ	ORAL	SOLUTION	Y
tofacitinib citrate	TOFACITINIB CITRATE ER	ORAL	TAB ER 24H	Y
tofacitinib citrate	XELJANZ XR	ORAL	TAB ER 24H	Y
tofacitinib citrate	TOFACITINIB CITRATE	ORAL	TABLET	Y

tofacitinib citrate	XELJANZ	ORAL	TABLET	Y
ustekinumab-ttwe	PYZCHIVA	INTRAVEN	VIAL	Y
ustekinumab-ttwe	PYZCHIVA	SUBCUT	SYRINGE	Y
ustekinumab-ttwe	PYZCHIVA	SUBCUT	VIAL	Y
abatacept	ORENCIA CLICKJECT	SUBCUT	AUTO INJCT	N
abatacept	ORENCIA	SUBCUT	SYRINGE	N
abatacept/maltose	ORENCIA	INTRAVEN	VIAL	N
adalimumab-aacf	ADALIMUMAB-AACF(CF) PEN (2 PK)	SUBCUT	PEN IJ KIT	N
adalimumab-aacf	ADALIMUMAB-AACF(CF) PEN CROHNS	SUBCUT	PEN IJ KIT	N
adalimumab-aacf	ADALIMUMAB-AACF(CF) PEN PS-UV	SUBCUT	PEN IJ KIT	N
adalimumab-aacf	IDACIO(CF) PEN CROHN'S-UC(6PK)	SUBCUT	PEN IJ KIT	N
adalimumab-aacf	IDACIO(CF) PEN PSORIASIS (4PK)	SUBCUT	PEN IJ KIT	N
adalimumab-aacf	IDACIO(CF) PEN	SUBCUT	PEN INJCTR	N
adalimumab-aacf	ADALIMUMAB-AACF(CF)	SUBCUT	SYRINGE	N
adalimumab-aacf	ADALIMUMAB-AACF(CF) (2 PK)	SUBCUT	SYRINGEKIT	N
adalimumab-aaty	ADALIMUMAB-AATY(CF) AI CROHNS	SUBCUT	AUTOINJKIT	N
adalimumab-aaty	ADALIMUMAB-AATY(CF) AUTOINJECT	SUBCUT	AUTOINJKIT	N
adalimumab-aaty	YUFLYMA(CF) AI CROHN'S-UC-HS	SUBCUT	AUTOINJKIT	N
adalimumab-aaty	YUFLYMA(CF) AUTOINJECTOR	SUBCUT	AUTOINJKIT	N
adalimumab-aaty	ADALIMUMAB-AATY(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-aaty	YUFLYMA(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-adaz	ADALIMUMAB-ADAZ(CF) PEN	SUBCUT	PEN INJCTR	N
adalimumab-adaz	HYRIMOZ(CF) PEN	SUBCUT	PEN INJCTR	N
adalimumab-adaz	HYRIMOZ(CF) PEN CROHN-UC START	SUBCUT	PEN INJCTR	N
adalimumab-adaz	HYRIMOZ(CF) PEN PSORIASIS	SUBCUT	PEN INJCTR	N
adalimumab-adaz	ADALIMUMAB-ADAZ(CF)	SUBCUT	SYRINGE	N
adalimumab-adaz	HYRIMOZ(CF)	SUBCUT	SYRINGE	N
adalimumab-adaz	HYRIMOZ(CF) PEDIATRIC CROHN'S	SUBCUT	SYRINGE	N
adalimumab-adbm	ADALIMUMAB-ADBM(CF) PEN	SUBCUT	PEN IJ KIT	N
adalimumab-adbm	ADALIMUMAB-ADBM(CF)PEN	SUBCUT	PEN IJ KIT	N
adalimumab-adbm	CYLTEZO(CF) PEN	SUBCUT	PEN IJ KIT	N
adalimumab-adbm	ADALIMUMAB-ADBM(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-adbm	CYLTEZO(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-afzb	ABRILADA(CF) PEN	SUBCUT	PEN IJ KIT	N
adalimumab-afzb	ABRILADA(CF) PEN (2 PACK)	SUBCUT	PEN IJ KIT	N
adalimumab-afzb	ABRILADA(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-aqvh	YUSIMRY(CF) PEN	SUBCUT	PEN INJCTR	N
adalimumab-atto	AMJEVITA(CF) AUTOINJECTOR	SUBCUT	AUTO INJCT	N
adalimumab-atto	AMJEVITA(CF)	SUBCUT	SYRINGE	N
adalimumab-bwwd	HADLIMA PUSHTOUCH	SUBCUT	AUTO INJCT	N

adalimumab-bwwd	HADLIMA(CF) PUSHTOUCH	SUBCUT	AUTO INJCT	N
adalimumab-bwwd	HADLIMA	SUBCUT	SYRINGE	N
adalimumab-bwwd	HADLIMA(CF)	SUBCUT	SYRINGE	N
adalimumab-fkjp	HULIO(CF) PEN	SUBCUT	PEN IJ KIT	N
adalimumab-fkjp	HULIO(CF) PEN	SUBCUT	PEN INJCTR	N
adalimumab-fkjp	HULIO(CF)	SUBCUT	SYRINGE	N
adalimumab-fkjp	HULIO(CF)	SUBCUT	SYRINGEKIT	N
adalimumab-ryvk	ADALIMUMAB-RYVK(CF) AUTOINJECT	SUBCUT	AUTOINJKIT	N
adalimumab-ryvk	ADALIMUMAB-RYVK(CF)	SUBCUT	SYRINGEKIT	N
anakinra	KINERET	SUBCUT	SYRINGE	N
apremilast	OTEZLA XR	ORAL	TAB ER 24H	N
apremilast	OTEZLA XR	ORAL	TB TBER DP	N
baricitinib	OLUMIANT	ORAL	TABLET	N
bimekizumab-bkzx	BIMZELX AUTOINJECTOR	SUBCUT	AUTO INJCT	N
bimekizumab-bkzx	BIMZELX	SUBCUT	SYRINGE	N
canakinumab/PF	ILARIS	SUBCUT	VIAL	N
certolizumab pegol	CIMZIA (2 PACK)	SUBCUT	KIT	N
certolizumab pegol	CIMZIA	SUBCUT	SYRINGEKIT	N
certolizumab pegol	CIMZIA (2 PACK)	SUBCUT	SYRINGEKIT	N
deucravacitinib	SOTYKTU	ORAL	TABLET	N
etrasimod arginine	VELSIPITY	ORAL	TABLET	N
golimumab	SIMPONI ARIA	INTRAVEN	VIAL	N
golimumab	SIMPONI	SUBCUT	PEN INJCTR	N
golimumab	SIMPONI	SUBCUT	SYRINGE	N
icotrokinra HCl	ICOTYDE	ORAL	TABLET	N
infliximab-abda	RENFLEXIS	INTRAVEN	VIAL	N
infliximab-dyyb	INFLECTRA	INTRAVEN	VIAL	N
infliximab-dyyb	ZYMFENTRA PEN	SUBCUT	PEN IJ KIT	N
infliximab-dyyb	ZYMFENTRA	SUBCUT	SYRINGEKIT	N
mirikizumab-mrkz	OMVOH	INTRAVEN	VIAL	N
mirikizumab-mrkz	OMVOH PEN	SUBCUT	PEN INJCTR	N
mirikizumab-mrkz	OMVOH	SUBCUT	SYRINGE	N
natalizumab	TYSABRI	INTRAVEN	VIAL	N
natalizumab-sztn	TYRUKO	INTRAVEN	VIAL	N
risankizumab-rzaa	SKYRIZI	INTRAVEN	VIAL	N
risankizumab-rzaa	SKYRIZI PEN	SUBCUT	PEN INJCTR	N
risankizumab-rzaa	SKYRIZI	SUBCUT	SYRINGE	N
risankizumab-rzaa	SKYRIZI ON-BODY	SUBCUT	WEAR INJCT	N
rituximab	RITUXAN	INTRAVEN	VIAL	N
rituximab-abbs	TRUXIMA	INTRAVEN	VIAL	N

