swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Icotyde

International non-proprietary name:	icotrokinra, icotrokinra hydrochloride
Pharmaceutical form:	film-coated tablets
Dosage strength(s):	200 mg
Route(s) of administration:	oral
Marketing authorisation holder:	Janssen-Cilag AG
Marketing authorisation no.:	70373
Decision and decision date:	approved on 07.10.2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
ELISA	Enzyme-Linked Immunosorbent Assay
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
hERG	Human Ether-à-go-go-Related Gene potassium channel
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
IL-23R	Interleukin-23 Receptor
INN	International non-proprietary name
ITT	Intention-to-treat
K_D	Equilibrium Dissociation Constant
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
mAbs	Monoclonal Antibodies
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
pM	Picomolar (10^{-12} mol/L)
PopPK	Population pharmacokinetics
RMP	Risk management plan
SAE	Serious adverse event
STAT	Signal Transducer and Activator of Transcription
SwissPAR	Swiss Public Assessment Report
TDAR	T-cell-dependent antibody response
TNBS	Trinitrobenzenesulfonic acid
TEAE	Treatment-emergent adverse event
T_{max}	Time to Maximum Observed Plasma Concentration

TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for icotrokinra, icotrokinra hydrochloride in the above-mentioned medicinal product.

Work-sharing procedure
The applicant requested a work-sharing procedure with UK, Canada and Switzerland.
The Access NAS (new active substance) work-sharing initiative is a collaboration between regulatory authorities – specifically Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the UK Medicines & Healthcare products Regulatory Agency (MHRA) and Swissmedic – and the pharmaceutical industry.
The work-sharing initiative involves the coordinated assessment of applications that have been filed in at least two jurisdictions.

2.2 Indication and dosage

2.2.1 Requested indication

Icotyde is indicated for the treatment of moderate to severe plaque psoriasis in adults and adolescents aged 12 years and older.

2.2.2 Approved indication

Icotyde is indicated for the treatment of moderate to severe plaque psoriasis in adults and adolescents 12 years of age and older who are candidates for phototherapy or systemic therapy.

2.2.3 Requested dosage

Summary of the requested standard dosage:

Patients aged 12 years and older (weighing ≥ 40 kg): 200 mg orally once daily.
Special patient groups

- Children < 12 years of age or with a body weight of < 40 kg: no data available
- Elderly patients (≥ 65 years): no dose adjustment required
- Patients with renal impairment: no dose adjustment required
- Patients with hepatic impairment: no dose adjustment required

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	21 November 2025
Formal control completed	21 December 2025
List of Questions (LoQ)	20 April 2026
Response to LoQ	19 June 2026
Preliminary decision	3 August 2026
Response to preliminary decision	18 August 2026
Final decision	7 October 2026
Decision	approval

3 Quality aspects

Swissmedic has peer-reviewed the assessment of the primary data submitted with this application conducted by the Access Partner Authority Health Canada, contributed its own perspective, and concurs with the assessment and overall conclusions (see section 2.1 Applicant's request / Work-sharing procedure).

4 Nonclinical aspects

4.1 Pharmacology

Icotrokinra bound to human, monkey and rat IL-23R with similar affinities (K_D of 2 to 7.1 pM, 3 pM and 12 to 23 pM, respectively). Binding affinities for mouse and rabbit IL-23R were substantially lower (86 000 pM and 420 pM). In humans, icotrokinra inhibited IL-23-induced STAT3 phosphorylation without any effect on IL-12-induced STAT4 phosphorylation, confirming its specificity for the IL-23R subunit of the IL-23R/IL-12Rβ1 heterodimer. The applicant further characterised the pharmacology of icotrokinra in humans, demonstrating inhibition of IL-23-induced STAT3 phosphorylation by diffuse large cell B-lymphoma cells, as well as IL-23 stimulated IFNγ production in human NK cells and whole blood from healthy and psoriatic donors. Pharmacological activity was confirmed in rats (by inhibition of IL-23-induced IL-17A release in splenocytes and whole blood) and monkeys (using a competitive ELISA demonstrating that icotrokinra inhibited binding of human IL-23 to cynomolgus monkey IL-23R). The investigations in humans and rats also confirmed that icotrokinra acts as a competitive IL-23R antagonist. Icotrokinra showed efficacy in a rat IL-23 induced skin inflammation model and a TNBS-induced colitis model.

There were no off-target pharmacological effects. Icotrokinra did not inhibit the hERG current at concentrations 400 000-fold human unbound C_{max} at therapeutic dose. There were no effects on cardiovascular function, respiration rate or body temperature in monkeys at plasma concentrations 57-fold human C_{max}. Safety pharmacology studies in rats did not reveal any effect of icotrokinra on the central nervous or respiratory system at exposures 48-fold human C_{max}.

4.2 Pharmacokinetics

After oral administration, icotrokinra was rapidly absorbed (T_{max} 0.5–2 h) and oral bioavailability was low (0.1–0.6%) in mice, rats and monkeys. Elimination half-life ($t_{1/2}$) was 0.9 h in mice and rats, 3 h in monkeys and 12 h in humans. A negative food effect was observed in both animals and humans. Systemic exposure increased with dose in all three animal species. Accumulation was noted after repeated administration, particularly in rats. There were no relevant sex-related differences in exposure. In long-term studies, most animals developed anti-drug antibodies (ADAs), which likely contributed to reduced clearance and increased systemic exposure. In contrast, no ADA formation was observed in pregnant rabbits.

Plasma protein binding was moderate in animals and humans (29-53%), with limited partitioning into blood cells. Icotrokinra showed low cellular permeability. Icotrokinra-derived radioactivity distributed into tissues including the skin, with highest exposure in the gastrointestinal tract wall (after oral administration only) and kidney. Distribution to the central nervous system was minimal. Transfer of icotrokinra to offspring was demonstrated in rats, although the relative contribution of placental and lactational transfer could not be determined.

Icotrokinra showed high metabolic stability in various *in vitro* systems. Unchanged icotrokinra was the predominant circulating and excreted species in rats and monkeys, with only minor metabolites detected. Metabolites identified in human plasma were not considered major circulating metabolites requiring additional nonclinical qualification.

After oral administration to rats and monkeys, icotrokinra was predominantly excreted via faeces as unabsorbed parent drug, with ≤1% of drug-related material recovered in urine. Most of the absorbed fraction was eliminated in urine as unchanged drug or metabolites.

Based on its peptide nature and the submitted *in vitro* data package, pharmacokinetic drug–drug interactions are unlikely.

4.3 Toxicology

The applicant conducted a full toxicology programme in accordance with ICH M3(R2). Repeat-dose toxicity studies were conducted in rats and monkeys, both of which are pharmacologically relevant species. In the toxicity studies, icotrokinra was administered orally, in line with the intended clinical route of administration. The duration of the repeat-dose toxicity studies (up to 6 months in rats and 9 months in monkeys) is appropriate for a product intended for long-term use.

