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One-Page Clinical Summary - Atopic Dermatitis
OPZELURA® (ruxolitinib) cream 1.5%

OPZELURA is approved for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis (AD) in non-immunocompromised patients 2 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. OPZELURA is also approved for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.[1] Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants, such as azathioprine or cyclosporine, is not recommended.

The efficacy and safety of OPZELURA for mild to moderate AD was evaluated in three Phase III, double-blind, randomized vehicle-controlled studies; adult and adolescent patients 12 years and older (TRuE-AD1 [N = 631]; TRuE-AD2 [N = 618]), as well as pediatric patients 2-11 years old (TRuE-AD3 [N=330]). Patients were randomly assigned to twice-daily application of OPZELURA, ruxolitinib cream 0.75%, or vehicle for 8 weeks.[2,3,4] Eligible patients could continue treatment in a 44-week extension period where OPZELURA or ruxolitinib cream 0.75% were applied as needed (Patients randomized to vehicle were randomized to either ruxolitinib cream 0.75% or 1.5% twice daily), stopping 3 days after lesion clearance, and restarting with lesion recurrence. No rescue treatment was permitted in all three studies.

EFFICACY

- In TRuE-AD1 and TRuE-AD2, a significantly greater proportion of patients who applied OPZELURA vs. vehicle achieved IGA Treatment Success (IGA-TS; primary endpoint; 53.8% and 51.3% vs 15.1% and 7.6%; P <0.0001), defined as IGA 0 or 1 with at least a 2-point improvement from baseline.[1,2]
    - After the 44-week extension where patients transitioned to as needed therapy, >70% of patients who had applied OPZELURA achieved clear or almost clear skin at Week 52, and mean affected body surface area was less than 2% (1.4-1.8%) based on treatment group.[3]
- In TRuE-AD3, significantly more patients who applied OPZELURA vs. vehicle achieved IGA Treatment Success (IGA-TS; primary endpoint; 56.5% vs 10.8% %; P <0.0001), defined as IGA 0 or 1 with at least a 2-point improvement from baseline.[4]
    - At the end of the open label 44-week long term extension, >72% of patients who had applied OPZELURA achieved clear or almost clear skin and mean affected body surface area was less than 2% (1.6%-1.9%) based on treatment group.
    - Patients remaining in the OPZELURA group from baseline through Week 52 spent ~50% of the long-term extension period off treatment due to lesion clearance.

ADDITIONAL STUDIES AND ANALYSES

- An open-label study (N = 46) that evaluated the short-term effect of twice-daily OPZELURA on pruritus saw a mean (SE) –3.4 (0.28) reduction in itch from baseline at Day 2 as measured by the peak pruritus numerical rating scale (PP-NRS; primary endpoint). Itch reduction (mean [SE]) was observed as early as 15 minutes (-2.3 [0.35]) and was measured by modified PP-NRS.[5]
- An indirect number needed to treat (NNT) analysis calculated using IGA-TS response rates at 4 weeks from the two pivotal Phase 3 studies in adolescents and adults with AD revealed a lower NNT for OPZELURA (3 and 2) compared to other topical therapies, including crisaborole (7 and 14) and roflumilast (6 [pooled]).[6,7] NNT analysis provide exploratory estimates of comparative effectiveness; such comparisons have inherent limitations.
- A retrospective observational cohort study using 18-month US claims data (N=1269) showed an average of 2.4 OPZELURA tubes filled per patient over 18 months, 91% (n=945) of patients remained biologic-free, and 36% (n=82) did not need continuation of their biologic therapy from baseline.[7]

SAFETY

- The Prescribing Information for OPZELURA includes boxed warnings for the risks of Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events (MACE), and Thrombosis.[1] Additional Warnings and Precautions also included in the Prescribing Information include Thrombocytopenia, Anemia and Neutropenia and for Lipid Elevations.
- The most common adverse reactions (AR) occurring in ≥1% patients treated with OPZELURA were nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increase, urticaria, folliculitis, tonsillitis, rhinorrhea, upper respiratory tract infection, COVID-19, application site reactions, pyrexia, and white blood cell decreased.
- A post-marketing safety analysis encompassing 14,000 patient-years of OPZELURA during the first year of market approval found that 585 (99.3%) of events were non-serious, and there were no adverse events associated with the class warnings for JAK inhibitors (2 cases of non-melanoma skin cancer possessed insufficient information for assessment of relatedness).[8]

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INDICATION

AQNEURSA™ (levacetylleucine) is indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥15 kg.

