

## Mounjaro® (tirzepatide) Medical Value Summary

### I. INDICATION<sup>1</sup>

- Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- Limitations of Use:
  - i. Has not been studied in patients with a history of pancreatitis
  - ii. Is not indicated for use in patients with type 2 diabetes

### II. DOSAGE AND ADMINISTRATION<sup>1</sup>

- The 2.5 mg dose is for treatment initiation and is not intended for glycemic control
- The recommended starting dosage is 2.5 mg injected subcutaneously once weekly
- After 4 weeks, increase to 5 mg injected subcutaneously once weekly
- If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose
- The maximum dosage is 15 mg subcutaneously once weekly
- Administer once weekly at any time of day, with or without meals
- Inject subcutaneously in the abdomen, thigh, or upper arm
- Rotate injection sites with each dose

### III. DOSAGE FORMS AND STRENGTHS<sup>1</sup>

- Injection: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL in single-dose pen

### IV. EFFICACY SUMMARY<sup>1</sup>

- The effectiveness of tirzepatide as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus was established in five trials. In these trials, tirzepatide was studied as monotherapy (SURPASS-1); as an add-on to metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors (SGLT2 inhibitors) (SURPASS-2, -3, and -4); and in combination with basal insulin with or without metformin (SURPASS-5). In these trials, tirzepatide (5 mg, 10 mg, and 15 mg given subcutaneously once weekly) was compared with placebo, semaglutide 1 mg, insulin degludec, and/or insulin glargine.
- In adult patients with type 2 diabetes mellitus, treatment with tirzepatide produced a statistically significant reduction from baseline in HbA<sub>1c</sub> compared to placebo. The effectiveness of tirzepatide was not impacted by age, gender, race, ethnicity, region, or by baseline BMI, HbA<sub>1c</sub>, diabetes duration, or renal function.

Trial Acronym	Concomitant therapy	Comparator	Efficacy (HbA <sub>1c</sub> [%] change from baseline) at primary endpoint <sup>a-c</sup>			
			Tirzepatide 5mg	Tirzepatide 10mg	Tirzepatide 15mg	Comparator
SURPASS-1	Monotherapy	Placebo	-1.8	-1.7	-1.7	-0.1
SURPASS-2	Metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors	Semaglutide 1mg	-2.0	-2.2	-2.3	-1.9
SURPASS-3	Metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors	Insulin degludec	-1.9	-2.0	-2.1	-1.3
SURPASS-4	Metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors	Insulin glargine	-2.1	-2.3	-2.4	-1.4
SURPASS-5	Basal Insulin with or without metformin	Placebo	-2.1	-2.4	-2.3	-0.9

<sup>a</sup>Observations: HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>.

<sup>b</sup>Placebo-to-treat population. Last observation carried forward (LOCF) was used to impute missing data.

<sup>c</sup>Least-squares (LS) mean adjusted for baseline value and other stratification factors.

<sup>d</sup>For AWARD-11 and -12, placebo multiple imputation, with respect to the baseline values, was used to model a wash-out of the treatment effect for subjects having missing data at final endpoint.

<sup>e</sup>ANCOVA pattern mixture model adjusted for baseline value and other stratification factors was used. AWARD-11 studied the 4mg and 4.5mg doses of TIRZEPATIDE.

### V. SAFETY SUMMARY<sup>1</sup>

**Please see full prescribing information including boxed warning for thyroid c-cell tumors available at:**

<https://pi.lilly.com/us/mounjaro-uspi.pdf?s=pi>

- **WARNING: RISK OF THYROID C-CELL TUMORS:** In both male and female rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether tirzepatide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.
- Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of tirzepatide and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with tirzepatide.

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This was developed by Lilly Medical and intended to be used by Population Health Decision Makers for medical, scientific, and educational purposes

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- Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with known serious hypersensitivity to tirzepatide or any of the excipients in tirzepatide.
- Pancreatitis: Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists. Observe patients for signs and symptoms, including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue tirzepatide and initiate appropriate management.
- Severe Gastrointestinal Disease: Use of tirzepatide has been associated with gastrointestinal adverse reactions, sometimes severe. Tirzepatide has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.
- The most common adverse reactions reported in  $\geq 5\%$  of tirzepatide-treated patients in placebo-controlled trials were nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain.

## VI. REAL-WORLD EVIDENCE<sup>2</sup>

- There are no head-to-head comparisons of tirzepatide versus semaglutide 2 mg. An adjusted indirect treatment comparison (aITC) of the efficacy of tirzepatide 5/10/15 mg versus semaglutide 2 mg in patients with type 2 diabetes was conducted.
- The primary analysis showed that the effects of tirzepatide 10 and 15 mg on the reduction of HbA1c and body weight were statistically significant and clinically meaningful compared to semaglutide 2 mg.
- The lowest dose of tirzepatide (5 mg) offered similar reductions from baseline in HbA1c and body weight versus the highest dose of semaglutide (2 mg).
- The incremental HbA1c reduction of 0.4% with tirzepatide 10 and 15 mg and greater body weight reduction of 3.2 kg with tirzepatide 10 mg and 5.2 kg with tirzepatide 15 mg compared to semaglutide 2 mg reported in this analysis may help more patients to reach these clinically relevant goals.

## VII. VALUE SUMMARY<sup>1</sup>

- Tirzepatide is an agonist for both GLP-1 and GIP receptors.
- In the SURPASS clinical trial program, treatment with tirzepatide 5 mg, 10 mg, and 15 mg in people with T2D resulted in:
  - a robust and clinically relevant lowering of HbA1c greater than placebo, semaglutide 1 mg, and basal insulin
  - a significant and clinically meaningful reduction in body weight
- Tirzepatide has a proven safety and tolerability profile similar to GLP-1RAs.
- Available as a once-weekly injection delivered via a single-dose pen device that has a hidden, attached, self-retracting needle and requires no reconstitution or mixing.

## REFERENCES

1. MOUNJARO (dulaglutide) Prescribing Information. Indianapolis, IN: Eli Lilly and Company, May 2022. <https://pi.lilly.com/us/mounjaro-uspi.pdf?s=pi>
2. Karan Vadhvani, Hiren Patel, Reema Mody, et al. Efficacy of tirzepatide 5, 10, and 15 mg versus semaglutide 2 mg in patients with type 2 diabetes: an adjusted indirect treatment comparison. Diabetes Obes. Metab. 2022 May 19.

# Long-term Efficacy and Safety of Extended Ofatumumab Use in Patients With RMS: ALITHIOS Study\*



- Ofatumumab is the first fully human anti-CD20 monoclonal antibody approved for the treatment of relapsing forms of MS in adults<sup>1</sup>
- It can be self-administered after the initial dose has been performed under the guidance of a health care professional<sup>1</sup>
- In the phase 3 ASCLEPIOS studies, ofatumumab significantly reduced the ARR, risk of 3- and 6-month CDW, number of T1 Gd+ lesions, and rate of neT2 lesions versus teriflunomide.<sup>1</sup> AEs from pooled ASCLEPIOS studies with incidence of at least 5% with ofatumumab and greater incidence than teriflunomide were URTI, systemic IRR, headache, local ISR, UTI, back pain, and decreased IgM<sup>1</sup>
- ALITHIOS is an ongoing phase 3b, open-label, long-term study evaluating the safety, tolerability, and effectiveness in eligible subjects who have participated in Novartis ofatumumab clinical MS studies (ASCLEPIOS I/II [phase 3] and APLIOS/APOLITOS [phase 2])<sup>3</sup>

**OBJECTIVE:** To assess the long-term efficacy of ofatumumab treatment for up to 4 years<sup>†</sup> in patients with RMS in the ongoing ALITHIOS extension study<sup>2</sup>

## Study design



ASCLEPIOS I/II  
Core period

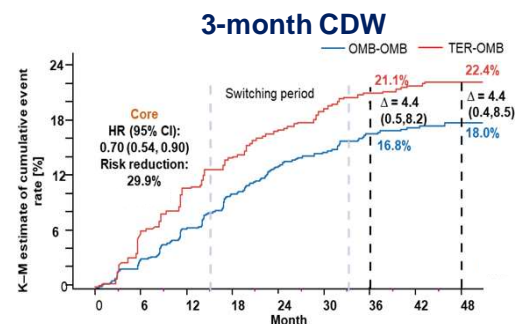
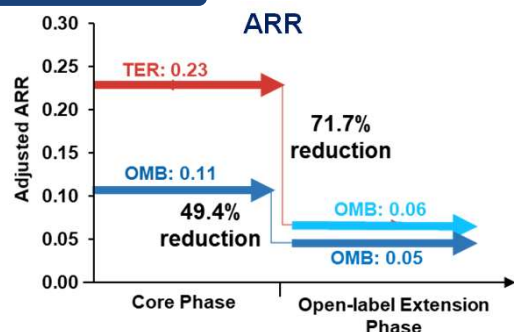
Total efficacy population  
N=1882

ALITHIOS  
open-label extension period

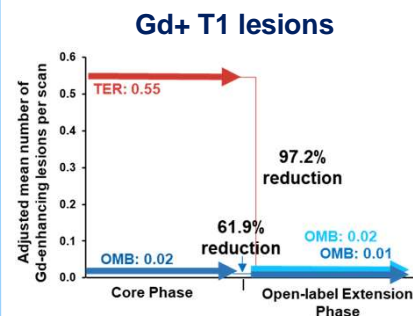
Continuous ofatumumab<sup>a</sup>  
N=690, 2761.4 PYs<sup>‡</sup>

