CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Division of Risk Management (DRM)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Reviewer Name	Donella Fitzgerald, PharmD, DRM
Associate Director	Jacqueline Sheppard, PharmD, DRM
Review Completion Date	March 13, 2026
Subject	Evaluation of Need for a REMS
Established Name	icotrokinra
Trade Name	Icotyde
Name of Applicant	Janssen Biotech Inc.
Therapeutic Class	Interleukin-23 receptor antagonist
Dosage Form(s)	200 mg oral tablet
Dosing Regimen	One tablet by mouth once daily

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1. Introduction

This review by the Division of Risk Management (DRM) evaluates whether a risk evaluation and mitigation strategy (REMS) for the new molecular entity (NME) Icotyde (icotrokinra) is necessary to ensure the benefits outweigh its risks. Janssen Biotech Inc. (Applicant) submitted a New Drug Application (NDA) 220149 for icotrokinra with the proposed indication for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who are candidates for systemic therapy or phototherapy. During the course of the review, the Division of Dermatology and Dentistry (DDD) revised the indication to the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40 kg who are candidates for systemic therapy or phototherapy. The Applicant did not submit a proposed REMS or risk management plan with this application.

2. Background

2.1. Product Information

Icotrokinra, a new molecular entity (NME),[a] is an interleukin-23 receptor (IL-23R) antagonist that is proposed for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who are candidates for systemic therapy or phototherapy. During the course of the review, the Division of Dermatology and Dentistry (DDD) revised the indication to the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40 kg who are candidates for systemic therapy or phototherapy. Icotrokinra is a first-in-class orally administered peptide that selectively binds to the IL-23R to competitively antagonize the binding of IL-23, resulting in inhibition of proximal IL-23R signaling and downstream effector functions such as cytokine secretion. Icotrokinra is proposed as a 200 mg oral tablet to be taken by mouth once daily for chronic treatment.[b] It is not currently approved in any jurisdiction.

2.2. Regulatory History

The following is a summary of the regulatory history for NDA 220149 relevant to this review:

- 07/18/2025: NDA 220149, icotrokinra, submission for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who are candidates for systemic therapy or phototherapy received.
- 11/04/2025: A Mid-cycle meeting was held between the Agency and the Applicant via teleconference. The Agency informed the Applicant that based on the currently available data, there were no safety issues that require a REMS for the application.

[a] Section 505-1 (a) of the FD&C Act: *FDAAA factor (F): Whether the drug is a new molecular entity*

[b] Section 505-1 (a) of the FD&C Act: *FDAAA factor (D): The expected or actual duration of treatment with the drug.*

3. Therapeutic Context and Treatment Options

3.1. Description of the Medical Condition

Psoriasis is a chronic inflammatory, immune-mediated skin disorder affecting approximately 7.5 million people in the United States (Warycha, 2021).[c] It is characterized by well-demarcated, erythematous scaly plaques on the skin. The plaques are typically found on the elbows, knees, lower back and scalp, but can develop anywhere on the body. Moderate to severe plaque psoriasis is typically defined as involvement of more than 5-10% of the body surface area (Feldman, 2022). Psoriasis can have a fluctuating relapsing course. Flares may be induced by factors such as infections, trauma, smoking and stress. Moderate-to-severe psoriasis can have a profound effect on quality of life, as it has been associated with increased risk of depression, sleep disturbances, social stigma and decreased work productivity (Kupetsky, 2013).[d]

3.2. Description of Current Treatment Options

There are numerous therapies available for the treatment of moderate-to-severe plaque psoriasis. The initial decision point when choosing psoriasis therapy is usually between local (topical) and full body (systemic or phototherapy) treatment. Because patients with moderate-to-severe psoriasis typically have more than 5% of their body surface area affected, the sole use of topical agents is not practical and often unsuccessful (Feldman, 2022). Topical agents such as emollients, corticosteroids, retinoids, vitamin D analogs, and calcineurin inhibitors, are often used as adjuncts for resistant, localized lesions in patients who are undergoing systemic treatment or phototherapy.

Biologic agents include the most effective therapies for moderate-to-severe plaque psoriasis (Feldman, 2022). A comparison of biologic therapies approved for the treatment of moderate-to-severe plaque psoriasis is included in the Appendix of this review. Several of the biologic agents were approved with a REMS that consisted of a Medication Guide (MG) and Communication Plan to mitigate the risks of infections and malignancies; this includes etanercept, adalimumab, certolizumab pegol, infliximab and ustekinumab. The REMS for these agents were released in 2011, with the exception of the ustekinumab REMS that was released in 2017. Brodalumab, an interleukin-17 receptor antagonist, was approved to treat moderate-to-severe plaque psoriasis in 2017 with a REMS to mitigate the risk of suicidal ideation and behavior including completed suicides. The REMS includes prescriber and pharmacy certification, as well as documentation of safe use conditions.