IMPORTANT SAFETY INFORMATION

Embryo-Fetal Toxicity

- Based on findings from animal reproduction studies, AQNEURSA may cause embryo-fetal harm when administered during pregnancy. The decision to continue or discontinue AQNEURSA treatment during pregnancy should consider the female's need for AQNEURSA, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal disease.

Pregnancy and Lactation

- For females of reproductive potential, verify that the patient is not pregnant prior to initiating treatment with AQNEURSA. Advise females of reproductive potential to use effective contraception during treatment with AQNEURSA and for 7 days after the last dose if AQNEURSA is discontinued.

- There are no data on the presence of levacetylleucine or its metabolites in either human or animal milk, the effects on the breastfed infant or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AQNEURSA and any potential adverse effects on the breastfed infant from levacetylleucine or from the underlying maternal condition.

Adverse Reactions

- The most common adverse reactions (incidence ≥5% and greater than placebo) are abdominal pain, dysphagia, upper respiratory tract infections, and vomiting.

Drug Interactions

- Avoid concomitant use of AQNEURSA with *N-acetyl-DL-leucine or N-acetyl-D-leucine.* The D-enantiomer, N-acetyl-D-leucine, competes with levacetylleucine for monocarboxylate transporter uptake, which may reduce the levacetylleucine efficacy.

- Monitor more frequently for P-gp substrate related adverse reactions when used concomitantly with AQNEURSA; AQNEURSA inhibits P-gp; however, the clinical significance of this finding has not been fully characterized.

To report SUSPECTED ADVERSE REACTIONS, contact IntraBio Inc. at 1-833-306-9677 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please click here for Full Prescribing Information for AQNEURSA.

AQNEURSA™ (levacetylleucine)

Written Testimony

Thank you for the opportunity to provide a written clinical synopsis on behalf of AQNEURSA™ (levacetylleucine). Please find below a concise clinical synopsis of AQNEURSA™ (levacetylleucine). I have also attached the Prescribing Information and Instructions for Use for your reference.

NPC is a rare autosomal recessive neurovisceral lysosomal storage disorder. Patients with NPC are unable to break down and transport lipids within their cells. As a result, these fats accumulate leading to dysfunction. The nervous system is particularly affected, resulting in progressive neurodegeneration and worsening symptoms such as difficulties with standing, walking, swallowing, and speaking. As NPC progresses, patients experience functional decline, persistent seizures, and cognitive impairment.

AQNEURSA is a chemically modified amino acid that was approved by the FDA in September 2024 for the treatment of neurological manifestations of Niemann-Pick disease type C or NPC in adults and pediatric patients weighing 15 kg or more. AQNEURSA is administered orally or through a feeding tube up to 3 times daily based on patient body weight and can be used with or without miglustat.

The efficacy and safety of AQNEURSA have been evaluated in a phase 3, pivotal, global, multicenter, randomized, double-blind, placebo-controlled, crossover study conducted over two 12-week treatment periods, followed by an extension phase. Sixty patients ≥4 years of age with a confirmed diagnosis of NPC were evaluated.

Per request of the FDA, the primary endpoint of the IB1001-301 Parent Study in the US was the calculated mean change in total score on the functional Scale for Assessment and Rating of Ataxia (fSARA), which is a modified version of the Scale for Assessment and Rating of Ataxia (SARA).

SARA

The SARA consists of 8 functional domain items that assess the interplay of the various neurological systems and neuronal networks which are disrupted in NPC (e.g., not just the cerebellum/ataxia) and manifest as functional impairments[1-3]. The total score for SARA can range from 0 to 40 with the following domains each accounting for the indicated number of points: Gait (0-8), Stance (0-6), Sitting (0-4), Speech (0-6), Finger-chase test (0-4), Nose-finger test (0-4), Fast alternating hand movements (0-4) and Heel-shin test (0-4)[2]. A lower score indicates less severe neurological symptoms/status.

fSARA

The fSARA is a modified version of the SARA that includes the 4 axial domains with equal representation in the total score. The total score for fSARA can range from 0 to 16 with the following domains each accounting for the indicated number of points: Gait (0-4), Speech (0-4), Stance (0-4), Sitting (0-4). A lower score indicates less severe neurological symptoms/status. The fSARA was not a predefined endpoint in the IB1001-301 clinical trial (primary, secondary, or exploratory) but rather an FDA analysis. The fSARA is not a validated tool to monitor NPC disease progression nor does it fully demonstrate the functional abilities of an individual with NPC.