Switched ofatumumab<sup>b</sup>  
N=677, 1271.1 PYs<sup>‡</sup>

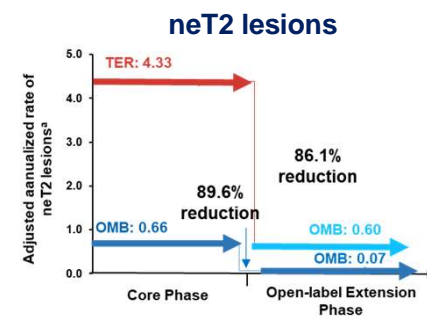
## Efficacy results



A similar trend was also observed for 6-month CDW (HR at core [95% CI]: 0.74 [0.56, 0.97])



95% reduction in the cumulative number of Gd+ T1 lesions with continuous use of ofatumumab versus switch



83.7% reduction in the cumulative number of neT2 lesions with continuous use of ofatumumab versus switch

AE, adverse events; ARR, annualized relapse rate; CD, cluster of differentiation; CDW, confirmed disability worsening; Gd+, gadolinium-enhancing; HR, hazard ratio; IgM, immunoglobulin M; IRR, injection-related reactions; ISR, injection site reaction; K-M, Kaplan-Meier; MS, multiple sclerosis; neT2, new or enlarging T2; OMB, ofatumumab; PY, patient-years; TER, teriflunomide; URTI, upper respiratory tract infection; UTI, urinary tract infection.  
\*This analysis represents chance findings. The open-label extension study is not blinded, not controlled, and includes inherent self-selection bias for remaining in the trial. No conclusions of statistical or clinical significance can be drawn. †Data cutoff: September 25, 2021, cutoff for core and extension periods refers to the first dose of ofatumumab in extension; ‡Total exposure to ofatumumab.  
\*Randomized to ofatumumab in the core; ‡Switch group refers to the patients started with teriflunomide in core and switched to ofatumumab in extension period.

1. KESIMP-TA. Prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2020. 2. Hauser SL et al. Poster presented at the AAN 2022 Annual Meeting; April 2-7, 2022, Seattle, WA. P5-004. 3. Hauser SL, et al. Mult Scler. 2022;13524585221079731.

This scientific information herein is consistent with an approved product label.

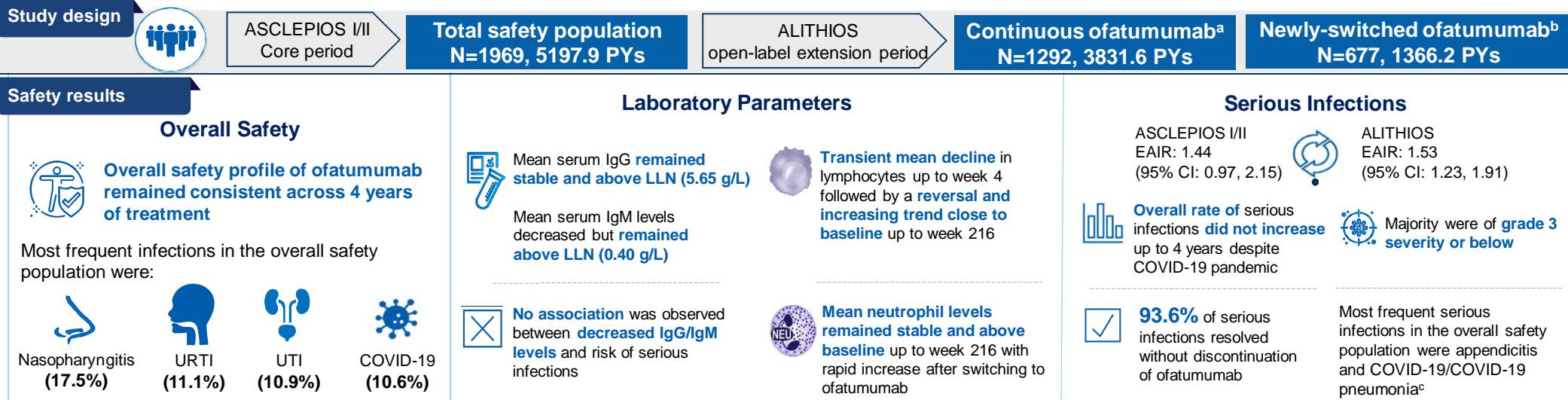
Adapted with permission from Hauser et al.<sup>2</sup>



# Long-term Efficacy and Safety of Extended Ofatumumab Use in Patients With RMS: ALITHIOS Study\*



**OBJECTIVE:** To assess the long-term safety and tolerability of ofatumumab treatment for up to 4 years<sup>†</sup> in patients with RMS<sup>2</sup>



## Long-term Efficacy Results<sup>1</sup>

- Treating patients early and continuously with ofatumumab was associated with fewer relapses, a reduced risk of 3-month and 6-month CDW, and a lower MRI lesion load compared with a switching strategy
- The long-term efficacy data support findings from 96-week core ASCLEPIOS studies, indicating that ofatumumab shows sustained efficacy in patients with RMS

## Long-term Safety Results<sup>2</sup>

- Cumulative safety data for up to 4 years show no new safety risk identified and suggest that extended ofatumumab treatment is well-tolerated in RMS patients
- The long-term safety data support findings from 96-week core ASCLEPIOS studies, indicating that ofatumumab is well-tolerated in patients with RMS

AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate per 100 PY; Ig, immunoglobulin; LLN, lower limit of normal; MRI, magnetic resonance imaging; PY, patient years; RMS, relapsing multiple sclerosis; SAE, serious adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection; W, week.

\*This analysis represent chance findings. The open-label extension study is not blinded, not controlled, and includes inherent self-selection bias for remaining in the trial. No conclusions of statistical or clinical significance can be drawn. <sup>†</sup>Data cutoff: September 25, 2021; cutoff for core and extension periods refer to the first dose of ofatumumab in extension.

<sup>a</sup>Includes all patients randomized to ofatumumab in ASCLEPIOS I/II, APLIOS and APOLITOS continued in ALITHIOS; or completed/discontinued ofatumumab during 1 of the 4 trials and continued in the safety follow-up of their respective trials, but did not enter ALITHIOS.

<sup>b</sup>Includes patients who were randomized to teriflunomide in ASCLEPIOS I/II and switched to ofatumumab on entering ALITHIOS; there are n=24 COVID-19-related SAEs in total, of which 1 patient has "suspected COVID-19".

<sup>c</sup>1. Hauser SL et al. Poster presented at the AAN 2022 Annual Meeting; April 2-7, 2022, Seattle, WA. P5-004. 2. Hauser SL et al. Poster presented at the AAN 2022 Annual Meeting; April 2-7, 2022, Seattle, WA. S14.004.

The content contained in this material is consistent with an approved product label and may be used for proactive communications.



## Written Testimony: Oregon Health Authority (OHA), Apretude

This document is a written testimony intended to summarize the key points below required for the Oregon Health Authority (OHA) review of *Apretude* (cabotegravir extended-release injectable suspension [CAB LA]) for intramuscular (IM) use.

### **Indication**

*Apretude* is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection.<sup>(PI,2,2.1)</sup> Individuals must have a negative HIV-1 test prior to initiating *Apretude* (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

### **Boxed Warnings (see attached Prescribing Information, Section 5, for further information)**

Individuals must be tested for HIV-1 infection prior to initiating *Apretude* or oral cabotegravir, and with each subsequent injection of *Apretude*, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection.<sup>(PI, 2.1.1)</sup>

### **Dosing**

Prior to initiating *Apretude*, an oral lead-in therapy may be used for about one month to assess the tolerability of *Apretude*.<sup>(PI, 2.4.1)</sup> *Apretude* is for IM gluteal injection only. Initiate *Apretude* with a single 600 mg (3 mL) injection given 1 month apart for 2 consecutive months on the last day of an oral lead-in if used or within 3 days and continue with the injections every 2 months thereafter.

### **Contraindications**

*Apretude* is contraindicated in patients: unknown or positive HIV-1 status; with previous hypersensitivity reaction (HSR) to CAB; coadministration with drugs where significant decreases in CAB plasma concentrations may occur.<sup>(PI, 6.6.1)</sup>

### **Warnings and Precautions (see attached Prescribing Information, Section 5, for further information)**<sup>(PI,6.7.1)</sup>

- Comprehensive management to reduce the risk of HIV-1 acquisition.
- Potential risk of developing resistance to *Apretude* if an individual acquires HIV-1 either before or while taking *Apretude* or following discontinuation of *Apretude*. Reassess risk of HIV-1.
- Residual concentrations of CAB may remain in the systemic circulation of individuals up to 12 months or longer.
- HSRs have been reported have been reported with other INSTIs. Discontinue *Apretude* immediately if signs or symptoms of HSRs develop.
- Hepatotoxicity has been reported in patients receiving CAB. Clinical and laboratory monitoring should be considered.
- Depressive disorders have been reported with *Apretude*. Prompt evaluation is recommended.