There was no acute toxicity in rats or monkeys at exposures up to 75- and >600-fold human C_{max} at therapeutic dose. The pivotal repeat-dose toxicity studies in rats and monkeys (including a TDAR assessment in monkeys) did not reveal any test item-related toxicity at exposures 15- to 61-fold (rats) and 351- to 392-fold (monkeys) human AUC at the end of the dosing phase. However, these safety margins should be interpreted with caution because almost all animals developed ADAs, which were neutralising in rats. In the 26-week rat study, exposure peaked after 8 weeks, reaching 69- to 195-fold human AUC at therapeutic dose, likely as a result of ADA-mediated accumulation, and declined thereafter. Consequently, exposures (and margins) at the end of dosing were lower than at earlier time points. Despite the presence of ADAs, the studies remain informative because systemic pharmacodynamic activity of icotrokinra was demonstrated at the end of the dosing period in both species. Nevertheless, in rats, the pharmacological activity expected based on the measured exposures may not have been fully achieved due to the presence of neutralising ADAs. Overall, the pivotal repeat-dose toxicity studies do not indicate a safety concern. However, animal studies have limited value for predicting immune responses to therapeutic proteins or peptides in humans.

Icotrokinra showed no evidence of genotoxicity.

The carcinogenicity studies in transgenic rasH2 mice (exposure 76-fold human AUC at therapeutic dose) and in rats (exposure 16-fold human AUC at therapeutic dose) showed no carcinogenic potential for icotrokinra. Although the interpretation of these studies was limited by the development of ADAs in both species and the fact that the mouse is a poor pharmacological responder, the overall weight of evidence provided by the applicant supports a low carcinogenic risk.

The fertility and early embryonic development studies did not reveal any adverse effects. At the NOAEL, exposure in males and females was 114- and 335-fold human AUC at therapeutic dose. No maternal or embryofetal toxicity could be identified in pregnant rats at exposures up to 297-fold human AUC at therapeutic dose. Maternal toxicity, including abortions, was observed in pregnant rabbits at 157-fold human AUC at therapeutic dose; however, no embryofetal toxicity was noted. The pre- and postnatal development study in pregnant rats did not reveal any adverse effects on the F0 or F1 generation either at exposures up to 127-fold human AUC at therapeutic dose. As stated above, safety margins in rats need to be interpreted with some caution. Although there was no reproductive toxicity at clinically relevant exposure to icotrokinra (and approved IL-23 mAbs), in the absence of human data, use of icotrokinra during pregnancy should be avoided as a precautionary measure.

The applicant did not conduct any toxicity studies in juvenile animals. It is agreed that the nonclinical toxicity studies with icotrokinra support dosing in adolescents (≥12 years).

Icotrokinra showed no phototoxicity potential *in vitro*.

There were no safety concerns with impurities.

All relevant nonclinical safety findings are included in the nonclinical part of the safety specification of the RMP. The PIP does not include any nonclinical measures. Based on the ERA, use of icotrokinra is not expected to pose any risk to the environment.

4.4 Nonclinical conclusions

The submitted nonclinical documentation is considered adequate to support the approval of icotrokinra in the proposed indication. All safety-relevant nonclinical data are included in the information for healthcare professionals.

5 Clinical aspects

Swissmedic has peer-reviewed the assessment of the primary data submitted with this application conducted by the Access Partner Authority MHRA, contributed its own perspective, and concurs with the assessment and overall conclusions (see section 2.1 Applicant’s request / Work-sharing procedure).

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Icotyde was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo-pro.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

ICOTYDE®

Composition

Active substances

Icotrokinra as icotrokinra hydrochloride.

Excipients

Tablet core: colloidal anhydrous silica, crospovidone, magnesium stearate, silicified microcrystalline cellulose
Film-coating: glyceryl monocaprylocaprate Type 1, iron oxide yellow (E172), macrogol poly (vinyl alcohol) graft polymer, polyvinyl alcohol partially hydrolyzed, talc, titanium dioxide (E171).

Pharmaceutical form and active substance quantity per unit

Icotyde 200 mg film-coated tablet.

Yellowish orange to yellowish brown, oval, film-coated tablet, approximately 19 mm in length and 9 mm in width debossed with ‘200’ on one side and ‘JNJ’ on the other side.

Each film-coated tablet contains 200 mg.

Indications/Uses

Icotyde is indicated for the treatment of moderate to severe plaque psoriasis in adults and adolescents 12 years of age and older who are candidates for phototherapy or systemic therapy.

Dosage/Administration

Dosage – Patients 12 years of age and older

The recommended dosage of Icotyde for adults is 200 mg taken orally once daily.

The recommended dosage of Icotyde for pediatric patients 12 years to less than 18 years of age who weigh at least 40 kg is 200 mg taken orally once daily.

The recommended dosage is based on clinical experience. In adults, the maximum duration of treatment was 90 weeks. In adolescents, the maximum duration of treatment was 83 weeks (see “Undesirable Effects”).

Icotyde film-coated tablets should be taken upon waking on an empty stomach with water. After taking Icotyde, the patient should wait at least 30 minutes before eating food. Icotyde film-coated tablets must be swallowed whole. Do not crush, split, or chew film-coated tablets (see “Pharmacokinetics”).

For alternate method of administration, Icotyde 200 mg film-coated tablets can be dispersed in water and administered orally (see “Dosage/Administration” – Alternative methods of administration).

If a patient shows no evidence of therapeutic benefit after 24 weeks, treatment discontinuation should be considered. Some plaque psoriasis patients with initial partial response may subsequently improve with continued treatment beyond 24 weeks.

Missed dose

If a patient misses a dose, instruct the patient to take the missed dose as soon as possible with a return to normal dosing schedule the following day.

Special populations

Pediatrics (< 18 years of age)

The safety and effectiveness of Icotyde have been established in pediatric patients (≥12 to <18 years of age) and weighing at least 40 kg with moderate to severe plaque psoriasis. Use of Icotyde in this indication is supported by evidence from two multi-center, randomized 52-week trials (ICONIC-LEAD and ICONIC-TOTAL) which included 72 pediatric subjects (≥12 to <18 years of age) (see “Undesirable effects” and “Properties/Effects” - Clinical efficacy).

The safety and efficacy of Icotyde have not been established in pediatric patients younger than 12 years of age or weighing less than 40 kg.

Elderly (≥ 65 years of age)

Of the 2400 subjects exposed to Icotyde in clinical trials for psoriasis, 242 (10%) were ≥ 65 years of age, and 36 (1.5%) were ≥ 75 years of age. No overall differences in safety and effectiveness of Icotyde have been observed between subjects 65 years and older and younger adult subjects.