Extensive analysis has been performed to examine the responsiveness of the fSARA in Spinocerebellar Ataxias. Moulaire et al. assessed and compared the temporal dynamics of the original SARA and the fSARA. Data was analyzed from four cohorts of patients with Spinocerebellar Ataxia (SCA), with a total data set comprising 1210 participants and 4092 visits. The linearity of the progression and the variability were assessed using an ordinal Bayesian mixed-effect model (Leaspy). Sample size calculations for therapeutic trials were performed with different scenarios to assess the responsiveness of the scales. This analysis demonstrated: After 3 years, the mean response on the fSARA is 0 points; After 8 years, the mean response on the f-SARA is +1 point.

IB1001-301 Parent Study Trial Results

In the IB1001-301 trial, the mean (SD) change on fSARA after 12 weeks of treatment with AQNEURSA was -0.61 (1.05), an improvement in neurological manifestations equivalent to reversing 2 years of disease progression as measured by f-SARA. The mean (SD) change on fSARA after 12 weeks of treatment with Placebo was -0.12 (1.24).

The fSARA demonstrated an improvement with AQNEURSA versus placebo, estimated mean difference (95% confidence interval [CI]) -0.4 (0.7, -0.2), two-sided p-value <0.001.

Secondary endpoints including the Modified Disability Rating Scale (mDRS), Spinocerebellar Ataxia Functional Index (SCAFI), EuroQoL-5 Dimension 5 Level Questionnaire (EQ-5DL-5L), and Investigator, caregiver, and patient Clinical Global Impression-Improvement (CGI-I) scales met significance and were supportive of the primary endpoint.

The most common adverse reactions include abdominal pain, difficulty swallowing (dysphagia), upper respiratory tract infections, and vomiting. For full safety information, please refer to the prescribing information provided to the committee.

IB1001-301 Extension Phase Study

Extension phase data are based on exploratory evaluations and should be considered descriptive in nature. In an open-label extension, there is a potential for enrichment in the remaining patient populations for those that tolerate and/or benefit from treatment. These data are not in the Prescribing Information for AQNEURSA. No conclusions regarding the benefits or risks of treatment can be established based solely on these data.

Following the initial phase (IB100-301 Parent Study), participants were allowed to continue into the open label extension which is still ongoing at our European trial sites. Enrollment in the Extension Phase Study also opened to a new cohort for additional participants with the age criteria now at birth.

The extension phase has data readouts at 12 and 18 months. The primary endpoint of the Extension Phase was the modified 5-domain Niemann-Pick disease type C Clinical Severity Scale (5-domain NPC-CSS). This is a validated clinical scale that evaluates Ambulation, Cognition, Fine motor skills, Speech, and Swallowing. A higher score indicates worse neurological status.

Fifty-three patients aged 5-67 years (45.3% female, 54.7% male) were enrolled in the EP. After 12 months, the mean (±SD) change from baseline on the 5-domain NPC-CSS was -0.27 (±2.42) with levacetylleucine vs +1.5 (±3.16) in the historical cohort* (95% CI -3.05 to -0.48; p = 0.009), corresponding to an 118% reduction in annual disease progression. After 18 months, the mean (±SD) change was +0.05 (±2.95) with levacetylleucine vs +2.25 (±4.74) in the historical cohort* (95% CI -4.06 to -0.35; p = 0.023). The 15-domain and 4-domain NPC-CSSs were consistent with the 5-domain NPC-CSS. The improvements in neurologic manifestations demonstrated in the placebo-controlled trial on the SARA end point were sustained over the long-term follow-up. Levacetylleucine was well tolerated, and no treatment-related adverse events or serious reactions occurred.

Summary

We respectfully request the committee to add AQNEURSA to your PDL, allowing patients with NPC to begin treatment without delay and help manage symptoms associated with this severely debilitating and fatal disease.

*The Natural History Cohort is derived from the Prospective Natural History Study in NPC. Patients with NPC in the Natural History Cohort demonstrated an annualized linear progression of 1.5 points on the 5-domain NPC-CSS.

Members of the Oregon Family and Social Services Administration Pharmacy and Therapeutics Committee:

Recordati Rare Diseases, Inc. ("RRD") submits this request to Oregon's State Pharmacy and Therapeutics Committee, in support of patients with rare urea cycle disorders (UCDs). As detailed below, the **availability of ammonia lowering medication is essential to patients who suffer from UCDs and specific organic acidemias**. RRD is seeking Carbaglu®(carglumic acid) tablets for oral suspension 200mg be the **preferred treatment** over generic carglumic acid for (i) adjunctive treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA), (ii) adjunctive treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency, and (iii) maintenance treatment of chronic hyperammonemia due to NAGS deficiency. This **request aligns with current FDA approval** for the different carglumic acid formulations currently available. Carbaglu® (carglumic acid) is currently approved for use in these three indications whereas generic carglumic acid is only approved for individuals with NAGS deficiency (Carbaglu PI).