rituximab-arrx	RIABNI	INTRAVEN	VIAL	N
rituximab-pvvr	RUXIENCE	INTRAVEN	VIAL	N
sarilumab	KEVZARA	SUBCUT	PEN INJCTR	N
sarilumab	KEVZARA	SUBCUT	SYRINGE	N
secukinumab	COSENTYX	INTRAVEN	VIAL	N
secukinumab	COSENTYX SENSOREADY (2 PENS)	SUBCUT	PEN INJCTR	N
secukinumab	COSENTYX SENSOREADY PEN	SUBCUT	PEN INJCTR	N
secukinumab	COSENTYX UNOREADY PEN	SUBCUT	PEN INJCTR	N
secukinumab	COSENTYX (2 SYRINGES)	SUBCUT	SYRINGE	N
secukinumab	COSENTYX SYRINGE	SUBCUT	SYRINGE	N
spesolimab-sbzo	SPEVIGO	INTRAVEN	VIAL	N
spesolimab-sbzo	SPEVIGO	SUBCUT	SYRINGE	N
tildrakizumab-asmn	ILUMYA	SUBCUT	SYRINGE	N
tocilizumab	ACTEMRA	INTRAVEN	VIAL	N
tocilizumab	ACTEMRA ACTPEN	SUBCUT	PEN INJCTR	N
tocilizumab	ACTEMRA	SUBCUT	SYRINGE	N
tocilizumab-aazg	TYENNE	INTRAVEN	VIAL	N
tocilizumab-aazg	TYENNE AUTOINJECTOR	SUBCUT	PEN INJCTR	N
tocilizumab-aazg	TYENNE	SUBCUT	SYRINGE	N
tocilizumab-anoh	AVTOZMA	INTRAVEN	VIAL	N
tocilizumab-anoh	AVTOZMA AUTOINJECTOR	SUBCUT	PEN INJCTR	N
tocilizumab-anoh	AVTOZMA	SUBCUT	SYRINGE	N
tocilizumab-bavi	TOFIDENCE	INTRAVEN	VIAL	N
upadacitinib	RINVOQ LQ	ORAL	SOLUTION	N
upadacitinib	RINVOQ	ORAL	TAB ER 24H	N
ustekinumab	STELARA	INTRAVEN	VIAL	N
ustekinumab	USTEKINUMAB	INTRAVEN	VIAL	N
ustekinumab	STELARA	SUBCUT	SYRINGE	N
ustekinumab	USTEKINUMAB	SUBCUT	SYRINGE	N
ustekinumab	STELARA	SUBCUT	VIAL	N
ustekinumab	USTEKINUMAB	SUBCUT	VIAL	N
ustekinumab-aauz	OTULFI	INTRAVEN	VIAL	N
ustekinumab-aauz	OTULFI	SUBCUT	SYRINGE	N
ustekinumab-aauz	USTEKINUMAB-AAUZ	SUBCUT	SYRINGE	N
ustekinumab-aauz	OTULFI	SUBCUT	VIAL	N
ustekinumab-aekn	SELARSDI	INTRAVEN	VIAL	N
ustekinumab-aekn	SELARSDI	SUBCUT	SYRINGE	N
ustekinumab-aekn	USTEKINUMAB-AEKN	SUBCUT	SYRINGE	N
ustekinumab-aekn	SELARSDI	SUBCUT	VIAL	N
ustekinumab-hmny	STARJEMZA	INTRAVEN	VIAL	N

ustekinumab-hmny	STARJEMZA	SUBCUT	SYRINGE	N
ustekinumab-hmny	STARJEMZA	SUBCUT	VIAL	N
ustekinumab-kfce	YESINTEK	INTRAVEN	VIAL	N
ustekinumab-kfce	YESINTEK	SUBCUT	SYRINGE	N
ustekinumab-kfce	YESINTEK	SUBCUT	VIAL	N
ustekinumab-srlf	IMULDOSA	INTRAVEN	VIAL	N
ustekinumab-srlf	IMULDOSA	SUBCUT	SYRINGE	N
ustekinumab-stba	STEQEYMA	INTRAVEN	VIAL	N
ustekinumab-stba	STEQEYMA	SUBCUT	SYRINGE	N
ustekinumab-stba	STEQEYMA	SUBCUT	VIAL	N
ustekinumab-ttwe	USTEKINUMAB-TTWE	INTRAVEN	VIAL	N
ustekinumab-ttwe	USTEKINUMAB-TTWE	SUBCUT	SYRINGE	N
ustekinumab-ttwe	USTEKINUMAB-TTWE	SUBCUT	VIAL	N
vedolizumab	ENTYVIO	INTRAVEN	VIAL	N
vedolizumab	ENTYVIO PEN	SUBCUT	PEN INJCTR	N
tofacitinib citrate	TOFACITINIB CITRATE	ORAL	SOLUTION	
tofacitinib citrate	TOFACITINIB CITRATE ER	ORAL	TAB ER 24H	
tofacitinib citrate	TOFACITINIB CITRATE	ORAL	TABLET	

Appendix 2: Outcomes Used for Assessment of Disease Progression in Clinical Trials for Selected Autoimmune Conditions

Table 1. Selected Outcomes Used for Assessment of Disease Progression[69-73]

Ankylosing Spondylitis		
Outcome Measure	**Domains**	**Scale and Scoring**
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) BASDAI50	Level of symptoms: 1. Fatigue 2. Pain in hips, back and neck 3. Pain in joints other than hips, back or neck 4. Discomfort in areas tender to touch or pressure Mean measurements of: 5. Intensity of morning stiffness 6. Duration of morning stiffness (0 to 2 hours scored on a 0-10 scale) • ≥ 50% improvement in BASDAI	VAS scale 0-10: 0 is no symptoms, 10 is very severe BASDAI score calculation: 1. Add scores for the first 4 questions 2. Add one half of the sum of question 5 and 6 3. Divide the result by 5 A BASDAI score ≥ 4 (on a scale of 0-10) indicates active disease that warrants consideration of therapy
Bath Ankylosing Spondylitis Functional Index (BASFI)	Severity of 10 functional abilities: 1. Putting on socks 2. Bend from the waist to pick up a pen from the floor 3. Reaching up to a high shelf 4. Getting up from an armless chair 5. Getting up off the floor 6. Standing unsupported 7. Climbing 12-15 steps unaided 8. Looking over the shoulder 9. Doing physically demanding activities 10. Doing a full day's activities	VAS scale 0-10: easy (0) to impossible (10) BASFI score calculation: Total all 10 items and divide by 10 for final score Reported as change in score from baseline
Assessment in Ankylosing Spondyloarthritis International Society (ASAS) Response ASAS20 ASAS40 ASAS Partial Remission	Combines measures of symptoms and disability in 4 disease measures: 1. Spinal inflammation (BASDAI questions 5 and 6) 2. Spinal pain 3. Patient global assessment of spondylitis 4. Functional impairment (BASFI score) • Improvement of ≥ 20% and ≥ 1 unit in ≥ 3 of disease measures above • No worsening of ≥ 20% and ≥ 1 unit in remaining unimproved measure • Improvement of ≥ 40% and ≥ 2 units in ≥ 3 of disease measures above • No worsening at all in remaining measure • Reflects low disease activity	Scale of 0 to 100, with higher score indicating more improvement. Assessment of response to therapy by percent in symptom improvement Value of ≤ 2 in each of the 4 domains