No dose adjustment of Icotyde is recommended for patients 65 years of age and older (see “Pharmacokinetics”).

Renal impairment

Based on a pharmacokinetic study, no dose adjustment of Icotyde is recommended for patients with mild, moderate or severe renal impairment (see “Pharmacokinetics”). Patients with end-stage renal disease (eGFR <15 mL/min/1.73m2), on dialysis, or with a current diagnosis or signs/symptoms of progressive, or uncontrolled renal disease were excluded from study participation. Therefore, no treatment recommendation can be made for these patients.

Hepatic impairment

Specific studies of Icotyde have not been conducted in patients with hepatic impairment.

No dose adjustment of Icotyde is recommended in patients with mild, moderate, or severe hepatic impairment (see “Pharmacokinetics”). Patients with AST or ALT >2x upper limit of normal or with a current diagnosis or signs or symptoms of severe, progressive, or uncontrolled liver disease were excluded from study participation.

Alternative methods of administration

For patients who have difficulty swallowing film-coated tablets, Icotyde 200 mg film-coated tablet can be dispersed in water. The following instructions should be followed:

- Place one Icotyde 200 mg film-coated tablet in a cup containing at least 120 mL of water. It may take a few minutes for the film-coated tablet to disperse. The film-coated tablet may not completely disperse. The mixture may look yellow, milky or cloudy, and small pieces may be seen in the water which are safe to swallow.
- Gently swirl the cup before drinking and swallow the full mixture.
- Rinse the cup with at least 120 mL of additional water and completely swallow contents to make sure the whole dose is taken. Icotyde film-coated tablet should be taken within 15 minutes of dispersion in water.

Contraindications

Clinically important untreated active infection (eg. untreated active TB disease). See warnings and precautions.
Hypersensitivity to the active substance or to any of the excipients listed in “Composition”.

Warnings and precautions

Infections

In the 16-week placebo-controlled trials in subjects with moderate to severe plaque psoriasis, the rate of serious infections for ICOTYDE-treated subjects was 0.2% compared to 0.4% of subjects who received placebo. Avoid treatment with Icotyde in patients with any clinically important active untreated infection until the infection is adequately treated. In patients with a chronic infection, a history of recurrent infection, or known risk factors for infection, Icotyde should be used with caution (See “Contraindications”).

Tuberculosis

Consider evaluating for tuberculosis (TB) infection prior to initiating treatment with Icotyde based on clinical judgment. Monitor patients for signs and symptoms of active TB disease during and after treatment with Icotyde. Patients with active TB disease should be adequately treated with anti-TB therapy prior to initiating Icotyde (See “Contraindications”).

Immunizations

Prior to initiating therapy with Icotyde, consider completion of all age-appropriate immunizations according to current immunization guidelines. No data are available on the response to live or inactive vaccines. Avoid use of live vaccines in patients during treatment with Icotyde. Live vaccines may be administered 3 days after discontinuation of Icotyde.

For recommendations on administration of live vaccines in infants potentially exposed during pregnancy, see “Pregnancy, Breast-feeding”.

Interactions

No formal drug-drug interaction studies have been conducted with Icotyde.
Based on in vitro studies, icotrokinra is not a CYP enzyme substrate, inhibitor, or inducer. Icotrokinra is not a substrate or inhibitor of P-glycoprotein (P-gp) or other major drug transporters. Therefore, no clinically relevant drug interactions have been identified.
Live vaccines/therapeutic infectious agents
Live vaccines should not be administered to patients during treatment with Icotyde. Live vaccines may be administered 3 days after discontinuation of Icotyde (see “Warnings and Precautions”).

Pregnancy, lactation

Pregnancy

There are insufficient human data on the use of Icotyde in pregnancy. Animal studies have shown no evidence of direct or indirect adverse health effects in relation to reproductive toxicity (see “Preclinical Data”).
For precautionary reasons, it is preferable to avoid use of Icotyde during pregnancy, unless the benefit of treatment outweighs the potential risks.
As a precautionary measure, administration of live vaccines to infants potentially exposed to Icotyde during pregnancy is not recommended. If there is a clear clinical benefit for the individual infant, administration of a live vaccine might be considered. Live vaccines may be administered 3 days after birth (see “Warnings and Precautions” and “Interactions”).

Breast-feeding

It is not known whether icotrokinra passes into breast milk (see “Preclinical Data”).
The developmental and health benefits of breast-feeding should be considered along with the mother’s clinical need for Icotyde and any potential adverse effects on the breastfed infant from Icotyde or from the underlying maternal condition.

Fertility

The effect of icotrokinra on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see “Preclinical Data”).

Effects on ability to drive and use machines

No studies on the effect of Icotyde on the ability to drive and use machines have been performed. Based on its pharmacologic characteristics, Icotyde has no or negligible influence on the ability to drive and use machines.

Undesirable effects

Adverse reactions are adverse events that occur during treatment, which can be distinguished from the symptoms of the underlying disease and for which a causal relationship to the use of the drug is plausible.

Clinical studies experience

The safety of Icotyde was evaluated in two Phase 3 placebo-controlled trials (ICONIC-LEAD and ICONIC-TOTAL) and two Phase 3 placebo- and active-controlled trials (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2) (see “Pharmacodynamic Properties - Clinical studies”). A total of 2400 subjects with plaque psoriasis 12 years of age and older received Icotyde 200 mg orally once daily. Of these, 2271 subjects were exposed for at least 6 months, and 1446 subjects were exposed to Icotyde for at least one year.

Adverse reactions from clinical trials are listed in Table 1 and are listed by MedDRA system organ class and according to the following convention: very common (≥1/10); common (<1/10, ≥1/100); uncommon (<1/100, ≥1/1,000); rare (<1/1,000, ≥1/10,000); very rare (<1/10,000).

Table 1: List of Adverse Reactions

System Organ Class	Frequency	Adverse reaction
Infections and Infestations	Common	Fungal infections[a]
Nervous system disorders	Common	Headache
Gastrointestinal disorders	Common	Nausea
General disorders	Common	Fatigue

[a] Fungal infections include tinea pedis (n=4), tinea versicolor (n=2), oral candidiasis (n=2), onychomycosis (n=1), skin candida (n=1), urinary tract candidiasis (n=1), vulvovaginal candidiasis (n=1), fungal skin infection (n=1), genital infection fungal (n=1), ear infection fungal (n=1), and laryngitis fungal (n=1).

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including concomitant medications and underlying disease. For these reasons, the

incidence of antibodies to icotrokinra in the studies described below should not be compared with the incidence of antibodies in other studies or to other products.
In four Phase 3 clinical studies through Week 52, 12.2% (291/2387) of subjects treated with Icotyde developed antibodies to icotrokinra. Of these subjects who developed antibodies to icotrokinra, none had antibodies that were classified as neutralizing antibodies (see also “Pharmacokinetics”).