Carbaglu® is a carbamoyl phosphate synthetase 1 (CPS 1) activator indicated in pediatric and adult patients as:

- Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA).
- Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency.
- Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS Deficiency (Carbaglu PI)

To put this into perspective, the incidence of NAGS deficiency is <1:2,000,000, for PA it is 1: 100,000, and MMA is 1: 50,000 (Ah Mew, et al., 2017 Chapman, et al., 2018). According to the Oregon state newborn screening website, Oregon has newborn screening for PA and MMA and not NAGS Deficiency. We are aware of less than 25 individuals with NAGS deficiency in the US.

Hyperammonemia is a medical emergency AND therapies need to be started as soon as possible to prevent decompensation and death. Individuals with the rare genetic diseases NAGS deficiency, PA and MMA do not break down nitrogen correctly resulting in toxic ammonia accumulation (Ah Mew, et al., 2017, Häberle, 2013). These diseases result in higher ammonia levels and require different ammonia lowering medications than more common hyperammonemia (Ali and Nagalli, 2023; Häberle, 2013). Thus, Carbaglu® (carglumic acid) is an essential treatment for these three rare conditions.

Those with inborn errors of metabolism must balance dietary needs for growth and development while simultaneously managing ammonia levels that result from normal catabolism or which are elevated due to stress, illness, growth, etc. Treatment requires both consistent daily management of triggers and management of protein intake and metabolism through prescribed diets and medications. It is imperative that patients and their healthcare team have access to treatments and lifesaving medication, particularly when it has been approved for their particular indication (Forny et al., 2021; Häberle, et al., 2019).

NAGS deficiency is typically identified in decompensating neonates that require hospitalization and immediate implementation of a complex management strategy (Ah Mew, 2013). The guidelines for diagnosis and management of UCDs by Häberle in 2012 are still in effect in stating Carbaglu® is recommended as first-line for the treatment of NAGS deficiency. Häberle (2019) also pointed out that there is potential toxicity of repeated boluses of sodium benzoate or phenylacetate. In our pivotal trial, Carbaglu® ensured control of metabolic parameters, prevented decompensation and neurological consequences, and no serious safety issues were identified.[8] Guidelines for PA and MMA were published by Forny in 2021 and include carglumic acid for acute metabolic decompensation.[6]

Since 2010, the standard of care has included daily Carbaglu® tablets for those with NAGS deficiency while the FDA approved the use for acute hyperammonemia with PA and MMA in 2021 (Carbaglu PI). In an NIH study by Dr. Mendel Tuchman, and as seen in our PI, Carbaglu® safely enhanced ammonia lowering, along with the standard of care. This medication has an extensive track record as the Reference Drug and an established record of quality, safety and efficacy. These are fragile patients that risk serious, life-threatening conditions without daily management including carglumic acid and other management strategies. The most common adverse reactions with Carbaglu® (>9%) are: vomiting, abdominal pain, pyrexia, tonsillitis, anemia, diarrhea, ear infection, infections, nasopharyngitis, hemoglobin decreased, headache, and neutropenia in individuals with PA or MMA (Carbaglu® PI). Please refer to the complete Important Safety Information and full Prescribing Information for Carbaglu® that was previously provided (Carbaglu® PI).

As the only carglumic acid approved for NAGS deficiency management AND acute crisis stemming from hyperammonemia due to propionic acidemia or methylmalonic acidemia, we humbly request to have Carbaglu® (carglumic acid) tablets for oral suspension 200mg be the **preferred treatment** over generic Carglumic acid and to not be considered interchangeable with generic carglumic acid. Moreover, Carbaglu® can be especially helpful in hospital settings to physicians by allowing them to address multilple rare disease indications.

References:

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Zoryve Cream 0.05%, 0.15%, and 0.3%/ Zoryve Foam 0.3%

- ZORYVE® (roflumilast) 0.3%, 0.15%, 0.05% cream and 0.3% foam, is a steroid-free, first -in -class, PDE-4 inhibitor indicated for topical treatment:
    - Atopic dermatitis in patients 2 years of age and older (recently approved as of October 2025)
    - Plaque psoriasis of the scalp and body 12 years of age and older (recently approved as of May 2025)
    - Plaque psoriasis 6 years of age and older
    - Seborrheic dermatitis 9 years and older[1–7]
- ZORYVE cream and foam has no label restrictions on application to affected skin areas, body surface area, nor duration of use and is the only topical product indicated for use in intertriginous areas in psoriasis.[1–7]
- All formulations of ZORYVE have been approved for once daily application, while the majority of other topicals indicated for dermatoses must be applied multiple times per day. [1–7]
- Safety and efficacy are consistent across all indications and age groups and have been studied in up to 64 weeks of continued use.[1–7]
- Most common adverse reactions (≥1%) of subjects across all indications include: headache, insomnia nausea, application site pain, diarrhea, vomiting, upper respiratory tract infection, rhinitis, nasopharyngitis, urinary tract infection, application site pain and conjunctivitis. [1–7]

