New Drug Overview

Icotyde (icotrokinra)

PDL Category: Immunological Agents

Introduction

Disease Background:

- Psoriasis is an inflammatory and chronic disease (*Feldman 2024*). It mainly affects the skin, nails, and/or joints (*Lebwohl et al 2026*).
  - The most frequently reported type of psoriasis is plaque psoriasis. It is estimated that about 80% to 90% of patients with psoriasis are effected with plaque psoriasis.
    - Plaque psoriasis is described as having well-defined demarcated plaques, which are generally red, pink, or dark brown in appearance and typically layered with a silvery scale. The plaques may differ in size and may be associated with pain or pruritus.
      - It is estimated that about 20% have moderate to severe disease that involves more than 5% of body or that affects regions such as the hands, feet, face, or genitals.
- While psoriasis equally affects men and women and generally is observed before 40 years of age, plaque psoriasis can occur at any age but it is most common to see the onset between ages 15 and 20 years and between ages 55 to 60 years (*Lebwohl et al 2026*).
- Psoriasis is recognized to be a immune-mediated disease, with T lymphocytes, dendritic cells, and cytokines performing a major role (*Feldman 2024*).
- PASI, known as Psoriasis Area and Severity Index, measures the overall severity and coverage of psoriasis. The composite score can be anywhere between 0 (normal) to 72 (maximal disease). This is generally used to monitor response of treatment in clinical trials (*Lebwohl et al 2026*).
- Treating psoriasis is dependent on the degree of severity (*Lebwohl et al 2026*).
  - Mild disease is typically characterized as affecting <3-5% of body surface area (BSA) and with little impact on quality of life. Topical therapies are used for mild disease.
  - Moderate disease is generally noted to involve more than 3-5% of BSA but no more than 10%. Quality of life has been impacted to some degree and/or symptoms not controlled with topical treatments. Systemic treatment and/or phototherapy are typically used as treatment for this stage.
  - Severe disease involves greater than 10% of BSA, quality of life has been impacted, and/or symptoms that consists of arthritis. Systemic treatments and/or phototherapy are typically used for this stage.
- Icotyde was FDA approved in 2026.

Pharmacology/Usage

- Icotyde (icotrokinra) is an interleukin-23 (IL-23) receptor antagonist.
  - Icotrokinra is a peptide that selectively binds to the IL-23 receptor (IL-23R) and antagonizes the binding of IL-23.
    - IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses.
      - Icotrokinra inhibits the IL-23/IL-23R-dependent release of proinflammatory cytokines.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Icotyde (icotrokinra)
• For the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40kg who are candidates for systemic therapy or phototherapy.	√

(Prescribing information: Icotyde 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Icotyde (icotrokinra)	Film-Coated Tablets: 200mg -Swallow whole; do not crush, split, or chew tablets.	PO	200mg QD. -Administer upon waking on an empty stomach with water. Wait at least 30 minutes after taking Icotyde before eating food.	• If a dose is missed, instruct patients to take the missed dose as soon as possible with a return to normal dosing schedule the following day. • Consider assessing patients for tuberculosis (TB) infection prior to starting treatment based on clinical judgement. • Complete all age-appropriate vaccinations according to current immunization guidelines. • For patients who have difficulty swallowing tablets, Icotyde can be dispersed in water using the following instructions: place one tablet in a cup containing at least 120ml of water. The tablet may not completely disperse but the mixture may look yellow, milky or cloudy and small pieces