Pediatric population

Pediatric subjects (12 years to less than 18 years of age)

The safety of Icotyde was evaluated in pediatric subjects 12 years to less than 18 years of age with plaque psoriasis in two Phase 3 placebo-controlled trials (ICONIC-LEAD and ICONIC-TOTAL). A total of 72 pediatric subjects were exposed to Icotyde 200 mg orally once daily. Of these, 71 were exposed for at least 6 months, and 67 were exposed for at least one year. The safety profile was consistent with the overall population.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

In clinical studies, single oral doses up to 1000 mg have been administered to healthy volunteers without dose-limiting toxicity.

Treatment

There is no specific treatment in the event of Icotyde overdose. In the event of an overdosage, administer appropriate symptomatic treatment.

Properties/Effects

ATC code

L04AC28

Mechanism of action

Icotrokinra is a peptide that selectively binds to the IL-23 receptor (IL-23R) with high affinity and competitively antagonizes the binding of IL-23. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses, but when produced in excess contributes to chronic inflammation associated with immune-mediated diseases. Icotrokinra inhibits the IL-23/IL-23R-dependent release of proinflammatory cytokines.

Pharmacodynamics

In evaluated subjects with plaque psoriasis receiving Icotyde 200 mg once daily in ICONIC-LEAD, significant reductions in serum levels of IL-17A, IL-17F, IL-22, β-defensin-2 and IL-19 were observed after 4 weeks and 16 weeks of treatment compared to baseline and placebo.
Icotyde reduced gene expression of the IL-23/Th17 pathway and psoriasis-associated gene expression profiles in psoriatic skin after 16 weeks and 24 weeks of treatment in subjects with plaque psoriasis. Gene expression levels of IL17A, IL17F, IL22, DEFB4A and IL19 were normalized to non-lesional skin after 24 weeks of treatment with Icotyde 200 mg once daily.
In addition, treatment with Icotyde resulted in improvement of histological measures of psoriasis after 24 weeks and 52 weeks with reductions in epidermal thickness and densities of T cells, including CD8+ tissue resident memory T cells.

Effect on QT/QTc interval and cardiac electrophysiology

At the recommended dose of Icotyde 200 mg, clinically relevant QTc interval prolongation was not observed.

Clinical efficacy

Plaque psoriasis

The efficacy of Icotyde 200 mg once daily was evaluated in 2492 subjects (72 pediatric subjects 12 years and older and weighing at least 40 kg and 2420 adult subjects) with plaque psoriasis who were eligible for systemic therapy or phototherapy in four Phase 3 randomized, multi-center, double-blind, placebo and/or active comparator-controlled trials (ICONIC-LEAD, ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and ICONIC TOTAL).
Efficacy measures and patient reported outcomes in the ICONIC trials included:

- The Investigator Global Assessment (IGA) is a 5-category scale: 0 = cleared, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe, that indicates the physician’s assessment of psoriasis focusing on plaque thickness/induration, erythema and scaling.
- The Psoriasis Area and Severity Index (PASI) is a composite score that assesses the fraction of body surface area involved with psoriasis and the severity of psoriatic lesions within the affected regions (plaque thickness/induration, erythema, and scaling). PASI numeric scores range from 0 to 72, with higher scores representing more severe disease.
- The Psoriasis Symptoms and Signs Diary (PSSD), includes patient reported outcomes that were designed to measure the severity of psoriasis symptoms (itch, pain, stinging, burning, and skin tightness) and signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding) using 0 to 10 numerical rating scale. Symptom summary score and sign summary score were derived, ranging from 0 to 100. The PSSD Itch score is an item-level

score derived from PSSD with scores ranging from 0 to 10. For all scores, a higher score indicates more severe disease.

- The Scalp-Specific Investigator Global Assessment (ss-IGA) is used to evaluate the disease severity of scalp psoriasis. The lesions are assessed based on a 5-point scale in terms of clinical signs of redness, thickness, and scaliness which are scored as absence of disease (0), very mild disease (1), mild disease (2), moderate disease (3), and severe disease (4).
- The Psoriasis Scalp Severity Index (PSSI) is a scalp-specific modification of the PASI based on the extent of involvement and the severity of erythema, infiltration, and desquamation. Involvement and severity of psoriasis on the PSSI is scored by physicians on a scale from 0 to 72, where 0 = no psoriasis and higher scores indicate more severe disease.
- Scalp Itch Numeric Rating Scale (NRS) is a single item instrument that evaluates the severity of scalp itch in adult and adolescent populations over the past 24 hours. The instrument uses an NRS score ranging from 0 (no scalp itch) to 10 (worst scalp itch imaginable).
- The Static Physician's Global Assessment of Genitalia (sPGA-G) is a 6-point scale to assess the severity of genital psoriasis. The sPGA-G evaluates erythema, plaque elevation, and scale of genital psoriatic lesions. The severity of genital psoriasis is assessed as clear (0), minimal (1), mild (2), moderate (3), severe (4), and very severe (5).
- The Genital Psoriasis Symptoms Scale (GPSS) Genital Itch NRS score is a patient reported assessment of 8 symptoms of genital psoriasis (itch, pain, discomfort, stinging, burning, redness, scaling, and cracking). The instrument uses an NRS that best describes the worst level of each symptom in the genital area in the past 24 hours, ranging from 0 (no severity) to 10 (worst imaginable severity). Genital Itch NRS score is derived from item 1 of the GPSS.
- The Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) Item 2 is a patient-reported instrument used to assess how frequently genital psoriasis symptoms have limited frequency of sexual activity in the last 7 days in the adult population (never [0], rarely [1], sometimes [2], often [3], or always [4]).
- The Physician's Global Assessment of Hands and Feet (hf-PGA) assesses the severity of hand and foot psoriasis using a 5-point scale to score the plaques on the hands and feet as: clear (0), almost clear (1), mild (2), moderate (3), or severe (4).
- The Modified Nail Psoriasis Severity Index (mNAPSI) is a physician-assessed score that assesses the severity of nail psoriasis. Each of the participant's ten fingernails are evaluated on 7 features. The first three features are each scored from 0 to 3 in severity and are (1) onycholysis and oil-drop dyschromia, (2) pitting, and (3) nail plate crumbling. The next four features are each scored 0 –absent or 1 –present, and are (1) leukonychia, (2) splinter hemorrhages, (3) nail bed hyperkeratosis, and (4) red spots in the lunula. The score ranges from 0-13 per nail, and 0-130 for all fingernails with higher numbers indicating more severe disease.