Atopic Dermatitis (Zoryve 0.05% and 0.15% Cream): [1–3]

- **Zoryve 0.05% Cream (FDA Approval – Oct 2025)**
    - ZORYVE 0.05% cream was evaluated in two Phase 3, randomized, double-blind, vehicle-controlled pivotal trials (INTEGUMENT-PED) evaluating the use of roflumilast 0.05% cream for the treatment of mild to moderate atopic dermatitis in patients aged 2-5 years.[1]
    - A significantly greater proportion of the roflumilast group achieved vIGA-AD success at week 4 (primary endpoint) versus the vehicle group (25.4% vs 10.7%; p<0.0001). Greater proportions of the roflumilast group achieved week 4 vIGA-AD 0/1 (35.4% vs 14.6%; p<0.0001) and EASI-75 (39.4% vs. 20.6%, p<0.0001). The primary endpoint at 4 weeks was intentional to demonstrate speed of resolution.
    - Starting within 24 hours after initial application, the Zoryve 0.05% group had a significantly greater reduction in pruritus compared with the vehicle group (nominal p≤0.0014).
    - Roflumilast was well tolerated and the most common treatment-emergent adverse events were upper respiratory tract infection (4.1%), diarrhea (2.5%), vomiting (2.1%), rhinitis (1.6%), conjunctivitis (1.4%), and headache (1.1%).
    - Patients aged 2-5 who received roflumilast 0.05% cream also enrolled in INTEGUMENT-OLE and the safety profile in this long-term study (up to 56 weeks) was consistent with the safety profile observed at week 4.[7]
- **Zoryve 0.15% Cream**
    - ZORYVE 0.15% cream was evaluated in two Phase 3, randomized, double-blind, vehicle-controlled pivotal trials (INTEGUMENT-1 and INTEGUMENT-2) evaluating the use of roflumilast 0.15% cream for the treatment of mild to moderate atopic dermatitis in patients 6 years or older.[2]
    - Among 1337 patients (654 patients in INTEGUMENT-1 and 683 patients in INTEGUMENT-2), significantly more patients treated with roflumilast achieved the primary end point (INTEGUMENT-1: 32.0% vs 15.2%, respectively; P < 0.001; INTEGUMENT-2: 28.9% vs 12.0%, respectively; P < 0.001) compared to vehicle.[2]
    - Roflumilast was well tolerated with low rates of treatment-emergent adverse events. At each time point, investigators noted no signs of irritation at the application site in 885 patients who were treated with roflumilast (95%), and 885 patients who were treated with roflumilast (90%) reported no or mild sensation at the application site.[2]
    - Additionally, across both trials, of the 98 patients with previous inadequate response, intolerance, or contraindication, 47 patients (34 patients treated with roflumilast; 13 treated with vehicle) had previously stopped crisaborole because of stinging, burning, and/or poor tolerability. None of these patients developed application-site adverse events during roflumilast or vehicle treatment.[2]

- Long-term safety and efficacy was published in a 52-week, Phase 3, multicenter, INTEGUMENT-OLE trial to investigate the long-term safety of roflumilast cream 0.15% in adults and children aged ≥6 years with atopic dermatitis. Once-daily nonsteroidal roflumilast cream 0.15% was well tolerated with no new safety signals for up to 56 weeks of treatment in patients ≥6 years of age. [3]
- No new safety signals were observed over up to 56 weeks of treatment. 96.3% of patients who experienced TEAEs had AEs of mild or moderate severity. At each visit, ≥98.1% of patients showed no evidence of irritation on investigator assessment of local tolerability. Application site pain was reported by 3 (0.5%) patients, and 0.4%–2.1% of patients reported severe stinging and/or burning at any visit.
- Roflumilast 0.15% cream demonstrated durable effectiveness in improving the signs and symptoms of AD, including pruritus through 56 weeks of treatment. Additionally, in the subset of patients who were proactively managed with twice weekly application of roflumilast 0.15% cream, the median duration of maintaining, "disease control," was 281 days. Of this patient population 57.7% (n=75) of these patients maintained, "disease control," through their final visit.