### **Efficacy Data**

- The efficacy of *Apretude* to reduce the risk of acquiring HIV-1 infection is supported by data from two Phase 3 randomized, multinational, double-blinded, double-dummy trials: HPTN 083 [NCT02720094] and HPTN 084 [NCT03164564].<sup>(PI,26.7.1)</sup>
- Patients were randomized to receive daily oral CAB 30 mg + daily oral TDF/FTC placebo for up to 5 weeks, followed by CAB LA 600 mg IM every 4 weeks x2 doses followed by CAB LA 600 mg IM every 8 weeks + daily oral TDF/FTC placebo or daily oral TDF/FTC 300 mg/200 mg and oral CAB placebo for 5 week, followed by daily oral TDF/FTC 300 mg/200 mg + CAB LA placebo IM every 4 weeks x2 doses then every 8 weeks thereafter.<sup>(PI,27.2.1)</sup>
- HPTN 083, a non-inferiority study, evaluated CAB LA vs. daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for PrEP in HIV-1 uninfected cisgender men and transgender women who have sex with men.<sup>(PI, 27.3.1)(Landovitz,2.4.1)</sup> The primary endpoint was the rate of incident HIV-1 infections.
- CAB LA was statistically superior to TDF/FTC at preventing HIV acquisition (HR=0.34, 95% CI 0.18-0.62,  $P<0.001$ ).<sup>(PI,27.5.3)(Landovitz,6.1.1)</sup> There were a total of 52 incident HIV infections with 13 incident infections in the CAB LA arm vs 39 incident infections in the TDF/FTC arm. Further testing revealed 1 of the infections in the CAB LA arm to be prevalent then yielding a 69% reduction in the risk of HIV-1 incident infection relative to TDF/FTC (HR=0.31, 95% CI 0.16-0.58,  $P=0.0003$ ).
- Based on a random subset of 390 patients receiving TDF/FTC, tenofovir concentrations were detectable ( $>0.31$  ng/mL) in 86% of patients and indicative of daily TDF ( $>40$  ng/mL) in 74.2% of patients.<sup>(Landovitz,5.4.1)</sup> Adherence was 91.5% of person-years as defined as injections having been received with a delay of  $<2$  weeks.
- Overall, 81.4% of patients who received CAB LA experienced at least 1 injection site reaction (ISR) during the course of the study.<sup>(Landovitz,7.4.1)</sup> The most common ISR reported was pain (60.8%); the events began a median of 1 day (IQR, 0 to 2) after injection and lasted a median of 3 days (IQR, 2 to 6).
- HPTN 084, a superiority study, evaluated CAB LA vs. daily oral TDF/FTC for PrEP in HIV-1 uninfected cisgender women. The primary endpoint was the rate of incident HIV-1 infections.<sup>(PI,29.1.1)</sup>
- CAB LA was statistically superior to TDF/FTC at preventing HIV acquisition (HR=0.12, 95% CI 0.05-0.31).<sup>(PI,29.3.3)(Delany-Moretlwe,1781.1.1)</sup> There were a total of 40 incident HIV infections with 4 incident infections in the CAB LA arm and 36 in the TDF/FTC arm. Further testing revealed 1 of the infections in the CAB LA arm to be prevalent then yielding a 90% reduction in the risk of HIV-1 incident infection relative to TDF/FTC (HR=0.10, 95% 0.04-0.27;  $P<0.0001$ ).
- Based on a random subset of 405 patients receiving TDF/FTC, tenofovir concentrations were detectable ( $>0.31$  ng/mL) in 55.9% of patients and indicative of receipt of daily TDF ( $>40$  ng/mL) in 42.1% of the plasma samples tested.<sup>(Delany-Moretlwe,1785.2.1)</sup> Adherence to CAB LA was 93.1%.
- ISRs were reported in 38% of patients in the CAB LA arm compared to 10.8% in the TDF/FTC arm.<sup>(Delany-Moretlwe,1785.6.1)</sup> The most common ISR symptom was pain and most injection site reactions were reported at the first injection and diminished over time.

### **Treatment Guidelines**

- *Apretude* is recommended for HIV prevention in adults reporting sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition in the CDC (IA rating) guidelines.<sup>(CDC,2.4.1)</sup>
- *Apretude* is recommended as PrEP for cisgender men and transgender women who have sex with men in the IAS-USA (AIIa rating) guidelines.<sup>(Saag,1662.Box4)</sup>

**This information is provided as professional service in response to your unsolicited request. ViiV Healthcare requests that the recipient of this information only share the contents with the Pharmacy and Therapeutics Committee members for the purposes of making evidence-based decisions regarding formulary inclusion.**

**References:** 1. ViiV Healthcare Local Label; 2. Landovitz R, et al. N Engl J Med. 2021;385(7):595-609; 3. Delany-Moretlwe S, et al. Lancet 2022; 399(10337):1779-1789. 4. US Public Health Service. CDC. Available at: <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>. Accessed August 3, 2022. 5. Saag MS, et al. JAMA. 2020;324(16):1651-1669.

## Written Testimony: Oregon Health Authority (OHA)– Updated data, Cabenuva

This document is a written testimony intended to summarize the key points below required for the Oregon Health Authority (OHA) review of *Cabenuva*<sup>®</sup> (cabotegravir extended-release injectable suspension [CAB LA]/rilpivirine extended-release injectable suspension [RPV LA]), co-packaged for intramuscular (IM) use.

### Updated Indication

*Cabenuva*, a 2-drug co-packaged product of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase (NNRTI), is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either CAB or RPV.<sup>(P1,2,1.1)</sup>

### Updated Dosing

Prior to initiating treatment, oral lead-in therapy may be considered to assess the tolerability of CAB and RPV with the recommended dosage used for approximately 1 month.<sup>(P1,2,3,1)</sup> *Cabenuva* is for IM gluteal injection only. *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) should be initiated on the last day of current antiretroviral therapy or oral lead-in and continue with injections of *Cabenuva* (400 mg CAB LA and 600 mg RPV LA) every month thereafter. *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) should be initiated on the last day of current antiretroviral therapy or oral lead-in for 2 consecutive months and continue with injections of *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) every 2 months thereafter.

- If oral lead-in is used, the recommended oral lead-in daily dose is one 30-mg tablet of *Vocabria* (cabotegravir) and one 25-mg tablet of *Edurant* (rilpivirine) taken with a meal for approximately 1 month (at least 28 days), followed by IM injections of *Cabenuva*.
- If a patient plans to miss a scheduled injection visit by more than 7 days, VOCABRIA in combination with EDURANT once daily may be used for up to 2 months to replace missed injection visits, or any other fully suppressive oral antiretroviral regimen may be used until injections are resumed.

### Efficacy Data

- Previously reviewed by Oregon Health Authority (OHA) on 08/05/2021:
  - 1). ATLAS and FLAIR week 48 pooled analysis
  - 2). FLAIR week 96 data

### Updated FLAIR Week 124 Data

**Background:** FLAIR was a randomized, multicenter, active-controlled, open-label, non-inferiority study which evaluated *Cabenuva* in virologically suppressed participants.<sup>(2)</sup>

- Patients were randomized to continue abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) or switch to *Cabenuva*.<sup>(2)</sup> At Week 96 participants on ABC/DTG/3TC had the option to transition to *Cabenuva* either as a direct to injection (DTI) group (n=111) or with an oral lead-in (OLI, n=121).

#### **Results – Week 124:**

- Virologic outcomes at Week 124 (after 24 weeks of *Cabenuva*) during the extension phase of FLAIR were similar between participants who received OLI or DTI. One participant (<1%) in each group had an HIV-1 RNA  $\geq 50$  copies/mL.<sup>(2)</sup>
- Most participants maintained virologic suppression: 110(99%) in the DTI group and 113 (93%) in the OLI group.<sup>(2)</sup>
- There was 1 additional participant with CVF since the 96 week analysis, totaling 4 participants over 124 weeks.<sup>(2)</sup>

#### **Safety Overview**

- The overall safety profile was consistent with that observed at Week 48 and when injection therapy with *Cabenuva* was initiated directly without the oral lead-in phase.<sup>(1,2)</sup>
- Injection site reactions (ISRs) were the most common AE, occurring after 914 (21%) of 4422 injection in the extension phase.<sup>(2)</sup> ISRs were numerically less common in the OLI arm (338/2128) than the DTI arm (576/2314).<sup>(2)</sup>

### Updated ATLAS 96 Week Data

**Background:** ATLAS was a randomized, multicenter, open-label non-inferiority study which evaluated *Cabenuva* in virologically suppressed patients.<sup>(Swindells, 186.4.1)</sup>

- Patients were randomized to continue on their current regimen (CAR) or switch to *Cabenuva*.
- Week 48 data established non-inferiority of *Cabenuva* vs current regimen.

#### **Results – Week 96:**

- Limited data are available due to a majority of patients transitioning to ATLAS-2M upon completing the maintenance phase.<sup>(Swindells,187.3.1)</sup>
- Of 52 patients included in the Week 96 analysis, no patients in the LA arm and 1 patient in the switch arm had HIV-1 RNA  $\geq 50$  copies/mL.<sup>(Swindells,189.2.1)</sup>
- There were no CVFs during the extension phase.<sup>(Swindells,189.2.15)</sup>

#### **Safety Overview**

- No new safety signals were identified.<sup>(Swindells,189.3.1)</sup>
- Most ISRs were mild or moderate in severity, except for 3 single Grade 3 AEs of injection site pain in the *Cabenuva* arm; none were considered serious by the investigators.<sup>(Swindells,189.5.4)</sup> The most commonly reported ISR was pain.