- Fingernail Physician's Global Assessment (f-PGA) is a physician-assessed score that is used to evaluate fingernail psoriasis on a scale of 0 to 4 as: clear (0), minimal (1), mild (2), moderate (3), or severe (4).
- The Dermatology Life Quality Index (DLQI) is a dermatology-specific health-related quality of life instrument designed to assess the impact of the disease on a patient's quality of life. DLQI scores range from 0 to 30, with a higher score indicating greater impact on patient's quality of life.
- The Children's Dermatology Life Quality Index (CDLQI) is a dermatology-specific health-related quality of life instrument designed to assess the impact of the disease on a pediatric patient's quality of life. CDLQI scores range from 0 to 30, with a higher score indicating greater impact on patient's quality of life.
- The Patient Reported Outcomes Measurement Information System-29 (PROMIS-29) is a health-related quality of life survey, assessing each of the 7 PROMIS domains (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles and activities). The questions are rated on a 5-point scale. There is also a single question on pain intensity rated on an 11-point scale. Two scores that summarize overall physical and mental health, the Physical Component Summary (PCS) score and Mental Component Summary (MCS) score, are computed based on the responses to the 29 items.

Adult and pediatric subjects 12 years of age and older with moderate to severe plaque psoriasis (ICONIC-LEAD)

ICONIC-LEAD enrolled 684 subjects (618 adult and 66 pediatric subjects 12 years of age and older) with moderate to severe plaque psoriasis defined as IGA score ≥3, a PASI score ≥12, and body surface area (BSA) involvement ≥10%.
Subjects were randomized to either Icotyde (200 mg orally once daily) or placebo for 16 weeks.
In ICONIC-LEAD, 65% of subjects were male, 72% of the subjects were White, 1.2% of the subjects were Black, and 24% of subjects were Asian; 13% were Hispanic or Latino. The mean age was 43 (Range: 12 to 85) years, the mean baseline weight was 86 kg, 10% were 12 years to less than 18 years of age, and 10% were 65 years of age and older. At baseline, subjects had a median affected BSA of 20%, median PASI score of 17, and 13% had a history of psoriatic arthritis. The proportion of subjects 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.

Clinical response

ICONIC-LEAD assessed responses at Week 16 compared to placebo for the 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 90% improvement in PASI scores from baseline (PASI 90).

Other evaluated outcomes against placebo included PASI 75 and PSSD Itch Score improvement from baseline (≥4-point reduction), at Week 4, PASI 90 and PSSD Symptom Score of 0 at Week 8, and IGA 0, PASI 100, PASI 75, PSSD Symptom Score of 0, PSSD Itch Score improvement from baseline (≥4-point reduction), and ss-IGA score of 0 or 1 with at least 2-grade improvement from baseline among those with a baseline ss-IGA score of at least 2 at Week 16.

Table 2 presents the efficacy results and patient-reported outcomes in adult and pediatric subjects 12 years of age and older from ICONIC-LEAD, demonstrating superiority of Icotyde compared to placebo.

Table 2: Efficacy Results and Patient-Reported Outcomes in Adult and Pediatric Subjects 12 Years and Older With Moderate to Severe Plaque Psoriasis; (ICONIC-LEAD)		
Endpoint	**Icotyde (N=456) n (%)**	**Placebo (N=228) n (%)**
IGA 0 or 1 and a ≥2-grade improvement from baseline		
Week 16 (Co-primary Endpoint)	295 (65%)	19 (8%)
Difference from placebo, % (95% CI)	56% (50%, 62%)[a]	
Week 24	338 (74%)	
PASI 90		
Week 8	98 (21%)	3 (1.3%)
Difference from placebo, % (95% CI)	20% (16%, 24%)[a]	
Week 16 (Co-primary Endpoint)	226 (50%)	10 (4.4%)
Difference from placebo, % (95% CI)	45% (40%, 50%)[a]	
Week 24	296 (65%)	
IGA 0		
Week 16	152 (33%)	3 (1.3%)
Difference from placebo, % (95% CI)	32% (27%, 37%)[a]	
Week 24	211 (46%)	
PASI 75		
Week 4	68 (15%)	5 (2.2%)
Difference from placebo, % (95% CI)	13% (9%, 17%)[a]	
Week 16	315 (69%)	25 (11%)
Difference from placebo, % (95% CI)	58% (52%, 64%)[a]	
Week 24	368 (81%)	
PASI 100		
Week 16	123 (27%)	1 (0.4%)
Difference from placebo, % (95% CI)	26% (22%, 31%)[a]	
Week 24	184 (40%)	
PSSD Symptom Score 0 (N)[b]	408	208
Week 16	82 (20%)	2 (1.0%)
Difference from placebo, % (95% CI)	19% (15%, 24%)[a]	
PSSD Itch NRS (≥4-point improvement) (N)[c]	350	176
Week 16	203 (58%)	23 (13%)
Difference from placebo, % (95% CI)	45% (37%, 52%)[a]	
DLQI score of 0 or 1 (N)[d]	398	200
Week 16	207 (52%)	22 (11%)
Difference from placebo, % (95% CI)	41% (34%, 47%)	

Key: IGA = Investigator's Global Assessment; CI = Confidence interval; PASI = Psoriasis Area and Severity Index; PSSD = Psoriasis Symptoms and Signs Diary; DLQI = Dermatology Life Quality Index

[a] p<0.001 for comparison between Icotyde and placebo; under error control and statistically significant.

[b] Includes subjects with baseline PSSD symptom score >0.

[c] Includes subjects with baseline PSSD Itch score ≥4.

[d] Includes subjects with baseline DLQI score >1. Note: These endpoints included were not multiplicity-controlled.

Maintenance and durability of response

In ICONIC-LEAD, adult subjects originally randomized to Icotyde and had PASI 75 or IGA 0/1 response at Week 24 were re-randomized to either continue Icotyde 200 mg once daily or withdrawn from therapy (i.e., receive placebo).

For adult subjects who were re-randomized and had an IGA 0/1 response at Week 24, 82% (123/150) of subjects who continued on Icotyde maintained IGA 0/1 response at Week 52 compared to 23% (35/150) of subjects randomized to placebo. For IGA 0/1 responders at Week 24 who were re-randomized to treatment withdrawal in ICONIC-LEAD, the median time to loss of IGA 0/1 response was 10.1 weeks. The median time to loss of IGA 0/1 response was not reached among subjects who were re-randomized to continue Icotyde 200 mg once daily since >50% of subjects in this treatment group maintained an IGA-0/1 response through Week 52.