Plaque psoriasis (Zoryve 0.3% Foam and 0.3% Cream):

- **Zoryve 0.3% Foam (FDA Approval – May 2025)**
  - ZORYVE 0.3% topical foam is approved for plaque psoriasis of the scalp and body in adults and adolescents aged 12 and older, offering a once-daily, steroid-free option.
  - Clinical trials (Phase 2 and Phase 3 ARRECTOR) showed 66.4% of patients with scalp psoriasis and 45.5% with body psoriasis achieved clear or almost clear skin (S-IGA/B-IGA success) after 8 weeks, with significant itch reduction (63.1% for body itch, 65.3% for scalp itch).
  - Common side effects include headache (3.1%), diarrhea (2.5%), nausea (1.7%), and nasopharyngitis (1.3%), with most being mild to moderate and no known serious side effects reported. [5]
- **Zoryve 0.3% Cream**
  - ZORYVE 0.3% cream was evaluated in two randomized, double-blind, multi-center, vehicle-controlled, 8 -week pivotal trials called DERMIS-1 and DERMIS-2, which included 881 patients with mild to severe plaque psoriasis. IGA success was achieved by a statistically significantly higher proportion of patients in the active ZORYVE 0.3% cream group versus vehicle group in DERMIS-1, 41.5% versus 5.8%, and in DERMIS-2, 36.7% vs 7.1%.
  - Additionally, ZORYVE 0.3% cream was effective for the use in intertriginous areas demonstrated by a statistically significantly higher proportion of patients in the active ZORYVE group versus vehicle group having an Intertriginous-IGA success in DERMIS-1, 71.5% vs 13.8%, and DERMIS-2 67.5% vs 17.4%.[4]

Seborrheic Dermatitis (Zoryve 0.3% Foam):[6]

- ZORYVE 0.3% foam was evaluated in two randomized, parallel group, double-blind, vehicle-controlled studies conducted in Canada and the US as well as a multicenter open-label study in the US for patients with seborrheic dermatitis.
- Within STRATUM, a phase III study to assess safety and efficacy in patients age 9 years or older with seborrheic dermatitis, IGA success was achieved by a statistically significantly higher proportion of patients in the active ZORYVE foam group versus vehicle group (79.5% vs 58.0%) with an odds ratio of 2.79.[1–6]

Summary:

- ZORYVE safety and tolerability has been consistently demonstrated across the clinical program, and via long-term safety trials. ZORYVE 0.3% cream is the only psoriasis topical therapy indicated for the use in intertriginous areas. ZORYVE 0.3% foam is the only approved therapy indicated for the treatment of seborrheic dermatitis for ages 9 years and older and scalp and body 12 years of age and older. [1–7]
- Arcutis requests for Zoryve cream 0.05%, 0.15%, and 0.3% strengths and Zoryve 0.3% foam be added as a **preferred agent** with **a single step through a preferred generic agent (TCS)** on formulary.

Zoryve Cream 0.05%, 0.15%, and 0.3%/ Zoryve Foam 0.3%

Citations:

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ANZUPGO® (delgocitinib): State Medicaid Written Testimony

This **reactive** document is a written testimony intended to summarize key points for the review of delgocitinib. Delgocitinib was approved by the FDA on July 23, 2025. **Please see Full Prescribing Information available at ANZUPGOHCP.com.**

Indication, Mechanism of Action, Dosage and Administration

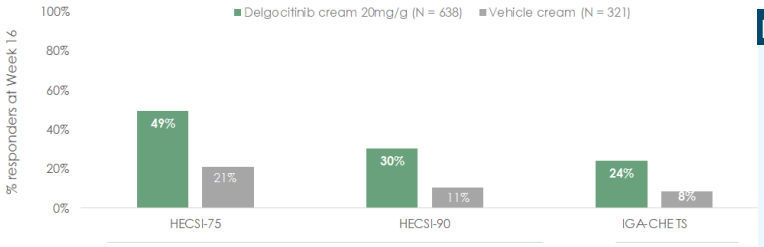
- Delgocitinib is the first and only FDA-approved treatment for moderate to severe chronic hand eczema (CHE) in adults. By blocking the activity of all four members of the Janus Kinase (JAK) family, delgocitinib broadly targets all subtypes of CHE, addressing the heterogeneous pathophysiology of the disease.[1-4]
- Delgocitinib is indicated for the treatment of moderate-to-severe CHE in adults who have had an inadequate response to, or for whom topical corticosteroids are not advisable.[1]
- The recommended dosage is the application of a thin layer of Anzupgo®, twice daily, to the affected areas only on the hands and wrists. Each gram of Anzupgo cream contains 20 mg of delgocitinib. Do not use more than 30 grams per 2 weeks or 60 grams per month. Use of ANZUPGO in combination with other JAK inhibitors or potent immunosuppressants is not recommended[1]