[c] Section 505-1 (a) of the FD&C Act: *FDAAA factor (A): The estimated size of the population likely to use the drug involved.*

[d] Section 505-1 (a) of the FD&C Act: *FDAAA factor (B): The seriousness of the disease or condition that is to be treated with the drug*

Other options for systemic therapy include retinoids and immunosuppressive or immunomodulatory drugs such as methotrexate, cyclosporine, apremilast, deucravacitinib. Non-pharmacological agents are also used in the treatment of moderate-to-severe plaque psoriasis. The use of ultraviolet light in therapeutic doses is used as phototherapy. Phototherapy can be used alone or in combination with saltwater baths. Dietary supplements such as turmeric, vitamin D and zinc have also been used.

Although there are numerous options for treatment, there is no cure for plaque psoriasis. It is a chronic disease that often requires long-term treatment. Current therapies have varying effectiveness in patients and may be associated with limitations related to parental administration, poor adherence, tolerability and safety. An unmet medical need remains for additional therapeutic options, especially oral agents.

4. Benefit Assessment

Efficacy of icotrokinra for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who are candidates for systemic therapy or phototherapy was evaluated in four multi-center, randomized, double-blind, placebo and/or active comparator-controlled trials (Trial PSO3001 [NCT06143878], Trial PSO3002 [NCT06220604], Trial PSO3003 [NCT06095115], and Trial PSO3004 [NCT06095102]) as summarized below in Table 1. Moderate-to-severe plaque psoriasis was defined as Investigator's Global Assessment (IGA) score ≥3, a Psoriasis Area and Severity Index (PASI) score ≥12, and body surface area (BSA) involvement ≥10%.

Table 1: Icotrokinra Clinical Development Program (Lim, 2026)

Trial ID	Design	Treatment/ Sample Size	Endpoint/Analysis
PSO3001	MC, R, DB, PG, PC trial (16 wks); ≥12 years of age	Icotrokinra/ 456 Placebo/ 228	Co-Primary: • IGA 0/1 and a ≥2-grade improvement from baseline at Week 16 • PASI-90 response at Week 16
PSO3002	MC, R, DB, PG, PC, AC (16 wks)	Icotrokinra/ 311 Placebo/ 156 Deucravacitinib/ 307	
PSO3004	MC, R, DB, PG, PC, AC (16 wks)	Icotrokinra/ 322 Placebo/ 82 Deucravacitinib/ 327	
PSO3003	MC, R, DB, PG, PC (16 wks); ≥12 years of age	Icotrokinra/ 208 Placebo/ 103	Primary: IGA 0/1 and a ≥2-grade improvement from baseline at Week 16

MC = multicenter; R = randomized; DB = double-blind; PG = parallel-group; PC = placebo-controlled; AC = active-controlled; wks = weeks

PSO3001: Subjects were randomized to receive either icotrokinra (200 mg orally once daily) or placebo for 16 weeks.

PSO3002 and PSO3004: Subjects were randomized to either icotrokinra 200 mg orally once daily, deucravacitinib 6 mg orally once daily or placebo. At Week 16, subjects originally randomized to placebo received icotrokinra 200 mg orally once daily thereafter. At Week 24, subjects originally randomized to deucravacitinib received icotrokinra 200 mg orally once daily thereafter.

PSO3003: Subjects were randomized to receive either icotrokinra 200 mg orally once daily or placebo for 16 weeks. At Week 16, subjects originally randomized to placebo switched to receive icotrokinra 200 mg orally once daily, and subjects randomized to icotrokinra at baseline remained on treatment through the end of study.

The coprimary endpoints for studies PSO3001, PSO3002 and PSO3004 were (1) IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16 and (2) PASI 90 at Week 16. For study PSO3003, the primary endpoint was IGA (overall) score of 0/1 and a ≥2-grade improvement from baseline at Week 16.

PHASE 3 STUDY RESULTS

Table 2: Icotrokinra Phase 3 Studies Primary Endpoint Results (DDD, 2026)

	Icotrokinra	Placebo	Difference	p-value
PSO3001				
IGA	64.7%	8.3%	56.4%	<0.001
PASI90	49.6%	4.4%	49.6%	<0.001
PSO3002				
IGA	68.5%	10.9%	57.6%	<0.001
PASI90	55.0%	3.8%	51.2%	<0.001
PSO3003				
IGA	56.7%	5.8%	51.1%	<0.001
PSO3004				
IGA	70.5%	8.5%	62.1%	<0.001
PASI90	57.1%	1.2%	56.0%	<0.001

In all four Phase 3 Studies, icotrokinra was superior to placebo for the co-primary or primary (PSO3003) endpoints with p-value <0.001 for each individual study. The clinical team concluded that icotrokinra is effective for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who are candidates for systemic therapy or phototherapy (DDD, 2026).[e]

During the course of the review, the DDD revised the indication to the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40 kg who are candidates for systemic therapy or phototherapy. The indication was revised to incorporate the minimum weight requirement from the inclusion criteria in the clinical trials.