For adult subjects who were re-randomized and had a PASI 90 response at Week 24, 84% (108/128) of subjects who continued on Icotyde maintained PASI 90 response at Week 52 compared to 21% (27/129) of subjects randomized to placebo. For PASI 90 responders at Week 24 who were re-randomized to treatment withdrawal in ICONIC-LEAD, the median time to loss of PASI 90 response was 10.1 weeks. The median time to loss of PASI 90 response was not reached among subjects who were re-randomized to continue Icotyde 200 mg once daily since >50% of subjects in this treatment group maintained a PASI 90 response through Week 52.

Adult subjects 18 years of age and older with moderate to severe plaque psoriasis (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, enrolled 1497 adult subjects with moderate to severe plaque psoriasis defined as IGA score ≥3, a PASI score ≥12, and BSA involvement ≥10%.

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

Baseline characteristics were consistent across both studies. In ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, 68% of subjects were male, 78% of subjects were White, 2% of subjects were Black, and 18% of subjects were Asian; 16% were Hispanic or Latino. The mean age was 46 (Range: 18 to 86) years, the mean baseline weight was 88 kg, and 10% of subjects were 65 years and older. At baseline, subjects had a median affected BSA of 21%, a median PASI score of 18; 14% had a history of psoriatic arthritis. The proportion of subjects with a baseline IGA score of 4 (severe) was 20%. At baseline, 72% had received prior systemic therapy, 33% of subjects had received prior phototherapy, and 26% had received prior biologic therapy.

Clinical response

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 assessed responses at Week 16 compared to placebo for the 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 response.

Other comparisons between Icotyde and deucravacitinib that were key secondary endpoints included:

- the proportion of subjects who achieved IGA 0/1 with at least 2-grade improvement from baseline, IGA 0, PASI 100, PASI 90, and PASI 75 at Week 16 and Week 24.
- the proportion of subjects who achieved PSSD symptom score of 0 at Week 16.

Other evaluated outcomes against placebo included the proportion of subjects who achieved PASI 75 and improvement in itch severity as measured by at least at 4-point reduction from baseline in PSSD Itch Score at Week 4, PASI 90 and PSSD Symptom Score of 0 (symptom-free) at Week 8, and IGA 0, PASI 100, PASI 75, PSSD Symptom Score of 0, PSSD Itch Score improvement from baseline (≥4-point reduction), and Scalp-Specific Investigator's Global Assessment (ss-IGA) score of 0 (absence of disease) or 1 (very mild disease) with at least 2-grade improvement from baseline among those with a baseline ss-IGA score of at least 2 at Week 16.

Table 3 presents the efficacy results and patient-reported outcomes in adult subjects with moderate to severe plaque psoriasis from ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, demonstrating superiority of Icotyde compared to placebo or deucravacitinib.

Table 3: Efficacy Results and Patient Reported Outcomes in Adults Subjects with Moderate to Severe Plaque Psoriasis; (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-ADVANCE 1			**ICONIC-ADVANCE 2**		
Endpoint	**Icotyde (N=311) n (%)**	**Deucra-vacitinib (N=307) n (%)**	**Placebo (N=156) n (%)**	**Icotyde (N=320) n (%)**	**Deucra-vacitinib (N=322) n (%)**	**Placebo (N=81) n (%)**
IGA 0 or 1 and ≥2-grade improvement from baseline						
Week 16 (Co-primary endpoint compared to placebo)	213 (68%)	154 (50%)	17 (11%)	227 (71%)	177 (55%)	7 (9%)
Difference, % (95% CI)		18% (11%, 26%)[a]	58% (50%, 64%)[b]		16% (9%, 23%)[a]	63% (53%, 70%)[b]
Week 24	230 (74%)	161 (52%)		220 (69%)	179 (56%)	
Difference, % (95% CI)		22% (14%, 29%)[a]			13% (6%, 21%)[a]	
Week 52	230 (74%)			233 (73%)		
PASI 90						

Table 3: Efficacy Results and Patient Reported Outcomes in Adults Subjects with Moderate to Severe Plaque Psoriasis; (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
Endpoint	Icotyde (N=311) n (%)	Deucravacitinib (N=307) n (%)	Placebo (N=156) n (%)	Icotyde (N=320) n (%)	Deucravacitinib (N=322) n (%)	Placebo (N=81) n (%)
Week 8	62 (20%)		2 (1.3%)	81 (25%)		0
Difference, % (95% CI)			19% (14%, 24%)[b]			25% (20%, 30%)[c]
Week 16 (Co-primary endpoint compared to placebo)	171 (55%)	91 (30%)	6 (3.8%)	184 (58%)	111 (34%)	1 (1.2%)
Difference, % (95% CI)		25% (18%, 33%)[a]	51% (44%, 57%)[b]		23% (16%, 30%)[a]	57% (49%, 62%)[b]
Week 24	205 (66%)	127 (41%)		208 (65%)	141 (44%)	
Difference, % (95% CI)		25% (17%, 32%)[a]			21% (14%, 29%)[a]	
Week 52	216 (69%)			230 (72%)		
IGA 0						
Week 16	114 (37%)	48 (16%)	3 (1.9%)	118 (37%)	57 (18%)	1 (1.2%)
Difference, % (95% CI)		21% (14%, 28%)[a]	35% (29%, 41%)[b]		19% (13%, 26%)[a]	36% (29%, 42%)[b]
Week 24	150 (48%)	63 (21%)		128 (40%)	68 (21%)	
Difference, % (95% CI)		28% (21%, 35%)[a]			19% (12%, 26%)[a]	
Week 52	163 (52%)			162 (51%)		
PASI 75						
Week 4	38 (12%)		4 (2.6%)	52 (16%)		3 (3.7%)
Difference, % (95% CI)			10% (4.8%, 14%)[b]			13% (5%, 18%)[c]
Week 16	231 (74%)	176 (57%)	18 (12%)	249 (78%)	198 (61%)	8 (10%)
Difference, % (95% CI)		17% (10%, 24%)[a]	63% (55%, 69%)[b]		17% (10%, 23%)[a]	68% (59%, 75%)[b]