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				may be seen in the water, which are safe to swallow. Swirl the cup and swallow. Add at least 120ml of additional water to the cup and completely swallow. • Monitor for potential adverse reactions when Icotyde is used in patients with an eGFR <60ml/min.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Icotyde was assessed in four multicenter, randomized, double-blind, placebo and/or active comparator-controlled trials (Trial PSO-1, Trial PSO-2, Trial PSO-3, and Trials PSO-4) that included subjects (N=2500; 2428 adults and 72 pediatric patients 12 years and older who weigh at least 40kg) with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy.
- *Trial PSO-1 and Trial PSO-2* enrolled adults (N=1505) with moderate-to-severe plaque psoriasis 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%.
  - Subjects were randomized to either Icotyde 200mg QD, deucravacitinib 6mg QD or placebo.
    - At week 16, subjects originally randomized to placebo received Icotyde 200mg QD thereafter.
    - At week 24, subjects originally randomized to deucravacitinib received Icotyde 200mg QD thereafter.
  - Baseline characteristics were consistent across both trials.
    - In Trial PSO-1 and Trial PSO-2, 68% of subjects were male, 78% were White, the mean age was 46 years and the mean baseline weight was 88kg. At baseline, subjects had a median affected BSA of 21%, a median PASI score of 18, and 14% had a history of psoriatic arthritis. The proportion with a baseline IGA score of 4 (severe) was 20%. In addition, at baseline, 72% had received prior systemic therapy, 33% of subjects had received prior phototherapy, and 26% had received prior biologic therapy.
  - Both trials assessed responses at week 16 for Icotyde compared to placebo for two co-primary endpoints:
    - The proportion of subjects who achieved IGA 0/1 response (defined as IGA score of 0 [cleared] or 1 [minimal] with a ≥2-grade improvement from baseline).
    - The proportion of subjects who achieved at least a 90% improvement in PASI scores from baseline (PASI 90).
    - Other assessed outcomes compared to placebo included IGA 0, PASI 75, PASI 100, Psoriasis Symptoms and Signs Diary (PSSD) Symptom Score of 0, and PSSD Itch Score improvement from baseline (≥4-point reduction).
    - Other comparisons between Icotyde and deucravacitinib that were secondary endpoints included:
      - The proportion of subjects who achieved IGA 0/1 score with at least 2-grade improvement from baseline, IGA 0 score, PASI 75, PASI 90, and PASI 100 at week 16 and week 24.
      - The proportion of subjects who achieved PSSD Symptom Score of 0 at week 16.
  - Results for Trial PSO-1 and Trial PSO-2 are presented in the tables below, which were adapted from the prescribing information.

Table 3. Efficacy results for Trial PSO-1

Endpoint	Icotyde (N=311)	Placebo (N=156)	Deucravacitinib (N=307)	Difference, %	
				Difference from placebo	Difference from deucravacitinib
IGA 0 or 1 ('cleared' or 'minimal') and a ≥2-grade improvement from baseline					
Week 16	213 (68%)	17 (11%)	154 (50%)	58	18
Week 24	230 (74%)	-	161 (52%)		22
IGA 0 ('cleared')					
Week 16	114 (37%)	3 (2%)	48 (16%)	35	21
Week 24	150 (48%)	-	63 (21%)	-	28
PASI 75					
Week 16	231 (74%)	18 (12%)	176 (57%)	63	17
Week 24	254 (82%)	-	196 (64%)	-	18
PASI 90					
Week 16	171 (55%)	6 (4%)	91 (30%)	51	25
Week 24	205 (66%)	-	127 (41%)	-	25
PASI 100					
Week 16	97 (31%)	2 (1%)	34 (11%)	30	20
Week 24	129 (41%)	-	49 (16%)	-	26
PSSD Symptom Score 0					
N	286	142	272	-	-
Week 16	68 (24%)	4 (3%)	25 (9%)	21	14
PSSD Itch Score Improvement (≥4-point reduction from baseline)					
N	251	115	-	-	-
Week 4	56 (22%)	8 (7%)	-	15	-
Week 16	155 (62%)	19 (17%)	-	45	-

Table 4. Efficacy results for Trial PSO-2

Endpoint	Icotyde (N=320)	Placebo (N=81)	Deucravacitinib (N=322)	Difference, %	
				Difference from placebo	Difference from deucravacitinib
IGA 0 or 1 ('cleared' or 'minimal') and a ≥2-grade improvement from baseline					
Week 16	227 (71%)	7 (9%)	177 (55%)	63	16
Week 24	220 (69%)	-	179 (56%)		13
IGA 0 ('cleared')					
Week 16	118 (37%)	1 (1%)	57 (18%)	36	19
Week 24	128 (40%)	-	68 (21%)	-	19
PASI 75					
Week 16	249 (78%)	8 (10%)	198 (61%)	68	17
Week 24	265 (83%)	-	216 (67%)	-	16
PASI 90					
Week 16	184 (58%)	1 (1%)	111 (34%)	57	23
Week 24	208 (65%)	-	141 (44%)	-	21
PASI 100					
Week 16	102 (32%)	1 (1%)	46 (14%)	31	18
Week 24	107 (33%)	-	52 (16%)	-	17
PSSD Symptom Score 0					
N	296	70	282	-	-
Week 16	64 (22%)	0	36 (13%)	22	9
PSSD Itch Score Improvement (≥4-point reduction from baseline)					
N	256	60	-	-	-
Week 4	54 (21%)	3 (5%)	-	16	-
Week 16	154 (60%)	9 (15%)	-	46	-

- Per the full-text study (*Gold et al 2025*), the coprimary endpoints were met in both trials, significantly in favor of icotrokinra as compared with placebo at week 16.
  - The authors also note that compared with deucravacitinib, icotrokinra met all key secondary endpoints at week 16 and week 24 in each study, demonstrating superiority.
  - The authors concluded that icotrokinra demonstrated superior clinical response rates versus placebo and deucravacitinib in phase 3 moderate-to-severe plaque psoriasis trials, with similar adverse event rates compared to placebo.