Ankylosing Spondylitis Disease Activity Score (ASDAS) ASDAS Calculator: http://www.asas-group.org/clinical-instruments/asdas_calculator/asdas.html	Measures severity of symptoms and signs of inflammation including: 1. Back pain 2. Patient global assessment of spondylitis 3. Peripheral pain and swelling (BASDAI score) 4. Duration of morning stiffness (BASDAI score) 5. CRP or ESR	Scale of 0-10: 0 is no symptoms, 10 is very severe ASDAS scores: < 1.3 – Inactive Disease 1.4 to 2.1 – Moderate Disease Activity 2.2 to 3.4 – High Disease Activity >3.5 – Very High Disease Activity Improvement Criteria: Change ≥ 1.1 – Clinically Important Improvement Change ≥ 2.0 – Major Improvement
Spondyloarthritis Research Consortium of Canada (SPARCC)	Assessment of inflammation in the sacroiliac joints on magnetic resonance imaging (MRI). • Six coronal slices are assessed. • The sacroiliac joints are divided into 4 quadrants (upper lilac, lower iliac, upper sacral, and lower sacral). • The presence of increased signals in each quadrant is recorded. The maximum score for 2 sacroiliac joints in each coronal slice is 8. Maximum score for 6 coronal slices = 48 • A score for "intense" is assigned each sacroiliac joint on each slice. A score of 1 is assigned if "intense signal" is seen in any quadrant of any joint on a single slice. Maximum score per slice is 2, and for 6 slices = 12 • A score for "deep" may be assigned each joint on each slice. A score of 1 is assigned if "deep" signal is seen in any quadrant of a sacroiliac joint on a single slice. Maximum score per slide is 2, and for 6 slices =12.	Maximum score is 72 points • Presence of bone marrow edema = 48 • Presence of intense edema = 12 • Presence of deep edema = 12
Rheumatoid Arthritis		
Outcome Measure	**Domains**	**Scale and Scoring**
Disease Activity Score (DAS)-28 DAS-28 calculator https://www.das-score.nl/das28/DAScalculators/dasculators.html	Clinical assessment of disease activity in combination with an acute phase reactant level 1. Assessment of 28 joints for swelling and tenderness - swollen joint count (SJC) - tender joint count (TJC) 2. General health (GH) - patient assessment of disease on a 0-100 scale where 100 means maximal disease activity 3. Either ESR or CRP adjusted with SJC and TJC scores	DAS-28 scoring ranges from 0 to 9.4: <2.6: Remission ≥2.6 and ≤3.2: Low Disease Activity >3.2 and ≤5.1: Moderate Disease Activity >5.1: High disease activity • DAS-28 reduction by 0.6 represents a moderate improvement. • DAS-28 reduction more than 1.2 represents a major improvement.
Health Assessment Questionnaire Disability Index (HAQ-DI)	Assess 8 domains of daily activity – patient self-reported 1. Dressing and Grooming 2. Arising	Scored 0 to 3: 0 - no difficulty 1 - with some difficulty

	3. Eating 4. Walking 5. Hygiene 6. Reach 7. Grip 8. Chores or Activities	2 - with much difficulty 3 - unable to do HAQ-DI calculation: Sum of all domains then divided by 8 to give total score ranging from 0 (best) to 3 (worst*)*
American College of Rheumatology (ACR) ACR 20 ACR 50 ACR 70	Definition of improvement in RA symptoms: • 20% improvement in tender and swollen joint counts • 20% improvement in 3 of 5 remaining ACR core set measures o patient global assessment (VAS score) o physician global assessment (VAS score) o self-reported physical disability (HAQ score) o an acute phase reactant (ESR or CRP) o patient pain assessment (VAS score) • 50% improvement in tender and swollen joint counts • 50% improvement in 3 of 5 remaining ACR core measures • 70% improvement in tender and swollen joint counts • 70% improvement in 3 of 5 remaining ACR core set measures	Scale ranges from 0 to 100, with higher scores indicating more improvement. 20% improvement 50% improvement 70% improvement
Plaque Psoriasis, Psoriatic Arthritis, and Generalized Pustular Psoriasis		
Outcome Measure	**Domains**	**Scale and Scoring**
Static Physicians Global Assessment Scale (sPGA)	The static PGA is a 0-5 ordinal rating ranging from “clear” to “very severe psoriasis” as evaluated by the provider	Scale of 0 – 5: 0 = clear; scores 1–5 = increasing severity Response to therapy indicated by a score of 0 or 1
Investigators Global Assessment (IGA)	Overall lesions are graded for induration, erythema, and scaling. 0 = clear 1 = minimal plaque elevation, faint erythema, minimal scaling 2 = mild plaque elevation, light red erythema, fine scale dominates 3 = moderate plaque elevation, moderate red erythema, coarse scale predominates 4 = severe plaque elevation, bright red erythema, thick scale predominates	IGA score ranges from 0 (clear skin) to 4 (severe disease).

Psoriasis Symptom Inventory (PSI)	Patient reported outcome in 8 areas: 1. Itch 2. Redness 3. Scaling 4. Burning 5. Cracking 6. Stinging 7. Flaking 8. Pain of Lesions	Scale of 0-4: 0 = not at all severe, 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe Score ranges from 0 – 32 Response to therapy indicated by scores < 8 with no single item rated higher than 1
Psoriasis Area and Severity Index (PASI) PASI-75 PASI-90	Measure of overall psoriasis severity and coverage on Head, Upper Extremities, Trunk, and Lower Extremities • Erythema • Induration • Scaling 75% Improvement in PASI score 90% Improvement in PASI score – clear or almost clear skin	Scale of 0-4: 0 is clear, 1-4 increasing severity PASI score: 1. Sum rows 1, 2, and 3 for each area of the body using a 0-4 scale 2. Add an area score based on percentage involvement from 0 (clear) to 6 (≥90% coverage) 3. Multiply score as rated for each body area (0.1, 0.2, 0.3, 0.4 for head, arms, trunk, and legs, respectively) 4. Add all the scores together Composite score range from 0 -72: 0 = normal 72 = maximal disease
PsA Response Criteria (PsARC)	Used by the National Institute of Health Care Excellence (NICE) to continue TNF inhibitor therapy with an assessment at baseline and 12 weeks 1. 66 swollen joint score 2. 68 tender joint score 3. Patient global assessment 4. Physician global assessment	**Response** = improvement in ≥ 2 of the 4 tests: -One of which must be the joint tenderness or swelling score -No worsening in any of the four measures • **Improvement** is defined as a decrease ≥ 30% in the swollen or tender joint score and ≥1 in either of the global assessments
Dermatology Quality of Life (DQLI)	10 question patient self-reported assessment 1. How itchy has your skin been? 2. How embarrassed are because of your skin? 3. Has your skin interfered with activities? 4. Has your skin influenced the clothes you wear/ 5. Has your skin affected social activities? 6. How your skin impacted your ability to participate in a sport? 7. Has your skin prevented you from working? 8. Has your skin caused any problems with friends? 9. Has your skin impacted sexual activities?	Scale of 0-3: 0 not at all, 1 a little, 2 a lot, and 3 very much Total score ranges from 0 to 30 Interpretation of DQLI score: 0 – 1 no effect at all on patient's life 2 – 5 small effects on patient's life 6 – 10 moderate effects on patient's life 11 – 20 very large effect on patient's life 21 – 30 extremely large effect on patient's life

	10. How much has the treatment for your skin affected your daily activities?	
Scalp-Specific Investigators Global Assessment (ss-IGA)	Assesses the disease severity of scalp psoriasis.	Lesions are scored on a 5-point scale: 0 = absence of disease 1 = very mild disease 2 = mild disease 3 = moderate disease 4 = severe disease
Psoriasis Scalp Severity Index (PSSI)	The PSSI is a scalp-specific modification of the PASI based upon the extent of involvement and the severity of erythema, infiltration, and desquamation.	Involvement and severity of psoriasis on the PSSI is scored by physicians on a scale from 0 to 72, where 0 = no psoriasis and higher scores indicate more severe disease.
Static Physicians Global Assessment of Genitalia (sPGA-G)	The sPGA-G is a 6-point scale to assess the severity of genital psoriasis at a given time point.	The sPGA-G evaluates erythema, plaque elevation, and scale of genital psoriatic lesions. The severity of genital psoriasis is assessed as clear (0), minimal (1), mild (2), moderate (3), severe (4), and very severe (5).
Physicians Global Assessment of Hands and Feet (hf-PGA)	The hf-PGA assesses the severity of hand and foot psoriasis using a 5-point scale to score the plaques on the hands and feet.	Psoriasis is scored on a 5-point scale: 0 = clear 1 = almost clear 2 = mild 3 = moderate 4 = severe
Generalized Pustular Psoriasis Global Assessment (GPPGA)	Clinician scores 3 components on a 5-point scale (0 = clear to 4 = severe): 1. Erythema 2. Pustules 3. Lesion scaling	Scoring: Ranges from 0 to 4 0 = clear 1 = almost clear 2 = mild disease: bright red erythema, discrete moderate-density pustules, fine scaling, or crusting 3 = moderate disease: bright red erythema, high-density pustules, moderate scaling, or crusting covering most or all lesions 4 = severe disease: deep, fiery red erythema, very high-density pustules with pustular lakes, and severe scaling or crusting cover most or all lesions
Crohn's Disease and Ulcerative Colitis		
Outcome Measure	**Domains**	**Scale and Scoring**
Crohn's Disease Activity Score (CDAI)	Evaluation of 8 clinical factors (each weighted and summed to reach a total score) 1. Number of liquid or soft stools each day for 1 week (weight x 2) 2. Abdominal pain (graded on a severity scale of 0-3) for 1 week (weight x 5)	Each factor is weighted and summed to achieve a total score • Scores ≤150 indicate minimal disease • Scores >150 indicate active disease • Scores >450 indicate extremely severe disease