Table 3: Efficacy Results and Patient Reported Outcomes in Adults Subjects with Moderate to Severe Plaque Psoriasis; (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
Endpoint	Icotyde (N=311) n (%)	Deucravacitinib (N=307) n (%)	Placebo (N=156) n (%)	Icotyde (N=320) n (%)	Deucravacitinib (N=322) n (%)	Placebo (N=81) n (%)
Week 24	254 (82%)	196 (64%)		265 (83%)	216 (67%)	
Difference, % (95% CI)		18% (11%, 25%)[a]			16% (9%, 22%)[a]	
Week 52	256 (82%)			268 (84%)		
PASI 100						
Week 16	97 (31%)	34 (11%)	2 (1.3%)	102 (32%)	46 (14%)	1 (1.2%)
Difference, % (95% CI)		20% (14%, 26%)[a]	30% (24%, 36%)[b]		18% (11%, 24%)[a]	31% (24%, 36%)[b]
Week 24	129 (41%)	49 (16%)		107 (33%)	52 (16%)	
Difference, % (95% CI)		26% (19%, 32%)[a]			17% (11%, 24%)[a]	
Week 52	152 (49%)			154 (48%)		
PSSD Symptom Score 0[d]	286	272	142	296	282	70
Week 8	24 (8%)		3 (2.1%)	27 (9%)		1 (1.4%)
Difference, % (95% CI)			6% (0.7%, 11%)[e]			8% (-0.5%, 12%)[f]
Week 16	68 (24%)	25 (9%)	4 (2.8%)	64 (22%)	36 (13%)	0
Difference, % (95% CI)		14% (8%, 21%)[a]	21% (15%, 27%)[b]		9% (2.7%, 15%)[c]	22% (15%, 27%)[b]
Week 52[g]	115 (45%)			88 (39%)		
PSSD Sign Score 0[h]	286	276	142	297	284	70
Week 16	55 (19%)	17 (6%)	3 (2.1%)	47 (16%)	27 (10%)	0
Difference, % (95% CI)		13% (8%, 19%)	17% (12%, 23%)		6% (0.9%, 12%)	16% (10%, 21%)
Week 52	102 (36%)			84 (28%)		

Table 3: Efficacy Results and Patient Reported Outcomes in Adults Subjects with Moderate to Severe Plaque Psoriasis; (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
Endpoint	Icotyde (N=311) n (%)	Deucravacitinib (N=307) n (%)	Placebo (N=156) n (%)	Icotyde (N=320) n (%)	Deucravacitinib (N=322) n (%)	Placebo (N=81) n (%)
PSSD Itch Score Improvement (≥4-point reduction from baseline)[i]	251	236	115	256	242	60
Week 4	56 (22%)		8 (7%)	54 (21%)		3 (5%)
Difference, % (95% CI)			15% (8%, 22%)[b]			16% (6%, 22%)[j]
Week 16	155 (62%)	127 (54%)	19 (17%)	154 (60%)	125 (52%)	9 (15%)
Difference, % (95% CI)		8% (-0.9%, 17%)	45% (35%, 54%)[b]		9% (0.2%, 18%)	46% (34%, 56%)[b]
Week 52	184 (73%)			193 (75%)		
DLQI score of 0 or 1	304	294	149	317	318	80
Week 16	172 (57%)	121 (41%)	17 (11%)	168 (53%)	127 (40%)	11 (14%)
Difference, % (95% CI)		15% (7%, 23%)[k]	45% (37%, 52%)[k]		13% (5%, 20%)[k]	39% (29%, 48%)[k]
Week 52	212 (70%)			204 (64%)		

Table 3: Efficacy Results and Patient Reported Outcomes in Adults Subjects with Moderate to Severe Plaque Psoriasis; (ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
Endpoint	Icotyde (N=311) n (%)	Deucravacitinib (N=307) n (%)	Placebo (N=156) n (%)	Icotyde (N=320) n (%)	Deucravacitinib (N=322) n (%)	Placebo (N=81) n (%)

Key: IGA = Investigator's Global Assessment; CI = Confidence interval; PASI = Psoriasis Area and Severity Index; PSSD = Psoriasis Symptoms and Signs Diary (PSSD); DLQI = Dermatology Life Quality Index

[a] p<0.001 for comparison between Icotyde and Deucravacitinib; under error control and statistically significant.

[b] p<0.001 for comparison between Icotyde and placebo; under error control and statistically significant.

[c] p=0.005 for comparison between Icotyde and placebo; under error control and statistically significant.

[d] Includes subjects with baseline PSSD symptom score >0.

[e] p=0.011 for comparison between Icotyde and placebo; under error control and statistically significant.

[f] p=0.025 for comparison between Icotyde and placebo; under error control and statistically significant.

[g] In ICONIC-ADVANCE 1 at Week 52, the Icotyde arm included 256 subjects with baseline PSSD symptom score >0 eligible for analysis. In ICONIC-ADVANCE 2 at Week 52, the Icotyde arm included 227 subjects with baseline PSSD symptom score >0 eligible for analysis.

[h] Includes subjects with baseline PSSD sign score >0.

[i] Includes subjects with baseline PSSD Itch score ≥4.

[j] p=0.004 for comparison between Icotyde and placebo; under error control and statistically significant.

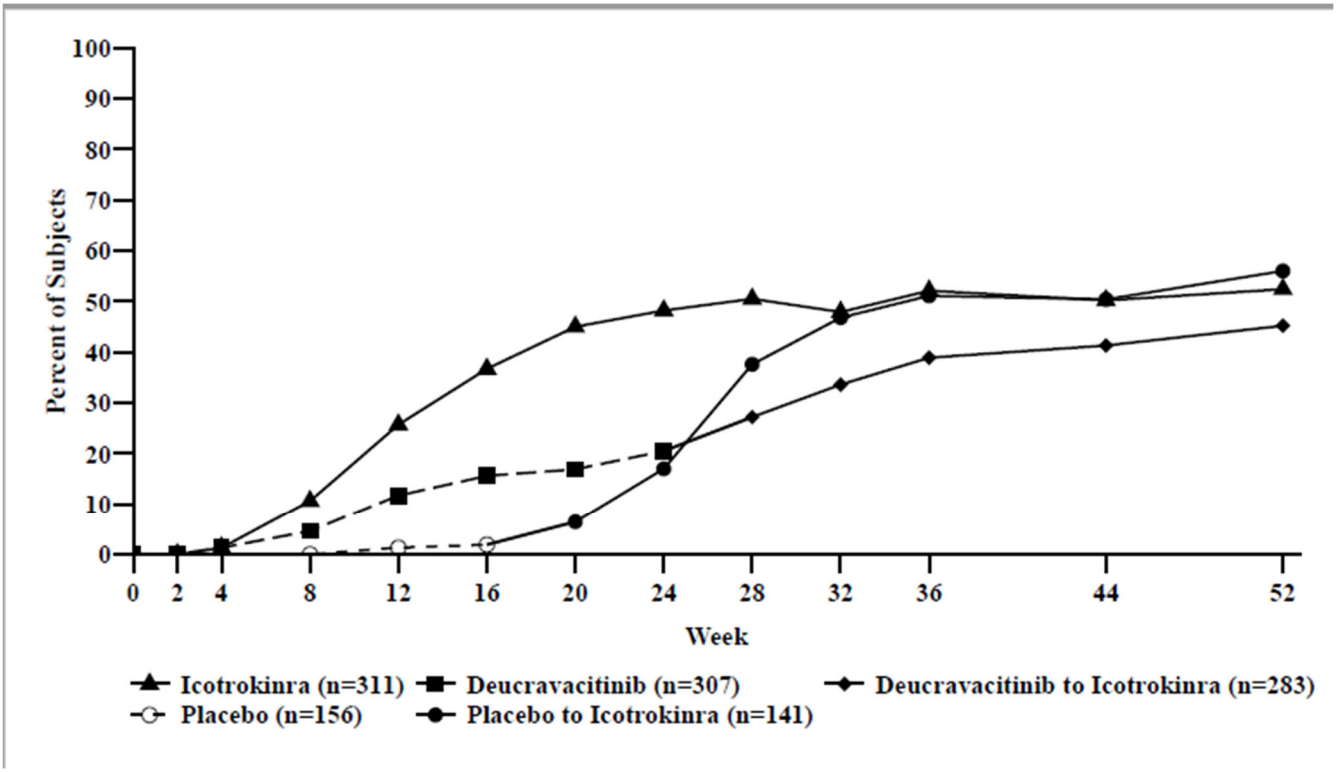
[k] Includes subjects with baseline DLQI score >1. Note: These endpoints included were not multiplicity-controlled.