- *Trial PSO-3* enrolled subjects (N=684, 618 adults and 66 pediatric subjects 12 years of age and older who weigh at least 40kg) with moderate-to-severe plaque psoriasis defined as Investigator's Global Assessment (IGA) score ≥3, a Psoriasis Area and Severity Index (PASI) score ≥12, and BSA ≥10%.
  - Subjects were randomized to receive either Icotyde 200mg QD or placebo for 16 weeks.
  - Regarding baseline characteristics, 65% of subjects were male, 72% were White, the mean age was 43 years, and the mean baseline weight was 86kg. At baseline, subjects had a median affected BSA of 20%, a median PASI score of 17, and 13% had a history of psoriatic arthritis. In addition, the proportion with a baseline IGA score of 4 (severe) was 25%. At baseline, 72% had prior systemic treatment, 30% of subjects had received prior phototherapy, and 34% had received prior biologic therapy.
  - This trial assessed responses at week 16 for Icotyde as compared to placebo for two co-primary endpoints:
    - The proportion of subjects who achieved IGA 0/1 response (defined as IGA score of 0 [cleared] or 1 [minimal] with a ≥2-grade improvement from baseline).
    - The proportion of subjects who achieved PASI 90.
    - Other outcomes assessed included IGA 0, PASI 75, PASI 100, PSSD Symptom Score of 0, and PSSD Itch Score improvement from baseline (≥4-point reduction).
  - Results for Trial PSO-3 are presented in the table below, which was adapted from the prescribing information.

Table 5. Efficacy results for Trial PSO-3

Endpoint	Icotyde (N=456)	Placebo (N=228)	Difference, % from placebo
IGA 0 or 1 ('cleared' or 'minimal') and a ≥2-grade improvement from baseline			
Week 16	295 (65%)	19 (8%)	56
IGA 0 ('cleared')			
Week 16	152 (33%)	3 (1%)	32
PASI 75			
Week 16	315 (69%)	25 (11%)	58
PASI 90			
Week 16	226 (50%)	10 (4%)	45
PASI 100			
Week 16	123 (27%)	1 (<1%)	26
PSSD Symptom Score 0			
N	408	208	-
Week 16	82 (20%)	2 (<1%)	19
PSSD Itch Score Improvement (≥4-point reduction from baseline)			
N	350	176	-
Week 4	67 (19%)	9 (5%)	14
Week 16	203 (58%)	23 (13%)	45

- In Trial PSO-3, adults who were randomized to Icotyde 200mg QD and were PASI 75 responders or IGA 0 or 1 responders at week 24 were re-randomized to continue Icotyde 200mg QD or withdrawn from therapy (ie, received placebo).
  - For adults who were re-randomized and had a PASI 90 response at week 24, 84% of subjects (108/128) who continued on Icotyde maintained PASI 90 response at week 52 compared to 21% of subjects (27/129) randomized to placebo. For PASI 90 responders at week 24 who were re-randomized to placebo, the median time to loss of PASI 90 response was about 10 weeks.
  - For adults who were re-randomized and had an IGA 0/1 response at week 24, 82% of subjects (123/150) who continued on Icotyde maintained IGA 0/1 response at week 52 compared to 23% of subjects (35/150) randomized to placebo. For IGA 0/1 responders at week 24 who were re-randomized to placebo, the median time to loss of IGA 0/1 response was about 10 weeks.
- Trial PSO-3 included 66 pediatric subjects 12 years of age and older who weigh at least 40kg.
  - The table below, adapted from the prescribing information, presents the efficacy results in pediatric subjects 12 years of age and older at week 16.