Efficacy[1,5-9]

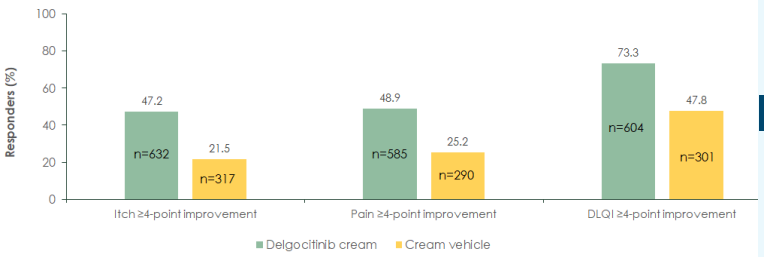
Delgocitinib was studied in two identical phase 3 trials including nearly 1000 patients, as well as an open-label long-term extension (LTE) trial:[5]

- **DELTA 1 & 2:** Delgocitinib achieved statistically significant improvements over cream vehicle in the primary and all secondary endpoints at all pre-specified timepoints.[5-9] The primary endpoint of Investigator's Global Assessment-CHE (IGA-CHE) treatment success at week 16 was met by 20% and 29% of delgocitnib patients vs 10% and 7% in the cream vehicle group in DELTA 1 & 2, respectively (DELTA 1 p=0.0055, DELTA 2 p<0.0001).
  - **Key patient- and clinician-reported secondary endpoints achieved:**
    - IGA-CHE treatment success: wks 4, 8
    - ≥4-point reduction from baseline in HESD* itch score: wks 2, 4, 8, 16
    - ≥4-point reduction from baseline in HESD* pain score: wks 4, 8, 16
    - 75% Improvement in HECSI**: wks 8,16
    - 90% Improvement in HECSI**: wk 16
    - ≥4-point reduction in Dermatology Life Quality Index score: wk 16
  - Relief from itch and pain was observed at days 1 and 3, respectively.[8]
  - 66% (n=421) of delgocitinib-treated patients achieved an IGA-CHE 0/1/2 response at week 16, compared to 39% (n=125) in the cream vehicle cohort.[6]

Pooled responders (%) from DELTA 1 & 2 clinician-reported endpoints: wk 16*



Pooled responders (%) from DELTA 1 & 2 patient-reported endpoints: wk 16*



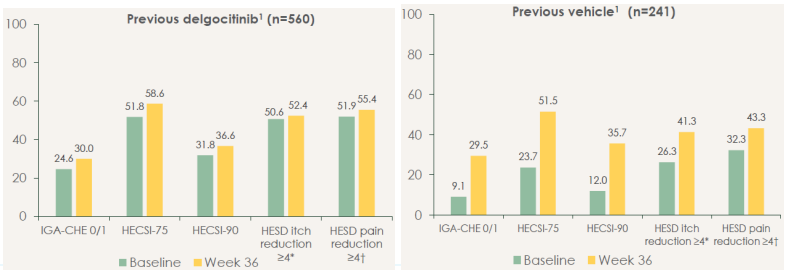
*p<0.001 for all endpoints
Inclusion Criteria of HESD itch score (weekly average) of ≥4 points

- **DELTA 3:** During the open-label LTE, all participants were treated as needed with twice-daily delgocitinib only when their IGA-CHE score was 2 or greater. Participants continuing delgocitinib maintained robust efficacy in all parameters, while participants switching to delgocitinib from cream vehicle saw marked improvements at week 36. In delgocitinib non-responders from DELTA 1 and 2, 48% achieved IGA-CHE 0/1 at some point within the DELTA 3 treatment period.[9]

Please see Full Prescribing Information in Section 14

*HESD = Hand Eczema Symptom Diary; **HECSI = Hand Eczema Severity Index

DELTA 3: % responders to as-needed treatment (IGA-CHE ≥2)



*Parent trial baseline itch score ≥4 (previous delgocitinib: n=557; previous vehicle: n=240);
†Parent trial baseline pain score ≥4 (previous delgocitinib: n=516; previous vehicle: n=217)