	3. General Well-being (subjective score of 0-4) for 1 week (weight x 7) 4. Presence of complications (weight x 20) 5. Use of diphenoxylate/atropine or opiates for diarrhea (weight x 30) 6. Presence of abdominal mass (graded as 0 [none], 2 [questionable] or 5 [definite]) (weight x 10) 7. Absolute deviation of Hematocrit from 47% (men) or 42% (women) (weight x 6) 8. Percentage deviation from standard weight (weight x 1)	
Mayo Clinic score (MCS) for grading activity of ulcerative colitis	Assessment Points **1. Stool Frequency** -Patient reporting a normal number of daily stools -3-4 more stools than normal 2 -≥ 5 more stools than normal 3 **2. Rectal Bleeding** -None 0 -Blood streaks seen with stool less than half the time 1 -Blood with most stools 2 -Pure blood passed 3 **3. Endoscopic Findings** -Normal or inactive colitis 0 -Mild friability, erythema, decreased vascularity 1 -Friability, marked erythema, absent vascular pattern, erosions 2 -Ulcerations and spontaneous bleeding 3 **4. Physician Global Assessment** -Normal 0 -Mild colitis 1 -Moderate colitis 2 -Severe colitis 3	The score can range from 0-12 with higher scores indicating worse severity. A critical component of this score is the endoscopic findings. Patients with lower scores but with an endoscopic score of 2 or greater are considered more severe regardless of the final score.

Simple Endoscopic Score for Crohn's Disease (SES-CD)[74]	Measures the endoscopic severity of inflammation and damage to the intestines in people with CD Five areas are evaluated: rectum, left colon, transverse colon, right colon, and terminal ileum Four features are scored for each of the 5 sections: size of ulcers, how much of the surface is covered by ulcers, how much the total surface area is affected and if there is stenosis. Each feature is score from 0 to 3, for a total score where higher numbers mean worse disease.	Scoring ranges from 0 to 15 for each of the 5 intestinal areas, except for stenosis because 3 represents an area through which the colonoscope cannot be passed and therefore can only be observed once 0-2 = remission 3-6 = mild endoscopic activity 7-15 = moderate endoscopic activity >15 = severe endoscopic activity
Abbreviations: CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; VAS = visual analog scale		

Appendix 3: FDA-Approved Targeted Immune Modulators

Table 2. FDA-Approved Targeted Immune Modulators for Selected Auto-Immune Conditions[28,76]

Drug – Route of Administration - Frequency	Molecular Target	Common Approved Indication(s)
Biologic DMARDs		
Adalimumab (HUMIRA) - SC every 2 weeks	TNF	AS, RA, PsA, PsO, CD, UC
Certolizumab Pegol (CIMZIA) – SC every 2 to 4 weeks		AS, RA PsA, PsO, CD
Etanercept (ENBREL) – SC every week		AS, RA, PsA, PsO
Golimumab - (SIMPONI and SIMPONI ARIA) – IV every 8 weeks, SC every 4 weeks		AS, RA, PsA, UC
Infliximab (REMICADE) – IV every 4 to 8 weeks, SC every 2 weeks		AS, RA, PsA, PsO, CD, UC
Anakinra (KINERET) – SC once daily	IL-1	RA
Canakinumab (ILARIS) – SC every 4 weeks		JIA
Sarilumab (KEVZARA) – SC every 2 weeks	IL-6	RA
Tocilizumab (ACTEMRA) – IV every 4 weeks, SC every 1 to 2 weeks		RA
Ustekinumab (STELARA) – IV one-time induction, SC every 8 to 12 weeks	IL-12 and IL-23	PsA, PsO, CD, UC
Bimekizumab (BIMZELX) – SC every 4 to 8 weeks	IL-17	AS, PsO, PsA, HS
Brodalumab (SILIQ) – SC every 2 weeks		PsO
Ixekizumab (TALTZ) – SC every 4 weeks		AS, PsA, PsO
Secukinumab (COSYNTEX) – IV every 4 weeks, SC every 4 weeks		AS, PsA, PsO, HS
Guselkumab (TREMFYA) – IV, SC every 8 weeks	IL-23	PsA, PsO, CD, UC

Icotrokinra (ICOTYDE) – PO once daily		PsO
Mirikizumab (OMVOH) – IV, SC every 4 weeks		UC, CD
Risankizumab (SKYRIZI) – SC every 12 weeks		PsA, PsO, CD, UC
Tildrakizumab (ILUMYA) – SC every 12 weeks		PsO
Vedolizumab (ENTYVIO) – IV every 8 weeks, SC every 2 weeks	Integrin receptor	CD, UC
Natalizumab (TYSABRI) – IV every 4 weeks		CD
Abatacept (ORENCIA) – IV every 4 weeks, SC every week	T-lymphocyte	RA, PsA
Rituximab (RITUXAN) – IV every 24 weeks	B-lymphocyte	RA
Spesolimab (SPEVIGO) – IV x 1 dose, SC every 4 weeks	IL-36	GPP
Targeted Synthetic DMARDs		
Baricitinib (OLUMIANT) – PO once daily	JAK 1,2	RA
Tofacitinib (XELJANZ & XEJANZ XR)- PO once or twice daily	JAK 1,2,3	AS, RA, PsA, UC
Upadacitinib (RINVOQ) – PO once daily	JAK 1	AS, RA, PsA, CD, UC
Apremilast (OTEZLA & OTEZELA XR) – PO once or twice daily	PDE4	PsA, PsO
Ozanimod (ZEPOSIA) – PO once daily	S1P receptor	UC
Etrasimod (VELSIPITY)– PO once daily		UC
Deucravacitinib (SOTYKTU) – PO once daily	TYK2	PsO, PsA
Abbreviations: AS=ankylosing spondylitis; CD=Crohn's Disease; DMARD=Disease-Modifying Antirheumatic Drug; FDA=Food and Drug Administration; IL=interleukin; GPP= Generalized Pustular Psoriasis; HS=hidradenitis suppurativa; IV=intravenous; JAK=Janus Kinase; JIA=juvenile idiopathic arthritis; PDE=phosphodiesterase; PO=oral; PsA=psoriatic arthritis; PsO=plaque psoriasis; S1P=sphingosine 1-phosphate; RA=rheumatoid arthritis; SC=subcutaneous; TNF=tumor necrosis factor; TYK2=tyrosine kinase 2; UC=Ulcerative Colitis		

Appendix 4: Abstracts of Comparative Clinical Trials

Upadacitinib vs adalimumab in patients with rheumatoid arthritis and a prior inadequate response or intolerance to a tumor necrosis factor inhibitor: 12-week results from the randomized, double-blind, SELECT-SWITCH study.[66]

Objectives: After the first tumor necrosis factor inhibitor (TNFi) failure, patients with rheumatoid arthritis (RA) often cycle to a second; however, switching mechanisms of action have been postulated to improve outcomes. The ongoing SELECT-SWITCH trial compared upadacitinib with adalimumab for active RA after first TNFi failure at 12 weeks.