Table 6. Efficacy results for Trial PSO-3, Pediatric subjects

Endpoint	Icotyde n (%)	Placebo n (%)	Difference, % from placebo
Number of randomized pediatric subjects	44	22	
IGA 0 or 1 (cleared or minimal) and a ≥2-grade improvement from baseline	37 (84%)	6 (27%)	56
PASI 90	31 (70%)	3 (14%)	56

- *Trial PSO-4* included subjects (N=311, 305 adults and 6 pediatric subjects 12 years of age and older who weigh at least 40kg) with moderate-to-severe plaque psoriasis who had a minimum BSA involvement of ≥1%, an IGA score of ≥2 and had failed to respond to at least one topical therapy for the treatment of plaque psoriasis. In addition, subjects in this trial had at least one of the following baseline conditions: Scalp-specific Investigator's Global Assessment (ss-IGA) score ≥3 (at least moderate plaque psoriasis of the scalp), static Physician's Global Assessment of Genitalia (sPGA-G) score ≥3 (at least moderate plaque psoriasis of the genital area), and/or Physician's Global Assessment of Hands and/or Feet (hf-PGA) score ≥3 (at least moderate plaque psoriasis of the hands and/or feet).
  - Subjects were randomized to receive either Icotyde QD or placebo for 16 weeks.
  - At week 16, subjects originally randomized to placebo switched to receive Icotyde QD, and subjects randomized to Icotyde at baseline remained on treatment through the end of study.
  - In this trial, baseline characteristics of subjects included 64% male, 78% White, a mean age of 45 years (range 12 to 87) and a mean baseline weight of 86kg. The proportion with affected BSA less than 10% was 36% with a median affected BSA of 12%. Subjects had a median PASI score of 14, and 16% had a history of psoriatic arthritis. The proportion with a baseline IGA score of 3 (moderate) and 4 (severe) were 73% and 22%, respectively. In addition, the proportion of subjects with ss-IGA score of 3 or greater was 81% and the proportion of subjects with sPGA-G score of 3 or greater was 45%. The proportion with hf-PGA score of 3 or greater was 23%. Scalp, genital, and hand/foot subpopulations were not mutually exclusive. Last, at baseline, 73% had received prior systemic therapy, 39% had received prior phototherapy, and 33% had received prior biologic therapy.
  - The primary endpoint of this trial was the proportion of subjects who achieved an IGA 0/1 response (defined as IGA score of 0 [cleared] or 1 [minimal] and a ≥2-grade improvement from baseline at week 16).
  - Other secondary endpoints assessed at week 16 included proportion of subjects who achieved an ss-IGA score of 0 (absence of disease) or 1 (very mild disease), Psoriasis Scalp Severity Index (PSSI) 90, improvement in scalp itch as measured by Scalp Itch Numerical Rating Scale (NRS) Score, sPGA-G score of 0 (clear) or 1 (minimal), improvement of genital itch severity as measured by a reduction of at least 4 points in the 11-point Genital Psoriasis Symptoms Scale

(GPSS) Genital Itch NRS score, and the patient-perceived impact of psoriasis of the genital area on limiting frequency of sexual activity (intercourse or other activities) as measured by the Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) Item 2.

- Results are presented in the table below, which was adapted from the prescribing information.

Table 7. Efficacy results for Trial PSO-4

Endpoint	Icotyde n (%)	Placebo n (%)	Difference, % from placebo
Number of randomized subjects	208	103	
IGA 0 or 1 and ≥2-grade improvement from baseline	118 (57%)	6 (6%)	51
Number of subjects with baseline ss-IGA score of ≥3	167	85	
ss-IGA 0 or 1 (scalp)	110 (66%)	9 (11%)	56
PSSI 90	96 (57%)	5 (6%)	52
Number of subjects with baseline Scalp Itch NRS score ≥4 & baseline ss-IGA score ≥3	131	58	
Scalp Itch NRS score (≥4-point improvement)	77 (59%)	5 (9%)	50
Number of subjects with baseline sPGA-G score of ≥3	98	42	
sPGA-G 0 or 1 (genitalia)	75 (77%)	9 (21%)	55
Number of subjects with baseline GPSS Genital Itch NRS score ≥4 & baseline sPGA-G score ≥3	69	31	
GPSS Genital Itch NRS score (≥4-point improvement)	44 (64%)	4 (13%)	50
Number of subjects with baseline GenPs-SFQ Item 2 score ≥2 & baseline sPGA-G score ≥3	55	25	
GenPs-SFQ Item 2 score 0 or 1 (genitalia)	44 (80%)	9 (36%)	43