Safety

- In DELTA 1 & 2 trials, adverse reactions reported in ≤ 1% of ANZUPGO recipients were application site reactions which included application site pain, paresthesia, pruritus, erythema, and bacterial skin infections including finger cellulitis, paronychia, and other skin infections, leukopenia, and neutropenia. Most adverse events (AEs) reported in the pivotal trials were mild or moderate in severity.[1]
- Topical delgocitinib showed over 30-fold lower systemic exposure than subtherapeutic oral dose and was at least 100-fold below the inhibitory concentration of 50% (IC50) value of delgocitinib (24 ng/mL)[10,11]

Please see Full Prescribing Information in Section 6

Matching-Adjusted Indirect Comparison (MAIC)*

A MAIC study evaluated **topical delgocitinib and dupilumab injection** for treating moderate-to-severe atopic dermatitis of the hands, a specific subtype of CHE. For this comparison, individual patient data for those with **atopic dermatitis of the hands** were taken from the DELTA 1 and 2 trials of delgocitinib, which studied a broader CHE population. These data were then compared to the aggregate published data from the LIBERTY AD-HAFT trial, which specifically assessed dupilumab for moderate-to-severe atopic dermatitis of the hands. **The study found that the efficacy of topical delgocitinib cream was comparable to the biologic dupilumab at 16 weeks in this atopic dermatitis patient group. While the observed differences in efficacy did not reach statistical significance, all results numerically favored delgocitinib over dupilumab.[12]**

Summary

- Delgocitinib, a topical pan-JAK inhibitor, is the first and only FDA-approved treatment for adults with moderate to severe Chronic Hand Eczema (CHE), designed to broadly address all subtypes of this condition. CHE is defined as hand eczema that lasts longer than 3 months or relapses twice or more per year, with persistent itch and skin pain as its most debilitating symptoms.[1-4]
- The steroid-free cream formulation[1], developed with patient input and minimal excipients, penetrates the dermis with low systemic exposure (0.6% bioavailability) and without penetration enhancers which can impact skin barrier (e.g., no propylene glycol), offering a safe and effective option for managing moderate-to-severe CHE.[13]

Please see Full Prescribing Information available at ANZUPGOHCP.com.

*Matching-Adjusted Indirect Comparison (MAIC) analyses are limited by potential unmeasured confounding factors, small effective sample sizes after matching, and reliance on published aggregate data, which should be carefully considered when interpreting findings as complementary rather than definitive evidence for treatment decisions.

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For State Formulary Decision Committee Members Only

Thank you for the opportunity to speak with you today.

Let's begin with unmet need in Recessive Dystrophic Epidermolysis Bullosa, or RDEB. This is a severe, ultra-rare genetic disorder caused by mutations in the COL7A1 gene, resulting in a deficiency or absence of type VII collagen. This leads to a lack of anchoring fibrils that normally connect the epidermis to the dermis, causing extreme skin fragility and blistering. Clinically, patients present with chronic, painful wounds that are slow to heal, highly susceptible to infection, and associated with squamous cell carcinoma and significant morbidity.

Current management is primarily supportive, relying on time-consuming and costly bandaging routines, along with symptomatic relief for pain and itch. While a topical non-cell-based gene therapy is available, it requires ongoing reapplication, and an unmet need remains for many patients—particularly those with extensive or chronic wounds—to achieve durable wound closure and sustained healing.

ZEVASKYN™ is an autologous gene-modified cellular sheet indicated for the treatment of wounds in adult and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB). These sheets are engineered to express type VII collagen at the dermal-epidermal junction and are designed for a one-time surgical application where applied. The COL7A1 transgene integrates into the host genome at the site of application and is maintained through cell division, supporting sustained expression of type VII collagen.

In the pivotal VIITAL study, patients treated with ZEVASKYN demonstrated clinically meaningful wound healing, with 81% of wounds achieving ≥50% healing at six months compared to 16% of control wounds which underwent the standard of care of bandaging. Among those, 65% achieved ≥75% healing compared to 7% for control, and 16% of wounds reached complete closure, compared to 0% for control. In addition to wound healing, patients reported significant reductions in pain, benefits that are unique to ZEVASKYN.

ZEVASKYN has an established safety profile. In clinical trials, the most common side effects were pruritus and procedural pain. Serious allergic reactions, including anaphylaxis, may occur with ZEVASKYN and lifelong monitoring for the development of cancer is advised. No cases of squamous cell carcinoma have been reported in ZEVASKYN-treated wounds, but SCC was observed in non-ZEVASKYN–treated sites in 4 patients.

ZEVASKYN is designed to promote durable wound healing and reduce pain with a single surgical application where its applied. As an autologous therapy, its gene-modified cellular sheets provide a personalized approach to managing wounds associated with RDEB, including large or chronic areas.