### **ATLAS-2M 48 & 96 Week Data**

**Background:** ATLAS-2M was a randomized, multicenter, international, open-label non-inferiority study which evaluated maintenance treatment with *Cabenuva* every 8 weeks vs every 4 weeks.<sup>(Overton,1996.2.1)</sup>

- Virologically suppressed adults, either already receiving *Cabenuva* every 4 weeks from the ATLAS study or oral standard of care, were randomized to either *Cabenuva* (600 mg CAB LA and 900 RPV LA) every 8 weeks or *Cabenuva* (400 CAB LA and 600 mg RPV LA) every 4 weeks.

#### **Results:**

- Week 48 data established non-inferiority of *Cabenuva* every 8-weeks vs. every 4-weeks (HIV-1 RNA  $\geq 50$  copies; 2% vs 1%) and remained through Week 96.<sup>(Overton,1999.5.1)</sup> <sup>(Jaeger,e683.4.1)</sup>
- There were 8 (1.5%) confirmed virologic failures in the every 8-week arm and 2 (0.4%) in the every 4-week arm at Week 48.<sup>(Overton,2000.2.1)</sup> One additional patient in the every 8-week dosing group met confirmed virologic failure.<sup>(Jaeger,e684.2.1)</sup>

#### **Safety Overview**

- 21% and 24% of patients in the every 8-week arm and every 4-week arms experienced a drug-related, non-ISR AE.<sup>(Overton,2001.Table3)</sup>
- ISRs were the most common AE reported. In both arms, 86% of ISRs had a duration of 1 to 7 days.<sup>(Overton,2002.2.1)</sup>
- In the every 8-week arm and the every 4-week arm, 1% (n=6) and 2%(n=11) of patients, respectively, withdrew from the study for injection-related reasons.<sup>(Overton,2001.Table3)</sup>
- The occurrence of AEs through 96 weeks were generally similar between the treatment arms and consistent with what was reported at Week 48. ISRs were the most common AEs reported and injection site pain was the most common ISR reported.<sup>(Jaeger,e684.4.1)</sup>

### **Use in Pediatrics**

The safety and effectiveness of *Cabenuva* have been established in adolescents aged 12 to younger than 18 years weighing at least 35 kg, which is supported by the trials in adults and the MOCHA (NCT03497676) trial in adolescents.<sup>(PI,23.1.1)</sup> Please see the full Prescribing Information for additional information.

### **Treatment Guidelines**

- *Cabenuva* is strongly recommended for virologically suppressed patients with HIV-1 in both DHHS (AI rating) and IAS-USA (AIIa rating) guidelines.<sup>(Saag,1657.Box 3)</sup><sup>(DHHS,I-33.5.1)</sup>

**References:** 1. ViiV Healthcare Local Label; 2. Swindells S, et al. *AIDS*. 2022;36:185-194; 3. Overton E, et al. *Lancet* 2020;396:1994-2005. 4. Jaeger H, et al. *Lancet HIV*. 2021;8(11):e679-89. 5. Saag MS, et al. *JAMA*. 2020;324(16):1651-1669; 6. DHHS Guidelines. Available at: [clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf](https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf). Updated Jun. 3, 2021. Accessed April 25, 2022.

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## Written Testimony: Oregon Health Authority (OHA) – Updated Data, Dovato

This document is a written testimony intended to summarize the key points below required for the Oregon Health Authority (OHA) review of *Dovato* (dolutegravir 50 mg/lamivudine 300 mg [DTG/3TC]).

### **Indication**

*Dovato*, a two-drug combination of DTG and 3TC, is indicated as a complete regimen for the treatment of HIV-1 infection in adults with no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of *Dovato*.<sup>(1)</sup>

### **Boxed Warnings (see attached Prescribing Information, Section 5, for further information)**

All patients with HIV-1 should be tested for the presence of hepatitis B virus (HBV) prior to or when initiating *Dovato*.<sup>(1)</sup> Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with HIV-1 and HBV and have discontinued 3TC, a component of *Dovato*.

### **Updated Dosing and Administration**

Prior to or when initiating *Dovato*, test patients for HBV infection. Pregnancy testing is recommended before initiation of *Dovato* in individuals of childbearing potential. The recommended dosage of *Dovato* in adults is one tablet taken orally once daily with or without food.<sup>(1)</sup> In patients taking *Dovato* and carbamazepine or rifampin, an additional tablet of *Tivicay* (DTG) 50 mg should be taken, separated by 12 hours from *Dovato*. Because *Dovato* is an FDC and dosage adjustments cannot be made to 3TC, *Dovato* is not recommended in patients with creatinine clearance < 30 mL/min.

### **Updated Efficacy Data**

- The efficacy of *Dovato* is supported by data from 2 randomized, double-blind, controlled trials (GEMINI-1 and GEMINI-2) in adults with no antiretroviral treatment history, and data from 2 randomized, open-label, controlled trials (TANGO and SALSA) in virologically suppressed adults.<sup>(1,4)</sup>

### **GEMINI 1&2 Results–Week 144**

Patients with screening plasma HIV-1 RNA of 1000 to ≤500,000 copies/mL were randomized 1:1 to receive DTG+3TC once daily or *Tivicay* 50 mg once daily + TDF/FTC.<sup>(1)</sup>

- In the Week 48 pooled analysis, virologic success was achieved in 91% of patients receiving DTG+3TC (N=716) and 93% receiving DTG + TDF/FTC (N=717); treatment difference: -1.7% (95% CI: -4.4%, 1.1%).<sup>(1)</sup> Through 144 weeks, 82% and 84% of patients, respectively, maintained virologic suppression.<sup>(2)</sup> None of the 12 patients receiving DTG+3TC or the 9 receiving DTG+TDF/FTC with confirmed virologic withdrawal (CVW) had treatment-emergent INSTI or NRTI substitutions detected through 144 weeks.<sup>(2)</sup> One DTG+3TC patient who did not meet CVW criteria developed M184V at Week 132 and R263R/K at week 144, conferring a 1.8-fold change in susceptibility to DTG; non-adherence to therapy was reported.
- Through week 144, overall AE profiles were similar between treatment groups and consistent with results from Week 48 and 96.<sup>(2)</sup> The most common AEs in the pooled safety population were diarrhea, nasopharyngitis, and headache.

### **TANGO Results–Week 144**

Patients were randomized to receive DOVATO once daily or continue their tenofovir alafenamide-based regimen (TBR) for up to 200 weeks.<sup>(1)</sup> Randomization was stratified by baseline third-agent class. The primary efficacy endpoint was the proportion of patients with plasma HIV-1 RNA ≥50 copies/mL (virologic non-response) at Week 48 (Snapshot algorithm, intent-to-treat population).

- In the primary analysis at Week 48, virologic non-response was <1% of patients receiving DTG/3TC (N=369) and <1% receiving TBR (N=372); treatment difference: -0.3% (95% CI: -1.2%, 0.7%).<sup>(1)</sup> Through 144 weeks, 0.3% and 1.3% of patients, respectively, experienced virologic non-response.<sup>(3)</sup> Zero patients receiving DTG/3TC and 3 patients (2 since Week 48) receiving TBR had CVW (no emergent resistance detected) through Week 144 and no resistance mutations were observed.<sup>(3)</sup>
- As observed at Week 48, cumulative incidence of drug-related AEs was higher in the DTG/3TC group than the TBR group at Week 96 (14% vs 3%, respectively) and Week 144 (15% vs 5%, respectively).<sup>(3)</sup> In the post-Week 48 analysis of AEs, rates of all AEs, drug-related AEs, serious AEs and AEs leading to discontinuation were similar between groups.
  - The most common AEs were nasopharyngitis, upper respiratory tract infection, diarrhea, and back pain.

### **SALSA Results–Week 48**

Patients were randomized to switch to DOVATO once daily or continue their current antiretroviral regimen (CAR) for up to 52 weeks.<sup>(4)</sup> Randomization was stratified by baseline third-agent class. The primary efficacy endpoint was the proportion of patients with virologic failure (plasma HIV-1 RNA ≥50 copies/mL) at Week 48 (FDA snapshot algorithm, intent-to-treat-exposed population).