Methods: Patients with inadequate response or intolerance to 1 non-adalimumab TNFi receiving stable methotrexate were randomized (1:1) to 15 mg once daily upadacitinib or 40 mg every-other-weekly adalimumab. The primary endpoint was achieving superiority in Disease Activity Score 28 (DAS28)–C-reactive protein

(CRP) ≤3.2 at week 12. Ranked secondary endpoints (week 12, superiority) were (1) achieving ≥50% improvement in American College of Rheumatology response criteria (ACR50); (2) achieving DAS28-CRP <2.6; change from baseline in (3) DAS28-CRP; (4) pain; (5) Health Assessment Questionnaire Disability Index (HAQ-DI).

Results: Overall, 492 patients were randomized. Baseline characteristics were balanced between groups. Week 12 DAS28-CRP ≤3.2 response was superior with upadacitinib (43.3%) vs adalimumab (22.4%; difference, 21.0% [95% CI: 12.9-29.1]; *P* < .0001) as were ACR50 (38.2% vs 26.8% [*P* = .0068]), DAS28-CRP <2.6 (28.4% vs 14.5%; *P* = .0002), mean changes in DAS28-CRP (−2.432 vs −1.840; *P* < .0001) and pain (−3.165 vs −2.373; *P* = .0005), but not in HAQ-DI (−0.523 vs −0.496; *P* = .5849). Safety was comparable between treatments.

Conclusions: The primary endpoint of the SELECT-SWITCH trial was met, with a higher percentage of patients with active RA who switched to upadacitinib after first TNFi failure achieving DAS28-CRP ≤3.2 at 12 weeks than those cycling to a second TNFi, adalimumab, with similar safety profile

Appendix 5: Medline Search Strategy
Ovid MEDLINE(R) ALL <1946 to July 08, 2026>

1	Adalimumab/	7946
2	Etanercept/	6785
3	tocilizumab.mp.	8593
4	Abatacept/	3646
5	Infliximab/	13096
6	Rituximab/	21540
7	golimumab.mp.	1956
8	apremilast.mp.	1523
9	tofacitinib.mp.	4552
10	certolizumab.mp.	1858
11	Certolizumab Pegol/	806
12	secukinumab.mp.	2970
13	Abatacept/	3646
14	Ustekinumab/	2265
15	Natalizumab/	2179
16	vedolizumab.mp.	2839
17	brodalumab.mp.	744
18	guselkumab.mp.	1144
19	anakinra.mp.	3403
20	canakinumab.mp.	1385
21	sarilumab.mp.	465
22	baricitinib.mp.	2427
23	guselkumab.mp.	1144
24	ixekizumab.mp.	1481

25	risankizumab.mp.	950
26	tildrakizumab.mp.	450
27	upadacitinib.mp.	2196
28	Janus Kinase Inhibitors/	3041
29	bimekizumab.mp.	520
30	deucravacitinib.mp.	378
31	Sphingosine 1 Phosphate Receptor Modulators/ or etrasimod.mp.	387
32	mirikizumab.mp.	229
33	spesolimab.mp.	232
34	deuruxolitinib.mp.	40
35	Receptors, Interleukin/ or icotrokinra.mp.	5213
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35	85198
37	limit 36 to (english language and full text and humans and yr="2025 -Current")	2270
38	limit 37 to (comparative study or guideline or meta-analysis or practice guideline or "systematic review")	357

Appendix 6: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ICOTYDE safely and effectively. See full prescribing information for ICOTYDE.

ICOTYDE™ (icotrokinra) tablets, for oral use
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------

ICOTYDE is an interleukin-23 (IL-23) receptor antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40 kg who are candidates for systemic therapy or phototherapy. (1)

----------DOSAGE AND ADMINISTRATION----------

- See the full prescribing information for recommended evaluation and immunizations prior to treatment. (2.1)
- Recommended dosage is 200 mg orally once daily. (2.2)
- Administer ICOTYDE on an empty stomach with water upon waking. (2.2)
- Wait at least 30 minutes after taking ICOTYDE before eating food. (2.2)
- For patients who have difficulty swallowing tablets, ICOTYDE can be dispersed in water. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 200 mg (3)

----------CONTRAINDICATIONS----------

None. (4)

----------WARNINGS AND PRECAUTIONS----------

Infections: Avoid treatment with ICOTYDE in patients with any clinically important active infection until the infection resolves or is adequately treated. If such an infection develops, discontinue ICOTYDE until the infection resolves. (5.1)
Tuberculosis (TB): Consider evaluating for TB prior to initiating treatment with ICOTYDE based on clinical judgement. Monitor patients for signs and symptoms of active TB during and after treatment with ICOTYDE. (5.2)
Immunizations: Avoid use of live vaccines during treatment with ICOTYDE. (5.3)

----------ADVERSE REACTIONS----------

Most common adverse reactions (≥1%) are headache, nausea, cough, fungal infection, and fatigue. (6.1)

----------USE IN SPECIFIC POPULATIONS----------

Moderate or Severe Renal Impairment: Monitor for potential adverse reactions when ICOTYDE is used in patients with eGFR <60 mL/min. (8.6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-526-7736 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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2.1 Recommended Evaluation and Immunizations Prior to Treatment Initiation
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4 CONTRAINDICATIONS
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*Sections or subsections omitted from the full prescribing information are not listed.

Appendix 7. Pharmacology and Pharmacokinetic Properties.[24,75]

Parameter	
Mechanism of Action	Interleukin-23 receptor antagonist
Oral Bioavailability	Tmax = 2 hours, food decreased area under the curve by 43% and Cmax decreased by 59%
Distribution and Protein Binding	Volume of distribution = 92,800 liters. Icotrokinra is 52% protein bound.
Elimination	37% to 81% of icotrokinra dose was recovered in feces within 24 hours as unchanged drug. Total body clearance: 6,550 liters/hour
Half-Life	12 hours
Metabolism	Metabolized by peptide catabolism into smaller peptides.

Appendix 8: Prior Authorization Criteria

Targeted Immune Modulators for Autoimmune Conditions

Goal(s):

- Promote use consistent with national clinical practice guidelines and medical evidence.
- Promote use of cost-effective products.

Length of Authorization:

- Up to 12 months

Requires PA:

- All targeted immune modulators for autoimmune conditions (both pharmacy and provider administered claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. Targeted Immune Modulators FDA-Approved for Ankylosing Spondylitis, Juvenile Idiopathic Arthritis, Rheumatoid Arthritis, and Non-Radiographic Axial Spondyloarthritis