Clinical guidelines

- As Icotyde was most recently FDA approved, there are currently no published guidelines addressing its use.
- **Joint American Academy of Dermatology- National Psoriasis Foundation (AAD-NPF) guidelines of care for the management and treatment of psoriasis with biologics. 2019** (*Menter et al 2019*).
  - Etanercept is recommended as a treatment option in adults with moderate-to-severe plaque psoriasis as monotherapy or as combination treatment with other specific agents, such as topicals or methotrexate.
  - Infliximab is recommended as a treatment option in adults with moderate-to-severe plaque psoriasis as monotherapy or as combination treatment with other specific agents, such as topicals. It may be combined with methotrexate or apremilast, among others.
  - Adalimumab is recommended as a treatment option in adults with moderate-to-severe plaque psoriasis as monotherapy or as combination treatment with other specific agents, such as topicals. It may be combined with methotrexate or apremilast, among others.

- Ustekinumab is recommended as a treatment option in adults with moderate-to-severe plaque psoriasis as monotherapy or as combination treatment with other specific agents, such as topicals. It may be combined with methotrexate or apremilast, among others.
- The following are recommended as a treatment option in adults with moderate-to-severe plaque psoriasis as monotherapy: secukinumab, ixekizumab, brodalumab, guselkumab, and tildrakizumab.
- Risankizumab is not FDA-approved but can be used as a treatment in adults with moderate-to-severe plaque psoriasis as monotherapy. (Note that since the date of this publication, risankizumab is now FDA approved for plaque psoriasis).

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Medications that interact with the immune system may increase the risk of infection.
    - Avoid treatment with Icotyde in patients with any clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Icotyde. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection and/or is not responding to standard therapy, monitor the patient closely and discontinue Icotyde until the infection resolves.
  - Consider evaluating patients for TB infection prior to starting Icotyde treatment based on clinical judgment.
    - Consider anti-TB therapy prior to starting Icotyde in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.
    - Monitor patients for signs and symptoms of active TB during and after Icotyde treatment.
    - Avoid administering Icotyde to patients with active TB.
  - Avoid use of live vaccines in patients during Icotyde treatment. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines.
    - Prior to starting Icotyde, complete immunizations per current immunization guidelines. No data are available on the response to live or inactive vaccines.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Icotyde) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included headache (0.8%), nausea (0.7%), cough (1%), fungal infection (1.1%), and fatigue (0.5%).

- **Drug interactions:** None.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that available data on use during pregnancy are not sufficient to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.
    - There is a pregnancy safety study for Icotyde. If a patient becomes pregnant while receiving Icotyde, healthcare providers can report Icotyde exposure by calling 1-800-526-7736 or visiting online at www.ICOTYDE.com.

- The safety and efficacy of use in the pediatric population younger than 12 years of age or who weigh less than 40kg have not been established.

Conclusion

- Psoriasis is an inflammatory and chronic disease (*Feldman 2024*). It mainly affects the skin, nails, and/or joints (*Lebwohl et al 2026*).
  - The most frequently reported type of psoriasis is plaque psoriasis. It is estimated that about 80% to 90% of patients with psoriasis are effected with plaque psoriasis (*Lebwohl et al 2026*).
- Icotyde is an IL-23 receptor antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adults and pediatric patients 12 years of age and older who weigh at least 40kg who are candidates for systemic therapy or phototherapy.
  - Consider assessing patients for TB infection prior to starting treatment with Icotyde based on clinical judgement.
  - Complete all age-appropriate vaccinations per current immunization guidelines.
- Avoid Icotyde treatment in patients with any clinically important active infection until the infection resolves or is adequately treated.
- The efficacy of Icotyde was assessed in 4 multicenter, randomized, double-blind, placebo and/or active comparator-controlled trials that included adults and pediatric patients 12 years and older who weigh at least 40kg with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy. It was found to be effective in all phase 3 studies.
  - Icotyde was found to be significantly more effective for co-primary endpoints as compared with placebo and for all key secondary endpoints as compared with deucravacitinib in two phase three studies (*Gold et al 2025*).
- While Icotyde is not currently reviewed in any guidelines due to it being FDA approved after guidelines were published, guidelines do list numerous biologic agents for use in plaque psoriasis. Comparators with Icotyde may include Sotyktu (deucravacitinib), etanercept, and adalimumab, among others.

- There is some evidence from phase 3 studies to suggest that Icotyde may be more effective than deucravacitinib for some endpoints when used in patients with moderate-to-severe plaque psoriasis; however, there is no evidence to suggest that Icotyde is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Icotyde remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.
- **PDL Placement:**

☐ Preferred

☒ Non-Preferred with Conditions

References

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