- In the primary analysis at Week 48, 1 patient (0.4%) in the DTG/3TC group (N=246) and 3 patients (1.2%) in the CAR group (N=247) had HIV-1 RNA ≥50 copies/mL, demonstrating non-inferiority; treatment difference: -0.8% (95% CI: -2.4%, 0.8%).<sup>(4)</sup> Zero patients met CVW criteria in either group and therefore, no resistance testing was performed.
- Drug-related AEs through Week 48 were more frequent in the DTG/3TC group (20%) than the CAR group (6%) but comparable post-Week 24 (5% vs 2%, respectively).<sup>(4)</sup> Drug-related AEs leading to withdrawal occurred in 4 patients in the DTG/3TC group and 1 patient in the CAR group.
- The most common AEs were weight increased, headache, and COVID-19.<sup>(4)</sup>

### **Treatment Guidelines**

The DHHS recommend the use of DTG plus 3TC as an initial regimen for most people with HIV-1, except for individuals with pre-treatment HIV RNA >500,000, hepatitis B virus (HBV) coinfection, or who will initiate ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available (AI rating).<sup>(DHHS, G-4, Table 6)</sup> The panel also provides recommendations to switch patients with suppressed viral loads to DTG plus 3TC in patients who have no evidence of resistance to either drug and do not have HBV coinfection, unless the patient is also on an HBV active regimen (AI rating).<sup>(5)</sup>

**References:** 1. ViiV Healthcare Local Label. 2. Cahn P, et al. *AIDS*. 2022;36:39-48. Doi: 10.1097/QAD.0000000000003070. 3. Osileyemi O, et al. *Clin Infect Dis*. 2022;ciaco36. Doi:10.1093/cid/ciac036. Online ahead of print. 4. Libre J, et al. *Clin Infect Dis*. 2022;ciac130. Doi: 10.1093/cid/ciac130. Online ahead of print. 5. DHHS Guidelines. Available at: [clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf](https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf). Updated January 20, 2022. Accessed August 4, 2022

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## Written Testimony: Oregon Health Authority (OHA) – Updated Data, *Triumeq*

This document is a written testimony intended to summarize the key points below required for the Oregon Health Authority (OHA) review of *Triumeq*® (abacavir/dolutegravir/lamivudine).

### Updated Indication

*Triumeq* and *Triumeq PD*, are a combination of DTG (integrase transfer inhibitor [INSTI]), ABC, and lamivudine (both nucleoside analogue reverse transcriptase inhibitors) indicated for the treatment of HIV-1 in adults and pediatric patients weighing  $\geq 10$  kg.<sup>(PI, 3.1.1)</sup> *Triumeq* and *Triumeq PD* alone is not recommended in patients with resistance-associated integrase substitutions or clinically-suspected INSTI resistance, because the dose of DTG in *Triumeq* and *Triumeq PD* is insufficient in these subpopulations.

### Boxed Warnings (see attached Prescribing Information, Section 5, for further information)

- Serious and sometimes fatal hypersensitivity reactions (HSRs) have occurred with ABC-containing products and is a multi-organ clinical syndrome.<sup>(PI, 2.1.1)</sup> Patients who carry the HLA-B\*5701 allele are at a higher risk and all patients should be screened prior to first use.
- Severe acute exacerbations of hepatitis B virus (HBV) have been reported in patients co-infected with HBV who have discontinued 3TC.

### Updated Dosing

The recommended dosage of *Triumeq* in adults is one tablet taken orally once daily, with or without food.<sup>(PI, 3.3.2)</sup>

Pediatric Population Body Weight	Number of Tablets (once daily)	Recommended Daily Dose
<b><i>Triumeq PD</i> Tablets (10 kg to &lt;25 kg)</b>		
10 kg to <14 kg	4	240 mg ABC, 20 mg DTG, and 120 mg 3TC
14 kg to <20 kg	5	300 mg ABC, 25 mg DTG, and 150 mg 3TC
20 kg to <25 kg	6	360 mg ABC, 30 mg DTG, and 180 mg 3TC
<b><i>Triumeq</i> Tablets (<math>\geq 25</math> kg)</b>		
$\geq 25$ kg	1	600 mg ABC, 50 mg DTG, and 300 mg 3TC

Do not interchange *Triumeq* and *Triumeq PD* on a milligram-per-milligram basis. In patients taking certain UGT1A or CYP3A inducers, an additional tablet of *Tivicay* should be taken, separated by 12 hours from *Triumeq*. Because *Triumeq* is an FDC and cannot be dose adjusted, it is not recommended in patients with creatinine clearance < 30 mL/min or patients with hepatic impairment.

### Use in Pediatrics

- The clinical data supporting use of *Triumeq* and *Triumeq PD* in pediatric patients with HIV-1 infection weighing  $\geq 10$  kgs is derived from previously conducted pediatric trials using the individual components of *Triumeq* and *Triumeq PD*.<sup>(PI, 29.1.1)</sup>

### ARROW

- ARROW (NCT02028676) evaluated ABC and 3TC (as either single entities or a fixed dose combination) once daily, in combination with a third antiretroviral in HIV-1 infected pediatric patients who weighed  $\geq 25$  kg.<sup>(PI, 48.3.1)</sup> At week 48 and 96, 72% and 67% of patients had an HIV-1 RNA <80 copies/mL.
- One event of Grade 4 hepatitis in the once-daily cohort was considered an uncertain causality by the investigator and no additional safety issues were identified in pediatric patients compared with historical data in adults.<sup>(PI, 16.5.1)</sup>

### IMPAACT P1093

- IMPAACT P1093 (NCT01302847) evaluated the pharmacokinetics, efficacy, safety, and tolerability of DTG, in HIV-1 infected infants, children, and adolescents ages  $\geq 4$  weeks to <18 years.<sup>(PI, 48.3.1)</sup> Across all 3 cohorts, 67% (18/27) of patients weighing  $\geq 10$  kg achieved HIV-1 RNA <50 copies/mL at Week 48 (FDA Snapshot).
- Overall, the safety data in this pediatric study was similar to adults.<sup>(PI, 16.6.1)</sup>

### Treatment Guidelines

The United States Department of Health and Human Services Panel lists “[Recommended Initial Regimens for Most People with HIV.](#)” (DHHS, G-3, Table 6) Included in these 4 regimens is *Triumeq* (dolutegravir [DTG] and abacavir/lamivudine [ABC/3TC]) in patients who are HLA-B\*5701 negative). *Triumeq* is also listed as a preferred INSTI regimen as an “[Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naïve.](#)” (DHHS, C-68, Table 4) The use of *Triumeq* requires HLA-B\*5701 testing before starting therapy. The use of DTG at conception has been associated with a small increase in the risk of NTDs, but this was not seen when DTG was started during pregnancy. However, in the most recent data from Botswana, there was no longer a significant difference in NTDs with the use of DTG-containing compared to non-DTG containing ARV regimens at conception.

Revisions to the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection to address the recent FDA approval of *Triumeq PD* have not yet occurred. (DHHS Pediatric, vi.2.3) The Panel notes that this will be addressed in a future update.

### References: 1. ViiV Healthcare Local Label. 2. DHHS Guidelines. Available at:

[clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf](https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf). Updated January 20, 2022. Accessed August 4, 2022. 3. HIV Clinical Guidelines: Pediatric ARV. Available at: <https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/pediatric-arv/guidelines-pediatric-arv.pdf>. Updated April 11, 2022. Accessed August 4, 2022.

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## Ocrevus® (ocrelizumab) Clinical Summary

Please consult complete Prescribing Information

### INDICATIONS AND USAGE<sup>1</sup>

OCREVUS is a CD20-directed cytolytic antibody indicated for the treatment of adult patients with

- Relapsing forms of multiple sclerosis (RMS), to include clinically isolated syndrome, relapsing-remitting disease (RRMS), and active secondary progressive disease
- Primary progressive MS (PPMS)

### PLACE OF OCREVUS IN THERAPY

- For PPMS, Ocrevus is the first and only disease-modifying therapy (DMT) that is FDA-approved.<sup>1</sup>
- In RMS, Ocrevus may be a treatment option for both treatment-naïve and treatment-experienced patients. The majority of patients in the pivotal trials had not received a DMT within 2 years prior to study entry (73.8%/72.9%; OPERA I/II).<sup>2</sup>

### EFFICACY IN RMS CLINICAL STUDIES (OPERA I, OPERA II; PI Study 1 and 2)<sup>1, 2</sup>

The efficacy of Ocrevus compared with subcutaneous interferon (IFN) beta-1a in RMS was evaluated in two identical, Phase III, randomized (1:1), double-blind, double-dummy, head-to-head comparative trials in 1,656 patients treated for 96 weeks. During the controlled treatment period, compared with IFN beta-1a, patients with Ocrevus had:

- Reduced annualized relapse rate (ARR, primary endpoint) by 46% and 47% in OPERA I and II (both  $p < 0.0001\%$ ).
- Delayed progression of disability confirmed at 12 and 24 weeks (12- and 24-week CDP) by 40% ( $p = 0.0006$  and  $p = 0.003$ , respectively).

### OPEN-LABEL EXTENSION OF RMS CLINICAL STUDIES (OPERA I, OPERA II)<sup>3</sup>

In the open-label extension (OLE) period of the OPERA studies, all patients received Ocrevus. At the end of Year 7.5 (Year 5.5 of OLE):

- Patients who continued receiving Ocrevus in the OLE continued to have persistent reduction in ARR (0.030), and patients switching from IFN beta-1a to Ocrevus had a rapid reduction in ARR (0.032),  $p = 0.90$ .
- A lower proportion of patients who continued Ocrevus in the OLE had 24-week CDP (25.2%) compared to patients who switched from IFN beta-1a to Ocrevus (29.1%),  $p = 0.12$ .
- The safety profile of Ocrevus in the OLE was generally consistent with the double-blind period.

### SAFETY STUDY OF 2-HOUR INFUSIONS (ENSEMBLE PLUS)<sup>1,4</sup>

In a randomized, double-blind substudy to the ENSEMBLE study, 580 patients with RRMS who had received the initial dose of Ocrevus (two 300 mg infusions, separated by 14 days) were randomized 1:1 to receive subsequent Ocrevus doses administered over an infusion time of approximately 3.5 hours ( $n = 291$ ) or 2 hours ( $n = 289$ ) every 24 weeks. The frequency and severity of infusion-related reactions (IRRs) were comparable between the conventional 3.5-hour infusion and shorter 2-hour infusion groups:

- A similar proportion of patients experienced an IRR during or within 24 hours following the first randomized infusion in the 3.5-hour infusion group (23.3%) vs. in the 2-hour infusion (24.4%).
- Most IRRs were mild or moderate. One patient in each group experienced a severe (Grade 3) IRR. There were no life-threatening, fatal, or serious IRRs.