5. Risk Assessment & Safe-Use Conditions

The safety of icotrokinra for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic or phototherapy was assessed primarily using data from the four Phase 3 trials

[e] Section 505-1 (a) of the FD&C Act*: FDAAA factor (C): The expected benefit of the drug with respect to such disease or condition.*

(PSO3001, PSO3002, PSO3003, PSO3004). The size of the overall safety database included 1816 pooled icotrokinra subjects exposed through the safety cutoff date.

Five deaths were reported in the icotrokinra psoriasis development program, all of which occurred in icotrokinra-treated subjects. The causes of death were reported as hematemesis, myocardial infarction, squamous cell carcinoma of the lung, gastrointestinal (GI) hemorrhage, and cocaine induced hypertensive cardiovascular disease. The DDD consulted the Division of Gastroenterology (DG) to assist with adjudication of the hematemesis and GI hemorrhage deaths. DG did not attribute these deaths to icotrokinra and stated that there are alternative, plausible explanations for the GI fatalities (DDD, 2026). DDD agreed with DG's analysis and subsequently concluded that all five deaths in the icotrokinra treated subjects were unlikely due to study drug.

Serious adverse events (SAEs) were reported in the icotrokinra clinical development program. SAEs that occurred in the pooled 16-week placebo-controlled period are presented by system organ class in table 3 below.

Table 3: Subjects with SAEs Through Week 16 by System Organ Class for Pooled Phase 3 Studies (PSO3001, PSO3002, PSO3003, PSO3004)

System Organ Class	Icotrokinra N= 1296 n (%)	Placebo N= 568 n (%)
Neoplasms benign, malignant and unspecified	6 (0.46%)	1 (0.2%)
Cardiac disorders	3 (0.23%)	0 (0.0%)
Hepatobiliary disorders	3 (0.23%)	1 (0.2%)
Respiratory, thoracic and mediastinal disorders	3 (0.23%)	1 (0.2%)
Gastrointestinal disorders	2 (0.15%)	0 (0.0%)
Infections and infestations	2 (0.15%)	2 (0.4%)
Nervous system disorders	2 (0.15%)	1 (0.2%)
Injury, poisoning and procedural complications	1 (0.08%)	4 (0.7%)
Musculoskeletal and connective tissue disorders	1 (0.08%)	1 (0.2%)
Skin and subcutaneous tissue disorders	1 (0.08%)	1 (0.2%)
Vascular disorders	0 (0.0%)	2 (0.4%)

The clinical team concluded that the proportion of subjects with one or more SAEs was similar in the icotrokinra and placebo groups (1.6% vs. 2.1%) through week 16. They also noted that the SAE SOC imbalances between icotrokinra and placebo did not seem to follow any pattern (DDD, 2026). An imbalance in the infections and infestations SOC was not identified, but based on icotrokinra's

mechanism of action, DDD plans to align its labeling with other approved IL-23 inhibitors by including potential infections, tuberculosis, and immunizations in the Warnings and Precautions.[f]

6. Expected Postmarket Use

Plaque psoriasis is typically diagnosed in the non-emergent outpatient setting with primary care physicians, nurse practitioners, physician assistants, pediatricians or dermatologists being the likely prescribers. If approved, the icotrokinra oral tablet will likely be dispensed from retail pharmacy settings and primarily be self-administered by the patient at home for chronic treatment. Based on the anticipated medication use process, monitoring for adverse reactions should be a collaborative effort between the prescriber and the patient.

No concerning care gaps have been identified within the intended scope of practice. The use of a Medication Guide may facilitate communicating the potential risks to patients and instruct them in when to seek additional medical attention. Labeling is sufficient to ensure the safe-use conditions described in Section 5 for mitigating the potential risks of infections, tuberculosis, and immunizations are followed in the expected postmarket setting.

7. Discussion of the Need for a REMS

Based on the efficacy and safety information currently available, DRM and DDD determined that a REMS is not necessary to ensure the benefits of icotrokinra outweigh the risks.

When evaluating factors of whether a REMS is necessary to ensure that the benefits outweigh the risks for icotrokinra, this reviewer considered the patient population, seriousness of the disease, expected benefit of the drug, expected duration of treatment, seriousness of known or potential adverse events, and the likely prescribing population.

Based on the information available at this time, there are no serious adverse events for icotrokinra that warrant a REMS. The potential risks of infections, tuberculosis and immunizations are known risks for IL-23 inhibitors and labeling for icotrokinra will be similar for the other products in the class. Thus, it is expected that the likely prescribers will be familiar with identifying and managing these potential risks.