Generic Name (BRAND NAME)	Ankylosing Spondylitis (AS)	Juvenile Idiopathic Arthritis (JIA)	Rheumatoid Arthritis (RA)	Non-Radiographic Axial Spondyloarthritis (nr-axSpA)
Tier 1 (Preferred First-Line)				
Adalimumab-bwwd (HADLIMA) syringe and autoinjector	≥18 y	≥2 yo	≥18 yo	
Etanercept (ENBREL)	≥18 yo	≥2 yo	≥18 yo	
Infliximab-abda (RENFLEXIS) vial	≥18 yo		≥18 yo	
Rituximab-pvvr (RUXIENCE) vial			≥18 yo	
Tier 2 (Second-Line)				
Adalimumab-fkjp 50 mg/mL (non-branded NDCs)	≥18 yo	≥2 yo	≥18 yo	
Adalimumab-atty (YUFLYMA)	≥18 yo	≥2 yo	≥18 yo	
Infliximab (REMICADE) vial	≥18 yo		≥18 yo	
Infliximab-axxq (AVSOLA) vial	≥18 yo		≥18 yo	
Tocilizumab-aazg (TYENNE) vial, autoinjector, and syringe		≥2 yo	≥18 yo	
Tofacitinib (XELJANZ and XELJANZ XR)	≥18 yo	≥2 yo	≥18 yo	
Tier 3 (Non-Preferred Third-Line)				
Abatacept (ORENCIA)		≥2 yo	≥18 yo	
Anakinra (KINERET)			≥18 yo	
Adalimumab (HUMIRA)	≥18 y	≥2 yo	≥18 yo	
Adalimumab-atto (AMJEVITA)	≥18 y	≥2 yo	≥18 yo	
Adalimumab-ryvk (SIMLANDI)	≥18 y	≥2 yo	≥18 yo	
Baricitinib (OLUMIANT)			≥18 yo	
Bimekizumab (BIMZELX)	≥18 yo			≥18 yo
Canakinumab (ILARIS)		≥2 yo		
Certolizumab (CIMZIA)	≥18 yo	≥2 yo	≥18 yo	≥18 yo
Golimumab (SIMPONI and SIMPONI ARIA)	≥18 yo	≥2 yo (SIMPONI ARIA)	≥18 yo	
Ixekizumab (TALTZ)	≥ 18 yo			≥18 yo
Rituximab (RITUXAN)			≥18 yo	
Sarilumab (KEVZARA)			≥18 yo	
Secukinumab (COSENTYX)	≥12 yo			≥18 yo
Tocilizumab (ACTEMRA)		≥2 yo	≥18 yo	
Upadacitinib (RINVOQ)	≥18 yo	≥2 yo	≥18 yo	≥18 yo

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 2. Targeted Immune Modulators FDA-Approved for Plaque Psoriasis, Psoriatic Arthritis, and Hidradenitis Suppurativa

Generic Name (BRAND NAME)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Hidradenitis Suppurativa (HS)
Tier 1 (Preferred First-Line)			
Adalimumab-bwwd (HADLIMA) syringe and autoinjector	≥18 yo	≥18 yo	≥12 yo
Etanercept (ENBREL)	≥4 yo	≥2 yo	
Infliximab-abda (RENFLEXIS) vial	≥18 yo	≥18 yo	
Ustekinumab-hmny (STARJEMZA) vial and syringe	≥6 yo	≥6 yo	
Tier 2 (Second-Line)			
Adalimumab-fkjp 50 mg/mL (non-branded NDCs)	≥18 yo	≥18 yo	≥18 yo
Adalimumab-atty (YUFLYMA)	≥18 yo	≥18 yo	≥12 yo
Infliximab (REMICADE) vial	≥18 yo	≥18 yo	
Infliximab-axxq (AVSOLA) vial	≥18 yo	≥18 yo	
Tofacitinib (XELJANZ & XELJANZ XR)		>2 yo	
Ustekinumab-kfee (YESINTEK)	≥6 yo	≥6 yo	
Ustekinumab-srif (IMULDOSA)	≥6 yo	≥6 yo	
Tier 3 (Non-Preferred Third-Line)			
Abatacept (ORENCIA)		≥2 yo	
Adalimumab (HUMIRA)	≥18 y	≥18 yo	≥12 yo
Adalimumab-atto (AMJEVITA)	≥18 y	≥18 yo	≥12 yo
Adalimumab-ryvk (SIMLANDI)	≥18 y	≥18 yo	≥12 yo
Apremilast (OTEZLA & OTEZLA XR)	≥ 6 yo & weighing ≥ 20 kg (OTEZLA) OR ≥ 50 kg (OTEZLA XR)	≥ 6 yo & weighing ≥ 20 kg (OTEZLA) OR ≥ 50 kg (OTEZLA XR)	
Bimekizumab (BIMZELX)	≥18 yo	≥18 yo	≥18 yo
Brodalumab (SILIQ)	≥18 yo		
Certolizumab (CIMZIA)	≥18 yo	≥18 yo	
Deucravacitinib (SOTYKU)	≥18 yo	≥18 yo	
Golimumab (SIMPONI and SIMPONI ARIA)		≥2 yo (SIMPONI ARIA) ≥18 yo (SIMPONI)	
Guselkumab (TREMFYA)	≥6 yo	≥6 yo	
Icotrokinra (ICOTYDE)	≥12 yo & weighing ≥ 40 kg		
Ixekizumab (TALTZ)	≥6 yo	>18 yo	

Generic Name (BRAND NAME)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Hidradenitis Suppurativa (HS)
Risankizumab (SKYRIZI)	≥6 yo	>6 yo	
Secukinumab (COSENTYX)	≥6 yo	≥2 yo	≥12 yo
Tildrakizumab (ILUMYA)	≥18 yo		
Upadacitinib (RINVOQ)		≥2 yo	
Ustekinumab (STELARA)	≥6 yo	≥6 yo	

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 3. Targeted Immune Modulators FDA-Approved for Crohn's Disease and Ulcerative Colitis

Generic Drug Name (BRAND NAME)	Crohn's Disease	Ulcerative Colitis
Tier 1 (Preferred First-Line)		
Adalimumab-bwwd (HADLIMA) syringe and autoinjector	≥6 yo	>18 yo
Infliximab-abda (RENFLEXIS) vial	≥ 6 yo	≥ 6 yo
Ustekinumab-hmny (STARJEMZA) vial and syringe	≥ 18 yo	≥18 yo
Tier 2 (Second-Line)		
Adalimumab-fkjp 50 mg/mL (non-branded NDCs)	≥6 yo	>18 yo
Adalimumab-atty (YUFLYMA)	≥6 yo	>18 yo
Infliximab (REMICADE)	≥6 yo	≥6 yo
Infliximab-axxq (AVSOLA)	≥6 yo	≥6 yo
Tofacitinib (XELJANZ and XELJANZ XR)		≥18 yo
Ustekinumab-kfee (YESINTEK)	≥ 18 yo	≥18 yo
Ustekinumab-srif (IMULDOSA)	≥ 18 yo	≥18 yo
Tier 3 (Non-Preferred Third-Line)		
Adalimumab (HUMIRA)	≥6 yo	≥5 yo
Adalimumab-atto (AMJEVITA)	≥6 yo	>18 yo
Adalimumab-ryvk (SIMLANDI)	≥6 yo	>18 yo
Certolizumab (CIMZIA)	≥18 yo	
Etrasimod (VELSIPITY)		≥18 yo
Golimumab (SIMPONI and SIMPONI ARIA)		≥15 kg (SIMPONI)
Guselkumab (TREMFYA)	≥18 yo	≥18 yo
Ozanimod (ZEPOSIA)		≥18 yo
Mirikizumab (OMVOH)	≥18 yo	≥18 yo
Risankizumab (SKYRIZI)	≥18 yo	≥18 yo
Upadacitinib (RINVOQ)	≥ 18 yo	≥18 yo
Ustekinumab (STELARA)	≥ 2 yo	≥ 2 yo
Vedolizumab (ENTYVIO)	≥18 yo	≥18 yo

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 4. Targeted Immune Modulators FDA-Approved for Other Indications not Listed in Table 1, 2 or 3

Generic Drug Name (BRAND NAME)	Other Indications
Adalimumab (HUMIRA) & biosimilars	• Uveitis (non-infectious) ≥2 yo
Abatacept (ORENCIA)	• Acute Graft Versus Host Disease (aGVHD) ≥ 2 yo
Anakinra (KINERET)	• DIRA • NOMID
Apremilast (OTEZLA)	• Oral Ulcers associated with Behcet's Disease ≥ 18 yo
Baricitinib (OLUMIANT)	• COVID ≥ 18 yo (hospitalized)
Canakinumab (ILARIS)	• FCAS ≥4 yo • FMF ≥ 4 yo • Gout flares unresponsive to NSAIDs and colchicine ≥18 yo • HIDS ≥ 4 yo • MKD ≥ 4 yo • MWS ≥ 4 yo • Stills Disease ≥ 2 yo • TRAPS ≥ 4 yo
Rituximab (RITUXAN) and biosimilars	• BL ≥ 6 mo • BLL ≥ 6 mo • B-AL ≥ 6 mo • CLL ≥ 18 yo • DLBCL ≥ 6 mo • GPA ≥ 2yo • MPA ≥ 2 yo • NHL ≥18 yo • Pemphigus Vulgaris ≥ 18 yo
Sarilumab (KEVZARA)	• Polymyalgia Rheumatica (PMR) ≥ 18 yo
Secukinumab (COSENTYX)	• Enthesitis-Related Arthritis (ERA) ≥ 4 yo
Spesolimab (SPEVIGO)	• Generalized Pustular Psoriasis Flares >12 yo and weighing >40 kg • Generalized Pustular Psoriasis after Flares >12 yo and weighing >40 kg
Tocilizumab (ACTEMRA) and biosimilars	• CRS ≥2 yo • COVID ≥ 2 yo (hospitalized) • GCA ≥18 yo • SSc-ILD ≥ 18 yo (ACTEMRA only)
Upadacitinib (RINVOQ)	• Atopic Dermatitis ≥ 12 yo • GCA ≥ 18 yo