### REAL WORLD EXPERIENCE: PERSISTENCE AND ADHERENCE<sup>5,6</sup>

An analysis of a U.S. commercial claims database evaluated persistence and adherence through 24 months to Ocrevus compared with other injectable, oral, or IV DMTs in 1,710 patients who either initiated or switched to a new DMT between April 2016 and December 2019. At 24 months:

- Persistence was higher in the Ocrevus group (75%) than the other IV (55%), oral (54%), and injectable (33%) DMT groups
- Adherence was higher in the Ocrevus group (80%) than the other IV (54%), oral (55%), and injectable (35%) DMT groups
- Patients in the other DMT groups had a 1.8- to 2.5-fold increased risk of nonpersistence and 2.2- to 3.0-fold increased risk of nonadherence compared with the Ocrevus group
- Persistence and adherence to all DMTs for MS were associated with lower total healthcare costs vs nonpersistence and nonadherence with a reduction of \$19,230 and \$16,091 in total healthcare costs (includes outpatient services, hospitalizations, and emergency department visits), respectively.

### CONTRAINDICATIONS<sup>1</sup>

Ocrevus is contraindicated in patients with an active hepatitis B virus infection and in patients with a history of life-threatening infusion reactions to Ocrevus.

### WARNINGS AND PRECAUTIONS<sup>1</sup>

- **Infusion reactions:** Management recommendations for infusion reactions depend on the type and severity of the reaction. Permanently discontinue Ocrevus if a life-threatening or disabling infusion reaction occurs.
- **Infections:** Delay Ocrevus administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with Ocrevus and after discontinuation, until B-cell repletion.
- **Progressive Multifocal Leukoencephalopathy (PML):** Withhold Ocrevus at the first sign or symptom suggestive of PML
- **Reduction in immunoglobulins:** Monitor the level of immunoglobulins at the beginning of treatment. Monitor during and after discontinuation of treatment with Ocrevus, until B-cell repletion, and especially when recurrent serious infections are suspected. Consider discontinuing Ocrevus in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.
- **Malignancies:** An increased risk of malignancy, including breast cancer, may exist with Ocrevus.
- **Immune-Mediated Colitis:** Immune-mediated colitis has been reported in the postmarketing setting. Monitor patients for new or persistent diarrhea or other gastrointestinal symptoms, and evaluate promptly if colitis is suspected

## ADVERSE REACTIONS<sup>1</sup>

The most common adverse reactions were:

- RMS (incidence  $\geq 10\%$  and  $>$  IFN beta-1a): upper respiratory tract infections and infusions reactions.
- PPMS (incidence  $\geq 10\%$  and  $>$  placebo): upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections.

## REFERENCES:

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5. Pardo G, Pineda ED, Ng CD, Bawa KK, Sheinson D, Bonine NG. Adherence to and persistence with disease-modifying therapies for multiple sclerosis over 24 months: a retrospective claims analysis. Neurol Ther. 2022;11(1):337-351.
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The document provides clinical information regarding SOTYKTU™. This document contains relevant information for SOTYKTU which may or may not be included in the [U.S. Prescribing Information \(USPI\)](#). BMS does not suggest or recommend the use of SOTYKTU in any manner other than as described in the USPI.

### SOTYKTU™ (deucravacitinib)<sup>1</sup>

**Indications:** Deucravacitinib is a tyrosine kinase 2 (TYK2) inhibitor indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

**Limitations of Use:** Deucravacitinib is not recommended for use in combination with other potent immunosuppressants.

**Mechanism of action:** Deucravacitinib is an inhibitor of TYK2. TYK2 is a member of the Janus kinase (JAK) family. Deucravacitinib binds to the regulatory domain of TYK2, stabilizing an inhibitory interaction between the regulatory and the catalytic domains of the enzyme. This results in allosteric inhibition of receptor-mediated activation of TYK2 and its downstream activation of Signal Transducers and Activators of Transcription (STATs) as shown in cell-based assays. JAK kinases, including TYK2, function as pairs of homo- or heterodimers in the JAK-STAT pathways. TYK2 pairs with JAK1 to mediate multiple cytokine pathways and also pairs with JAK2 to transmit signals as shown in cell-based assays. The precise mechanism linking inhibition of TYK2 enzyme to therapeutic effectiveness in the treatment of adults with moderate to severe plaque psoriasis is not currently known.

**Dosage and administration:** 6 mg taken orally once daily, with or without food. Do not crush, cut, or chew the tablets.

### POETYK PSO-1 and POETYK PSO-2 (Registrational Studies)

**POETYK PSO-1** was a 52-week, phase 3, multicenter, randomized, double-blind, placebo- and active comparator (apremilast)-controlled study that evaluated the efficacy and safety of deucravacitinib in 666 patients aged ≥ 18 years with moderate to severe plaque psoriasis. Patients were randomized 2:1:1 to receive oral deucravacitinib 6 mg once daily (QD; n = 332), placebo twice daily (BID; n = 166), or apremilast 30 mg BID (n = 168) for 16 weeks. After 16 weeks, patients randomized to placebo switched to deucravacitinib 6 mg QD and patients randomized to deucravacitinib continued the same treatment until Week 52. For patients randomized to apremilast, those with 50% improvement from baseline in PASI (PASI 50) at Week 24 continued the same treatment, while those with PASI < 50 were switched to deucravacitinib 6 mg QD.<sup>2</sup>

**POETYK PSO-2** was a 52-week, phase 3, multicenter, randomized, double-blind, placebo- and active comparator (apremilast)-controlled study to evaluate the efficacy and safety of deucravacitinib in 1020 patients aged ≥ 18 years with moderate to severe plaque psoriasis.<sup>3,4</sup> Patients were randomized in a 2:1:1 ratio to receive oral deucravacitinib 6 mg QD (n = 511) for 24 weeks, placebo BID (n = 255) for 16 weeks, or apremilast 30 mg BID (n = 254) for 24 weeks. For patients initially randomized to deucravacitinib, there was a randomized withdrawal period in which those with PASI ≥ 75 at Week 24 were rerandomized 1:1 to receive placebo or continue deucravacitinib until Week 52, while those with PASI < 75 at Week 24 continued deucravacitinib through Week 52. Patients initially randomized to placebo switched to deucravacitinib 6 mg QD at Week 16 through Week 52. For patients initially randomized to apremilast, those who achieved PASI ≥ 75 at Week 24 were switched to placebo through Week 52, while those with PASI < 75 at Week 24 were switched to deucravacitinib 6 mg QD through Week 52.<sup>4</sup>

### **Co-primary efficacy endpoints at Week 16**

- **75% improvement from baseline in PASI (PASI 75):** In **PSO-1**, a significantly greater proportion of patients in the deucravacitinib arm achieved PASI 75 at Week 16 than in the placebo arm (58.4% vs 12.7%, respectively;  $P < 0.0001$ ). Patients in the deucravacitinib arm had significantly greater PASI 75 response rates than patients in the apremilast arm at Week 16 (58.4% vs 35.1%, respectively;  $P < 0.0001$ ) and Week 24 (69.3% vs 38.1%, respectively;  $P < 0.0001$ ).<sup>2</sup> In **PSO-2**, a significantly greater proportion of patients in the deucravacitinib arm achieved PASI 75 at Week 16 than in the placebo arm (53.0% vs 9.4%, respectively;  $P < 0.0001$ ). Patients in the deucravacitinib arm had significantly greater PASI 75 response rates than patients in the apremilast arm at Week 16 (53.0% vs 39.8%, respectively;  $P = 0.0004$ ) and Week 24 (58.7% vs 37.8%, respectively;  $P < 0.0001$ ).<sup>3</sup>
- **Static physician global assessment score (sPGA) 0/1:** In **PSO-1**, a significantly greater proportion of patients in the deucravacitinib arm achieved sPGA 0/1 response at Week 16 than in the placebo arm (53.6% vs 7.2%, respectively;  $P < 0.0001$ ). Patients in the deucravacitinib arm had significantly greater sPGA 0/1 response rates than patients in the apremilast arm at Week 16 (53.6% vs 32.1%, respectively;  $P < 0.0001$ ) and Week 24 (58.7% vs 31.0%, respectively;  $P < 0.0001$ ).<sup>2</sup> In **PSO-2**, a significantly greater proportion of patients in the deucravacitinib arm achieved sPGA 0/1 response at Week 16 than in the placebo arm (49.5% vs 8.6%, respectively;  $P < 0.0001$ ). Patients in the deucravacitinib arm had significantly greater sPGA 0/1 response rates than patients in the apremilast arm at Week 16 (49.5% vs 33.9%, respectively;  $P < 0.0001$ ) and Week 24 (49.8% vs 29.5%, respectively;  $P < 0.0001$ ).<sup>3</sup>