8. Risk Management Activities Proposed by the Applicant

The Applicant did not propose any risk management activities for icotrokinra beyond routine pharmacovigilance and labeling. The Applicant stated that the "the risks associated with this drug can be adequately managed by the product labeling, medication guide, and routine pharmacovigilance activities" (Janssen, 2025).

[f] Section 505-1 (a) of the FD&C Act: *FDAAA factor (E): The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.*

9. Conclusion & Recommendations

Based on the available data, a REMS is not necessary for icotrokinra to ensure the benefits outweigh the risks. The potential safety concerns associated with IL-23 receptor antagonists, such as icotrokinra, are well documented and healthcare providers who treat plaque psoriasis are familiar with them and the importance of patient monitoring.

Should the DDD have any concerns or questions or if new safety information becomes available, please send a consult to DRM.

10. References

Division of Dermatology and Dentistry. Draft Unireview for icotrokinra, NDA 220149, February 20, 2026

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Kupetsky EA, Keller M. Psoriasis vulgaris: an evidence-based guide for primary care. J AM Board Fam Med 2013;26:787-801

Warycha MA, What is Psoriasis? CareMount Medical 2018-2021. What is Psoriasis?– Healthcare Services in New York | Multi-Specialty Practices (caremountmedical.com)

11. Appendix

Table 4: FDA Approved Biologic Treatments for Moderate-to Severe Psoriasis

Product Trade Name (Generic) Year of Approval	Mechanism of Action	Indication	Administration	Important Safety and Tolerability Issues	Risk Management Approaches/Boxed Warning, Medication Guide (MG), Instructions for Use (IFU)
FDA Approved Biologic Treatments for Moderate-to Severe Psoriasis					
Skyrizi (risankizumab) 2019	IL-23 inhibitor	moderate-to-severe plaque psoriasis, psoriatic arthritis, Crohn's disease	SC and IV injections	hypersensitivity reactions, infections, tuberculosis (TB), hepatotoxicity in Crohn's treatment	MG, IFU
Ilumya (tildrakizumab) 2018	IL-23 inhibitor	moderate-to-severe plaque psoriasis	SC injection	hypersensitivity reactions, infections, TB	MG
Siliq (brodalumab) 2017	IL-17A receptor antagonist	moderate-to-severe plaque psoriasis in pts who failed to respond or lost response to other systemic therapies	SC injection	SIB, infections, TB, Crohn's disease	REMS for Suicidal Ideation and Behavior (SIB), boxed warning for SIB, MG, IFU
Tremfya (guselkumab) 2017	IL-23 inhibitor	moderate-to-severe plaque psoriasis, psoriatic arthritis	SC injection	hypersensitivity reactions, infections, TB	MG, IFU
Taltz (ixekizumab) 2016	IL-17A inhibitor	Moderate-to-severe plaque, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis	SC injection	Infections, TB, hypersensitivity, Inflammatory Bowel Disease (IBD)	MG
Cosentyx (secukinumab) 2015	IL-17A inhibitor	Moderate-to-severe plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, enthesitis-related arthritis	SC injection	Infections, TB, IBD, hypersensitivity reactions	MG, IFU

Stelara (ustekinumab) 2009	IL-12 and 23 inhibitor	Moderate-to-severe plaque psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis	SC and IV injections	Infections, TB, malignancies, hypersensitivity reactions, Posterior reversible encephalopathy syndrome	MG
Cimzia (certolizumab) 2008	TNF-alpha inhibitor	Crohn's disease, moderate-to-severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, moderate-to-severe plaque psoriasis	SC injection	Infections, malignancies, heart failure, hypersensitivity reactions, neurologic reactions, hematological reactions	Boxed warning for serious infections, TB, lymphoma and other malignancies; MG, IFU
Humira (adalimumab) 2002	TNF-alpha inhibitor	Rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, plaque psoriasis, uveitis	SC injection	Infections, malignancies, anaphylaxis or hypersensitivity reactions, demyelinating disease, heart failure	Boxed warning for serious infections and malignancy; MG, IFU
Remicade (infliximab) 1998	TNF-alpha inhibitor	Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis	IV injection	Infections, malignancies, hepatotoxicity, heart failure, cytopenias, hypersensitivity, demyelinating disease, cardiovascular/cerebrovascular reactions	Boxed warning for serious infections and malignancy; MG
Enbrel (etanercept) 1998	TNF-alpha inhibitor	Rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis	SC injection	Infections, demyelinating disease, lymphoma, heart failure, anaphylaxis or allergic reactions	Boxed warning for serious infections and malignancies; MG, IFU
Other Treatments: phototherapy, topical treatments, non-biologic therapies, dietary supplements (turmeric, St. John's wort, fish oil, vitamin D, zinc, aloe vera)					

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