Abbreviations: BL = Burkitt Lymphoma; BLL = Burkitt-like Lymphoma; B-AL = mature B-cell acute leukemia; CLL = Chronic Lymphocytic Leukemia; COVID = Covid-19 infection; CRS = Cytokine Release Syndrome; DIRA = Deficiency of Interleukin-1 Receptor Antagonist; DLBCL = Diffuse Large B-Cell Lymphoma; FCAS = Familial Cold Autoinflammatory Syndrome; FMF = Familial Mediterranean Fever; GCA = Giant Cell Arteritis; GPA = Granulomatosis with Polyangiitis (Wegener's Granulomatosis); HIDS: Hyperimmunoglobulin D

Generic Drug Name (BRAND NAME)	Other Indications
Syndrome; MKD = Mevalonate Kinase Deficiency; mo = months old; MPA = Microscopic Polyangiitis; MWS = Muckle-Wells Syndrome; NHL = Non-Hodgkin's Lymphoma; NOMID = Neonatal Onset Multi-Systemic Inflammatory Disease; NSAIDs = non-steroidal anti-inflammatory drugs; SSc-ILD = Systemic Sclerosis-Associated Interstitial Lung Disease; TRAPS = Tumor Necrosis Factor Receptor Associated Periodic Syndrome; yo = years old	

Table 5. First-Line Conventional Therapy Recommended for Select Conditions

Conditions	Recommended Conventional Therapy Prior To a Targeted Immune Modulator
Arthritis (Juvenile Idiopathic, Psoriatic, Rheumatoid)	• DMARD therapy: Methotrexate, leflunomide, sulfasalazine or hydroxychloroquine for ≥ 6 months; AND • Concurrent DMARD therapy with plans to continue concomitant use. Biologic therapy is recommended in combination with DMARDs (e.g., methotrexate) for those who have had inadequate response with DMARDs.
Ankylosing Spondyloarthritis	• At least 2 NSAIDs over 4 weeks for each medication • Patients with predominant peripheral manifestations should try sulfasalazine or one glucocorticoid injection, if appropriate.
Atopic Dermatitis	4-week trial of either one the following treatments in pediatrics and adults: • Moderate to high potency topical corticosteroid (e.g., clobetasol, desoximetasone, desonide, mometasone, betamethasone, halobetasol, fluticasone, or fluocinonide) OR a topical calcineurin inhibitor (e.g., tacrolimus) AND for adults only: • Oral immunomodulator therapy (e.g., cyclosporine, methotrexate, mycophenolate mofetil or azathioprine) for at least 12 weeks
Crohn's Disease	• Mercaptopurine, methotrexate, or azathioprine for ≥6 months
Generalized Pustular Psoriasis	• Acitretin, methotrexate, or cyclosporine for ≥ 3 months
Hidradenitis Suppurativa (HS)	• 90-day trial of oral antibiotics (e.g., tetracyclines, doxycycline, minocycline). May add oral clindamycin or rifampin for acute, symptomatic lesions resistant to tetracycline therapy.
Plaque Psoriasis	• Topical high potency corticosteroid (e.g., betamethasone dipropionate 0.05%, clobetasol propionate 0.05%, fluocinonide 0.05%, halcinonide 0.1%, halobetasol propionate 0.05%; triamcinolone 0.5%) for a minimum of 4 weeks; AND • At least one other topical agent: calcipotriene, tazarotene, anthralin for a minimum of 8 weeks; AND • Phototherapy for at least 8 weeks; AND • At least one other systemic therapy: acitretin, cyclosporine, or methotrexate for at least 16 weeks
Ulcerative Colitis	• 5-aminosalicylate products, mercaptopurine, or azathioprine for ≥6 months
Abbreviations: DMARD = Disease Modifying Anti-Rheumatic Drug; NSAID = non-steroidal anti-inflammatory drug	

Table 6. FDA-recommended Baseline Safety Tests for Sphingosine 1-Phosphate Receptor Modulators

	Negative Pregnancy Test	LFTs	CBC & lymphocyte count	Ophthalmic Exam	Baseline ECG (see notes)	Skin Exam for Malignancy	Varicella Zoster Antibodies

Etrasimod (VELSIPITY)	X	X	X	X	X	X	X
Ozanimod (ZEPOSIA)	X	X	X	X	X		X
Abbreviations: CBC=complete blood count; ECG=electrocardiogram; FDA =Food and Drug Administration; LFTs=liver function tests							

Sphingosine 1-Phosphate Receptor Modulators Clinical Notes:

- Patients on antiarrhythmics, beta-blockers or calcium channel blockers or with risk factors for bradycardia (h/o MI, age >70 yrs., electrolyte disorder, hypothyroidism) may be more prone to development of symptomatic bradycardia and should be initiated on etrasimod or ozanimod with caution. A cardiology evaluation should be performed before considering treatment in patients with significant QT prolongation, heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension, a history of with second-degree Mobitz type II or higher AV block, sick-sinus syndrome, or sinoatrial heart block.
- An ophthalmology evaluation should be repeated 3-4 months after etrasimod or ozanimod initiation with subsequent evaluations based on clinical symptoms.

Table 7. Baseline Documentation of Disease Severity and Measurements to Assess Response to Therapy for Selected Conditions

Indication	Disease Severity Definitions
Ankylosing Spondylitis	• **Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)**: Score ≥ 4 (on a scale of 0-10) indicates active disease that warrants consideration of biologic therapy. Response to therapy indicated by 50% improvement on BASDI score (BASDI50) or a change from baseline ≥ 2 units on overall score. • **Assessment of Spondyloarthritis International Society (ASAS)**: Scale of 0-10 where 0 is no symptoms, 10 is very severe. Response to therapy is at least 40% improvement from baseline (ASAS40). • **Ankylosing Spondylitis Disease Activity Score (ASDAS)**: Scale of 0-10 where 0 is no symptoms, 10 is very severe. Disease activity ≥ 2.1 warrants consideration of biologic therapy. ASDAS scores: < 1.3 – Inactive Disease 1.4 to 2.1 – Moderate Disease Activity 2.2 to 3.4 – High Disease Activity >3.5 – Very High Disease Activity Response to therapy is indicated by a decrease of > 1.1 in ASDAS score.
Atopic Dermatitis or Plaque Psoriasis	Functional impairment as indicated by **Dermatology Life Quality Index (DLQI)** ≥ 11 or **Children's Dermatology Life Quality Index (CDLQI)** ≥ 13 (or severe score on another validated tool) AND one or more of the following: • At least 10% body surface area involved, or • Hand, foot, face, or mucous membrane involvement Response to therapy indicated by: • **Eczema Area and Severity Index score (EASI 50)**: 50% reduction in EASI (score ranges from 0 to 72) or **Psoriasis Area and Severity Index (PASI 50):** 50% reduction in PASI