### **PASI 75 and sPGA 0/1 results beyond Week 16**

- **PASI 75:** In **PSO-1**, patients treated continuously with deucravacitinib from Day 1 maintained PASI 75 responses through Week 52, with 65.1% achieving PASI 75 at Week 52. Patients who switched from placebo to deucravacitinib at Week 16 demonstrated a PASI 75 response rate at Week 52 and percentage change in PASI score from baseline to Week 52 comparable to those observed in patients who received continuous deucravacitinib from Day 1 (PASI 75 response rate: 68.3% vs 65.1%; change in PASI score: -80.5% vs -78.4%, respectively).<sup>2</sup> In **PSO-2**, most Week 24 PASI 75 responders who were rerandomized to continuous treatment with deucravacitinib maintained PASI 75 response through Week 52, with 80.4% achieving PASI 75 at Week 52. In contrast, among Week 24 PASI 75 responders who were rerandomized to placebo (withdrawal of deucravacitinib), 31.3% achieved PASI 75 at Week 52; the median time to loss of PASI 75 response in patients rerandomized to placebo was 85 days.<sup>3</sup>
- **sPGA 0/1:** In **PSO-1**, patients treated continuously with deucravacitinib from Day 1 maintained sPGA 0/1 responses through Week 52, with 52.7% achieving sPGA 0/1 at Week 52. Patients who switched from placebo to deucravacitinib at Week 16 had a sPGA 0/1 response rate at Week 52 comparable to that observed in patients who received continuous deucravacitinib from Day 1 (53.8% vs 52.7%, respectively).<sup>2</sup> In **PSO-2**, most Week 24 PASI 75 responders who were rerandomized to continuous treatment with deucravacitinib maintained sPGA 0/1 response through Week 52, with 70.3% achieving sPGA 0/1 at Week 52.<sup>5</sup>

**PSO-1 and PSO-2 Years 1 and 2 safety data found in table on Page 2.**

### **Secondary efficacy endpoints**

For statistical analysis of secondary endpoints, the co-primary endpoints (PASI 75 and sPGA 0/1) had to demonstrate statistical significance. Hierarchical testing was used for comparisons of deucravacitinib with apremilast and with placebo separately; statistical significance ( $P < 0.025$ ) had to be achieved for each preceding secondary endpoint to proceed to the next secondary endpoint.<sup>2,4</sup>



- **90% improvement from baseline in PASI (PASI 90):** In **PSO-1**, a significantly greater proportion of patients achieved PASI 90 at Week 16 with deucravacitinib than with placebo or apremilast (35.5% vs 4.2% and 19.6%, respectively;  $P < 0.0001$  vs placebo and  $P = 0.0002$  vs apremilast); this difference remained significant vs apremilast at Week 24 (42.2% vs 22.0%, respectively;  $P < 0.0001$ ).<sup>2</sup> In patients who received continuous deucravacitinib from Day 1, PASI 90 response was maintained through Week 52, with 44.0% achieving PASI 90 at Week 52.<sup>5</sup> In **PSO-2**, a significantly greater proportion of patients achieved PASI 90 at Week 16 with deucravacitinib than with placebo or apremilast (27.0% vs 2.7% and 18.1%, respectively;  $P < 0.0001$  vs placebo and  $P = 0.0046$  vs apremilast); this difference remained significant vs apremilast at Week 24 (32.5% vs 19.7%, respectively;  $P < 0.0001$ ).<sup>3</sup>
- **100% improvement from baseline in PASI (PASI 100):** In **PSO-1**, a significantly greater proportion of patients achieved PASI 100 at Week 16 with deucravacitinib than with placebo or apremilast (14.2% vs 0.6% and 3.0%, respectively;  $P < 0.0001$  for both comparisons); this difference remained significant vs apremilast at Week 24 (17.5% vs 6.5%, respectively;  $P = 0.0007$ ).<sup>2</sup> In patients who received continuous deucravacitinib from Day 1, PASI 100 response was maintained through Week 52, with 19.3% achieving PASI 100 at Week 52.<sup>5</sup> In **PSO-2**, a significantly greater proportion of patients achieved PASI 100 at Week 16 with deucravacitinib than with placebo or apremilast (10.2% vs 1.2% and 4.3%, respectively;  $P < 0.0001$  vs placebo and  $P = 0.0051$  vs apremilast); PASI 100 response rates at Week 24 were 13.1% with deucravacitinib vs 6.7% with apremilast.<sup>3</sup>
- **Scalp-specific Physician Global Assessment (ss-PGA) 0/1:** In **PSO-1**, among patients with scalp psoriasis at baseline (ss-PGA  $\geq 3$ ), a significantly greater proportion achieved an ss-PGA 0/1 response at Week 16 with deucravacitinib than with placebo or apremilast (70.3% vs 17.4% and 39.1%, respectively;  $P < 0.0001$  for both comparisons); this difference remained significant vs apremilast at Week 24 (72.2% vs 42.7%;  $P < 0.0001$ ).<sup>2</sup> In patients treated continuously with deucravacitinib from Day 1, ss-PGA 0/1 response was maintained through Week 52, with 65.6% achieving ss-PGA 0/1 at Week 52. Likewise, 69.7% of patients who switched from placebo to deucravacitinib at Week 16 achieved ss-PGA 0/1 response rates at Week 52 comparable to those observed in patients who received continuous deucravacitinib from Day 1.<sup>5</sup> In **PSO-2**, among patients with scalp psoriasis at baseline (ss-PGA  $\geq 3$ ), a significantly greater proportion achieved an ss-PGA 0/1 response at Week 16 with deucravacitinib than with placebo or apremilast (59.7% vs 17.3% and 36.7%, respectively;  $P < 0.0001$  for both comparisons); this difference remained significant vs apremilast at Week 24 (59.0% vs 41.6%, respectively;  $P = 0.0003$ ).<sup>3</sup>

### POETYK PSO-LTE (Non-registrational Study)

**POETYK PSO-LTE** is an ongoing, phase 3, open-label, single-arm study to evaluate the long-term safety and efficacy of deucravacitinib in patients with moderate to severe plaque psoriasis. Patients who completed PSO-1 or PSO-2 could enroll in PSO-LTE after 52 weeks, in which they receive open-label deucravacitinib 6 mg QD (N = 1519). An interim analysis was completed with a cutoff date of October 1, 2021.<sup>6,7</sup> The proportions of patients who achieved PASI 75, PASI 90 and sPGA 0/1 at 2 years as observed were similar regardless of prior treatment received in the parent trials. At Week 60, the proportions of deucravacitinib treated patients who achieved PASI 75 and sPGA 0/1 as observed were 79.4% and 60.0%, respectively. The sensitivity analyses supported as-observed results, with comparable response rates seen using treatment failure rules (TFR) or modified nonresponder imputation (mNRI). PASI 75 response rate at Week 60 was 77.7% using TFR and 75.7% using mNRI; sPGA 0/1 response rate was 58.7% using TFR and 57.1% using mNRI.<sup>7</sup>

### Integrated safety analysis of POETYK PSO-1, PSO-2, and PSO-LTE: Summary of safety in Years 1 and 2

Event	PSO-1 and PSO-2: Year 1 safety pool (Weeks 0–52)						PSO-1, PSO-2, and PSO-LTE: Year 2 safety pool	
	Deucravacitinib (n = 1364; total PY, 969.0)		Placebo (n = 666; total PY, 240.9)		Apremilast (n = 422; total PY, 221.1)		Deucravacitinib (n = 1519; total PY, 2482.0) <sup>b</sup>	
	n (%)	EAIR/100 PY	n (%)	EAIR/100 PY	n (%)	EAIR/100 PY	n (%)	EAIR/100 PY
Any AE	995 (72.9)	229.2	347 (52.1)	217.4	299 (70.9)	281.1	1214 (79.9)	154.4
SAEs	55 (4.0)	5.7	14 (2.1)	5.7	9 (2.1)	4.0	145 (9.5)	6.1
AEs leading to discontinuation	43 (3.2)	4.4	23 (3.5)	9.3	26 (6.2)	11.6	69 (4.5)	2.8
Deaths	2 (0.1) <sup>a</sup>	0.2	1 (0.2)	0.4	1 (0.2)	0.4	10 (0.7)	0.4
<b>Most common AEs (EAIR <math>\geq 5</math>/100 PY) in any active treatment arm</b>								
Nasopharyngitis	229 (16.8)	26.1	54 (8.1)	22.7	54 (12.8)	25.9	271 (17.8)	12.9
URTI	124 (9.1)	13.4	33 (5.0)	13.5	27 (6.4)	12.4	150 (9.9)	6.5
COVID-19	5 (0.4)	0.5	NR	NR	NR	NR	124 (8.2)	5.1
Headache	80 (5.9)	8.5	21 (3.2)	8.6	53 (12.6)	26.0	99 (6.5)	4.2
Arthralgia	55 (4.0)	5.7	NR	NR	NR	NR	85 (5.6)	3.5
Diarrhea	69 (5.1)	7.3	28 (4.2)	11.5	54 (12.8)	26.5	84 (5.5)	3.5

<sup>a</sup> One additional death occurred between Week 16 and 52 due to hepatocellular carcinoma in a patient with a history of hepatitis C virus infection and liver cirrhosis.

<sup>b</sup> This represents the pooled PSO-1 and PSO-2 population enrolled in the LTE through the 120-day cutoff date of October 1, 2021.