	• **Dermatology Life Quality Index (DLQI**): 4-point reduction in DLQI • **Investigators Global Assessment (IGA)** score: 2-point reduction in IGA (score ranges from 0 (clear) to 4 (severe)
Generalized Pustular Psoriasis	• **Generalized Pustular Psoriasis Global Assessment (GPPGA):** Assessment of severity of skin erythema, pustules, and scaling. Each symptom is scored on a 5-point scale (0 = clear to 4 = severe). Score ≥3 indicates moderate to severe flares with ≥ 5% BSA covered with erythema and pustules. • **Generalized Pustular Psoriasis Index and Severity Index (GPPASI)** assess lesion severity on a 5-point scale (0 = clear to 4 = severe). Area of involvement is scored by the percentages of head, trunk, upper limb, and lower limb on a 7-point scale. Total score ranges from 0 to 72 with higher scores indicating higher disease severity. • For continued renewal of spesolimab for the prevention of flares, the severity of GPP as measured by the GPPGA or GPPASI total score at initiation should be maintained (not worsen), patients should experience fewer flares compared to baseline, and the reduction in the number of flares should be sustained.
Hidradenitis Suppurative	• The Hurley clinical staging system describes disease severity by 3 stages: stage 1 indicates abscess formation, single or multiple, without sinus tracts and scar formation; stage 2 indicates recurrent abscesses with tract formation and scarring, single or multiple, widely separated lesions; and stage 3 indicates diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area. • **Hidradenitis Suppurativa Clinical Response (HiSCR**): response to therapy is defined as 50, 75, or 90% reduction in total abscess and inflammatory nodule count with no increase in abscesses or draining tunnels (reported as HiSCR50, HISCR75, HiSCR90, respectively). • Baseline assessment: Document number of abscesses and inflammatory nodules. • Response to therapy indicated by a 50% reduction in total abscess and inflammatory nodule count AND no increase in abscesses and draining fistulas.

Approval Criteria	
1. What diagnosis is being treated?	Record ICD-10 code.

Approval Criteria		
2. Does the condition meet the definition of severe disease defined as follows: • Psoriasis and atopic dermatitis are severe in nature when resulting in functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's DLQI ≥ 13 (or severe score on another validated tool) AND one or more of the following: o At least 10% body surface area involvement; OR o Hand, foot, face, or mucous membrane involvement OR • Moderate-to-severe HS (e.g., Hurley Stage II or III) ? Notes: A. Most systemic targeted immune modulators are not FDA-approved for treatment of mild symptoms. C. Alopecia areata is excluded.	**Yes:** Go to # 4	**No:** Go to #3.
3. Is there documentation that the condition is of sufficient severity that it impacts the patient's health? Note: documentation should include chart notes describing at least one of the following: - The patient has been hospitalized for the condition in the past year - The condition causes recurrent (at least 2) emergency or urgent care visits in the past year - The condition currently impacts the member's ability to complete activities of daily living including walking, bathing, dressing, toileting, brushing teeth, or eating - The condition impacts the member's ability to attain, maintain, or regain independence in self-care including using the telephone, shopping, preparing meals, housekeeping, using transportation, taking medication(s), working, attending school, or managing finances - The condition, if untreated, can be reasonably expected to cause disability, impact age-appropriate growth or development, or result in increased morbidity and mortality based on published medical literature.	**Yes:** Go to #4	**No:** Pass to RPh. Deny, medical necessity.

Approval Criteria		
4. Has baseline disease severity been documented as outlined for conditions described in **Table 7**?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness.
5. Does the requested use meet FDA-approved criteria for this condition and age as defined in Table 1,2,3 or 4 above OR a recognized medically accepted indication supported by compendial or high-quality evidence?	**Yes:** Go to #7	**No:** Go to #6
6. Is there documentation of 1) inadequate response, contraindication or intolerance to FDA-approved targeted immune modulators AND 2) prescribing by, or in consultation with, a relevant specialist for the condition?	**Yes**: Go to #7	**No:** Pass to RPh. Deny; medical appropriateness.
7. Has baseline screening for latent or active tuberculosis been completed and if positive, has the patient started tuberculosis treatment? *(Note: this requirement does not apply to requests for apremilast.)	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness. If patient meets all other criteria, may approve once for up to 3 months to allow time for screening for ongoing therapy to avoid interruptions in care.
8. Is this a request for continuation of therapy?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #9
9. Is there documentation of one of the following: • treatment failure or inadequate response to conventional treatment in outlined Table 5 OR • contraindication or intolerance to first-line conventional treatments outlined in Table 5 OR • request is for a condition not outlined in Table 5?	**Yes:** Go to #10 Document each therapy with dates. If applicable, document intolerance or contraindication(s).	**No**: Pass to RPh. Deny; medical appropriateness

Approval Criteria		
10. Is the request for 1) a preferred Tier 1 product in Table 1, 2 or 3 OR 2) a preferred Tier 2 product if there is no Tier 1 product listed for the indication?	**Yes:** Go to #12	**No:** Go to #11
11. Is there documentation that therapy with an agent from each of the preferred tiers would be inappropriate? Note: documentation could include inadequate response after ≥3 months with at least one product from each preferred tier, contraindication or intolerance to products from each preferred tier, or lack of products FDA-approved for the requested indication in tiers. Message: Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics Committee.	**Yes:** Go to #12	**No**: Pass to RPh. Deny; medical appropriateness. Require trial of at least one product from each tier.
12. Is the request for a JAK inhibitor (e.g., tofacitinib, baricitinib, or upadacitinib)?	**Yes:** Go to #13	**No:** Go to #14
13. Is the patient currently on other biologic therapy or on a potent immunosuppressant like azathioprine, tacrolimus, OR cyclosporine? Note: Tofacitinib, baricitinib, and upadacitinib may be used concurrently with methotrexate or other nonbiologic DMARD drugs. Tofacitinib, baricitinib, or upadacitinib are not recommended to be used in combination with other JAK inhibitors, biologic DMARDs, azathioprine, or cyclosporine.	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Approve baricitinib or upadacitinib for up to 6 months. Approve tofacitinib for up to 6 months at a maximum dose of 10 or 11 mg daily for Rheumatoid Arthritis OR 10 mg twice daily for 8 weeks then 5 or 10 mg twice daily for Ulcerative Colitis
14. Is the prescription for a sphingosine 1-phosphate receptor modulator (etrasimod or ozanimod)?	**Yes:** Go to #15	**No:** Go to #18

Approval Criteria		
15. Have baseline safety assessments been completed as outlined in **Table 6**?	**Yes:** Go to #16	**No:** Pass to RPh. Deny; medical appropriateness.
16. Does the patient have preexisting cardiac disease, risk factors for bradycardia, or is on an anti-arrhythmic, beta-blocker, or calcium channel blocker?	**Yes:** Go to #17	**No:** Go to #18
17. Has the patient had a cardiology consultation before initiation (see clinical notes attached to **Table 6**)?	**Yes:** Go to #18	**No:** Pass to RPh. Deny; medical appropriateness.
18. Duration of initial approval based on indication	AS, Plaque psoriasis, RA, AD: 6 months HS: 12 weeks UC/Crohn's: 12 months Other: length of treatment or 1 year, whichever is longer	

Renewal Criteria		
1. Has the patient been adherent to both biologic and DMARD therapy (if DMARD therapy has been prescribed in conjunction with the biologic therapy)?	**Yes:** Go to #2	**No:** Pass to RPh. Deny; medical appropriateness.
2. Have the patient's symptoms improved with therapy according to the outcomes for conditions described in **Table 7**? For conditions, not listed in Table 7, go to #3	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness.
3. Has the patient's condition improved as assessed by the prescribing provider and provider attests to patient's improvement?	**Yes:** Approve for 12 months. Document assessment and provider attestation received.	**No:** Pass to RPh; Deny; medical appropriateness.

P&T/DUR Review: 10/26 (DM); 10/25 (DM); 8/24; 6/23; 10/22; 6/2; 10/21; 10/20; 2/20; 5/19; 1/19; 1/18; 7/17; 11/16; 9/16; 3/16; 7/15; 9/14; 8/12
Implementation: 1/1/27; 1/1/26; 1/1/25; 9/1/24; 7/1/23; 1/1/23; 7/1/22; 1/1/22; 1/1/2021; 7/1/2019; 3/1/19; 3/1/18; 9/1/17; 1/1/17; 9/27/14; 12/12