Abbreviations: AE, adverse event; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; NR, not reported; PY, patient-year; SAE, serious adverse event; URTI, upper respiratory tract infection. Adapted with permission from Alexis A, et al. Poster presentation at WCDC: January 14–19, 2022; Kauai, HI, and Virtual.<sup>8</sup> and Warren RB, et al. Poster presentation at SDDS; March 11–13, 2022; San Diego, CA.<sup>6</sup>

**References:** 1. SOTYKTU [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company, September 2022. 2. Armstrong AW, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. J Am Acad Dermatol. 2022.3. Strober B, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 POETYK PSO-2 trial. J Am Acad Dermatol. 2022.4. Strober B, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 POETYK PSO-2 trial. Supplementary material. J Am Acad Dermatol. 2022. 5. Warren RB, et al. Deucravacitinib, an oral, selective tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: 52-week efficacy results from the phase 3 POETYK PSO-1 and POETYK PSO-2 trials. Oral presentation at the European Academy of Dermatology and Venereology (EADV) 30th Congress; September 29–October 2, 2021; Virtual. Presentation 2857. 6. Warren RB, et al. Deucravacitinib long-term safety in plaque psoriasis: 2-year results from the phase 3 POETYK PSO program. Poster presentation at the San Diego Dermatology Symposium (SDDS); March 11–13, 2022; San Diego, CA. 7. Warren RB, et al. Deucravacitinib long-term efficacy and safety in plaque psoriasis: 2-year results from the phase 3 POETYK PSO program. Poster presentation at the European Academy of Dermatology and Venereology (EADV) Spring Symposium; May 12–14, 2022; Ljubljana, Slovenia.8. Alexis A, et al. Deucravacitinib, an oral, selective tyrosine kinase 2 (TYK2) inhibitor: infection-related adverse events in the phase 3 POETYK PSO-1 and PSO-2 trials. Poster presentation at the 2022 Winter Clinical Dermatology Conference – Hawaii® (WCDC); January 14–19, 2022; Kauai, HI, and Virtual.



OSU College of Pharmacy - Drug Use Research & Management  
OHA Health Policy & Analytics, Office of Delivery System Innovation  
500 Summer Street Northeast, E35  
Salem, OR 97301-1079

October 4, 2022

Dear OSU College of Pharmacy - Drug Use Research & Management,

Thank you for your request about Sotyktu® (deucravacitinib) which has been forwarded to Medical Information by Uchechukwu Mordi. You have requested information regarding a written testimony request for Sotyktu (deucravacitinib) for Oregon Medicaid.

Please note that Bristol Myers Squibb does not recommend the use of SOTYKTU in any manner inconsistent with that described in the Full Prescribing Information. Please review the end of this letter for full indications and boxed warnings, and consult the attached Full Prescribing Information for SOTYKTU.

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# SOTYKTU™ - Medicaid Summary

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## Summary

Thank you for your unsolicited request regarding the Medicaid Summary for SOTYKTU™ (deucravacitinib).

As requested, please find the following attached:

### – Oregon Medicaid Summary

#### Important Safety Information

- **Hypersensitivity:** Hypersensitivity reactions such as angioedema have been reported in subjects receiving SOTYKTU. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue SOTYKTU.
- **Infections:** SOTYKTU may increase the risk of infections. Serious infections have been reported in subjects with psoriasis who received SOTYKTU. The most common serious infections reported with SOTYKTU included pneumonia and COVID-19. Avoid use of SOTYKTU in patients with an active or serious infection. Consider the risks and benefits of treatment prior to initiating SOTYKTU in patients:
  - with chronic or recurrent infection
  - who have been exposed to TB
  - with a history of a serious or an opportunistic infection
  - with underlying conditions that may predispose them to infection.

Closely monitor patients for the development of signs and symptoms of infection during and after treatment with SOTYKTU. A patient who develops a new infection during treatment with SOTYKTU should undergo prompt and complete diagnostic testing; appropriate antimicrobial therapy should be initiated; and the patient should be closely monitored. Interrupt SOTYKTU if a patient develops a serious infection. Do not resume SOTYKTU until the infection resolves or is adequately treated.

- **Viral reactivation:** Herpes virus reactivation (e.g. herpes zoster, herpes simplex), was reported in clinical trials with SOTYKTU. In the 16-week placebo-controlled period, herpes simplex infections were reported in 17 subjects (6.8/100 PY) treated with SOTYKTU, and 1 subject (0.8/100 PY) treated with placebo. Multidermatomal herpes zoster was reported in a subject who received SOTYKTU. During PSO-1, PSO-2, and the open-label extension trial in which subjects who completed the controlled trials could enroll, the majority of subjects who reported events of herpes zoster while receiving SOTYKTU were under 50 years of age. The impact of SOTYKTU on chronic viral hepatitis reactivation is unknown. Subjects with positive screening tests for hepatitis B or C, chronic hepatitis B, or untreated hepatitis C, were excluded from clinical trials. Consider viral hepatitis screening and monitoring for reactivation in accordance with clinical guidelines before starting therapy and during therapy with SOTYKTU. If signs of reactivation occur, consult a hepatitis specialist. SOTYKTU is not recommended for use in patients with active hepatitis B or hepatitis C.
- **Tuberculosis (TB):** In clinical trials, of 4 subjects with latent TB who were treated with SOTYKTU and received appropriate TB prophylaxis, no subjects developed active TB (during the mean follow-up of 34 weeks). One subject, who did not have latent TB, developed active TB after receiving 54 weeks of SOTYKTU. Evaluate patients for latent and active TB infection prior to initiating treatment with SOTYKTU. Do not administer

SOTYKTU to patients with active TB. Initiate treatment of latent TB prior to administering SOTYKTU. Consider anti-TB therapy prior to initiation of SOTYKTU in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients receiving SOTYKTU for signs and symptoms of active TB during treatment.

- **Malignancy and lymphoproliferative disorders:** Malignancies, including lymphomas, were observed in clinical trials with SOTYKTU. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with SOTYKTU, particularly in patients with a known malignancy (other than a successfully treated non-melanoma skin cancer and patients who develop a malignancy when on treatment with SOTYKTU).
- **Rhabdomyolysis and elevated CPK:** Cases of rhabdomyolysis were reported in subjects treated with SOTYKTU resulting in interruption or discontinuation of SOTYKTU dosing. Treatment with SOTYKTU was associated with an increased incidence of asymptomatic CPK elevation and rhabdomyolysis compared to treatment with placebo. Discontinue SOTYKTU if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Instruct patients to promptly report any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.
- **Laboratory abnormalities:**
  - Triglyceride elevations – Treatment with SOTYKTU was associated with increases in triglyceride levels. The effect of this elevated parameter on cardiovascular morbidity and mortality has not been determined. Periodically evaluate serum triglycerides according to the clinical guidelines for hyperlipidemia while patients are receiving treatment with SOTYKTU. Manage patients according to clinical guidelines for the management of hyperlipidemia.
  - Liver enzyme elevations – Treatment with SOTYKTU was associated with increased incidence of liver enzyme elevation compared to treatment with placebo. Liver serum transaminase elevations  $\geq 3$  times the upper limit of normal were reported in subjects treated with SOTYKTU. Evaluate liver enzymes at baseline and thereafter according to routine patient management. If treatment-related increases in liver enzymes occur and drug-induced liver injury is suspected, interrupt SOTYKTU until a diagnosis of liver injury is excluded.
- **Immunizations:** Prior to initiating therapy with SOTYKTU, consider completion of all age-appropriate immunizations according to current immunization guidelines including prophylactic herpes zoster vaccination. Avoid use of live vaccines in patients treated with SOTYKTU. The response to live or non-live vaccines has not been evaluated.
- **Potential risks related to JAK inhibition:** It is not known whether TYK2 inhibition may be associated with the observed or potential adverse reactions of JAK inhibition. In a large, randomized, postmarketing safety trial of a JAK inhibitor in RA patients 50 years of age and older with at least 1 cardiovascular risk factor, higher rates of all-cause mortality, including sudden cardiovascular death, MACE, overall thrombosis, deep venous thrombosis, pulmonary embolism, and malignancies (excluding non-melanoma skin cancer) were observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. SOTYKTU is not approved for use in RA.

**For full prescribing information, please refer to the enclosed SOTYKTU package insert.**



**Product Indication: Sotyktu® (deucravacitinib):**

SOTYKTU is a tyrosine kinase 2 (TYK2) inhibitor indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Please refer to the end of this information packet for the following:

- Reporting adverse event cases or product quality complaints, or to provide information on exposure to a BMS product during pregnancy or lactation.

With the aim to continuously improve the quality of our service we would like to request you complete a brief satisfaction survey. It will only take you 3 minutes to complete. The survey can be accessed at the below link:

[Click here](#)

We trust that you will find this information helpful. If you have further questions or require additional information, please contact BMS Medical Information Department at 1-800-321-1335.

Sincerely,  
BMS Medical Information

## For Your Consideration:

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### **Adverse Event / Pregnancy**

If you become aware of a patient who has experienced an adverse event with a BMS product, has received treatment with a BMS product during pregnancy or lactation, or has become pregnant while her partner received treatment with a BMS product, please contact us at 1-800-721-5072.

### **Investigational Product Statement**

There may be information included that pertains to an investigational therapy that has not yet been approved for use in your country. The safety and efficacy of investigational therapies and/or uses have not been established. There is no guarantee that the investigational therapies will receive health authority approval or become commercially available in any country for the uses being investigated.