Response over time

Icotyde showed early onset of efficacy in adult subjects with IGA 0 responses observed as early as Week 8, with continued improvement through Week 24 and maintained through Week 52

in ICONIC-ADVANCE 1 (see Figure 1).

Figure 1: Proportion of Adult Subjects with Moderate to Severe Plaque Psoriasis with IGA 0 Response through Week 52 (ICONIC-ADVANCE 1)



Efficacy in adult subjects switching from deucravacitinib to Icotyde

In ICONIC-ADVANCE 1, among 122 subjects who received deucravacitinib who failed to achieve an IGA 0/1 response at Week 24 and were switched to Icotyde, 58% achieved IGA 0/1 response with a ≥2-grade improvement from baseline after 28 weeks of treatment.

In ICONIC-ADVANCE 1, among 156 subjects who received deucravacitinib who failed to achieve a PASI 90 response at Week 24 and were switched to Icotyde, 56% achieved a PASI 90 response after 28 weeks of treatment.

Adult and pediatric subjects 12 years of age and older with moderate to severe plaque psoriasis involving special areas (ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2)

In ICONIC-LEAD, among subjects with ss-IGA score of at least 2 at baseline, 72% of subjects randomized to Icotyde achieved ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline compared to 15% of subjects randomized to placebo at Week 16 ($p<0.001$).

In ICONIC-ADVANCE 1, among subjects with ss-IGA score of at least 2 at baseline, 72% of subjects randomized to Icotyde achieved ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline compared to 21% of subjects randomized to placebo at Week 16 (p<0.001).

In ICONIC-ADVANCE 2, among subjects with ss-IGA score of at least 2 at baseline, 74% of subjects randomized to Icotyde achieved ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline compared to 19% of subjects randomized to placebo at Week 16 (p<0.001).

In ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2, improvements were also observed in psoriasis involving scalp, genitalia, nail, or hands/feet in subjects treated with Icotyde (Table 4).

Table 4: Summary of Clinical Response in Subjects With Plaque Psoriasis Involving Scalp, Genitalia, Nails and Hand/Foot; (ICONIC-LEAD, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-LEAD		ICONIC-ADVANCE 1		ICONIC-ADVANCE 2	
Endpoint	Icotyde (N=456)	Placebo (N=228)	Icotyde (N=311)	Placebo (N=156)	Icotyde (N=320)	Placebo (N=81)
ss-IGA 0/1 (scalp) (N)[a]	344	165	216	104	206	53
Week 16	249 (72%)	23 (14%)	161 (75%)	22 (21%)	149 (72%)	11 (21%)
Week 24	278 (81%)		174 (81%)		159 (77%)	
Week 52			174 (81%)		161 (78%)	
sPGA-G 0/1 (genitalia) (N)[b]	92	44	72	30	72	23
Week 16	65 (71%)	17 (39%)	57 (79%)	6 (20%)	58 (81%)	8 (35%)
Week 24	74 (80%)		62 (86%)		57 (79%)	
Week 52[c]			59 (82%)		60 (85%)	
hf-PGA 0/1 (hand/foot) (N)[d]	104	47	70	29	95	24
Week 16	77 (74%)	11 (23%)	49 (70%)	9 (31%)	58 (61%)	2 (8%)
Week 24	79 (76%)		55 (79%)		69 (73%)	
Week 52			52 (74%)		79 (83%)	
f-PGA 0/1 (nails) (N)[e]	137	66	101	45	104	22
Week 16	69 (50%)	14 (21%)	53 (52%)	10 (22%)	53 (51%)	3 (14%)
Week 24	87 (64%)		56 (55%)		68 (65%)	
Week 52			71 (70%)		74 (71%)	
mNAPSI (nails) (N)[f], mean percent change from baseline (SD)	194	100	137	70	139	40
N[f]	187	98	130	69	135	39
Week 16	-37.9 (105.42)	1.7 (133.97)	-24.8 (107.78)	49.3 (261.27)	-40.6 (58.00)	12.2 (116.72)
N[f]	187		123		131	
Week 24	-44.6 (111.30)		-51.3 (60.95)		-57.6 (61.10)	
N[f]			121		125	
Week 52			-57.9 (117.31)		-81.2 (32.47)	

Table 4: Summary of Clinical Response in Subjects With Plaque Psoriasis Involving Scalp, Genitalia, Nails and Hand/Foot; (ICONIC-LEAD, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2)

	ICONIC-LEAD		ICONIC-ADVANCE 1		ICONIC-ADVANCE 2	
Endpoint	Icotyde (N=456)	Placebo (N=228)	Icotyde (N=311)	Placebo (N=156)	Icotyde (N=320)	Placebo (N=81)

Key: ss-IGA = Scalp Specific Investigator's Global Assessment; s-PGA-G = Static Physician's Global Assessment of Genitalia; hf-PGA = Physician's Global Assessment of Hands and Feet; f-PGA = Fingernail Physician's Global Assessment; mNAPSI = Modified Nail Psoriasis Severity Index
[a] Includes subjects with baseline ss-IGA score ≥3.
[b] Includes subjects with baseline sPGA-G score ≥3.
[c] In ICONIC-ADVANCE-2 at Week 52, the Icotrokinra arm included 71 subjects with sPGA-G ≥3 eligible for analysis.
[d] Includes subjects with baseline hf-PGA score ≥3.
[e] Includes subjects with baseline f-PGA score ≥2.
[f] Includes subjects with baseline mNAPSI score >0 and a post-baseline assessment at the appropriate week.
Note: Data from Deucravacitinib arms for ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 are not shown.

Adult and pediatric subjects 12 years of age and older with plaque psoriasis involving special areas (scalp, genitalia, or hands/feet) (ICONIC-TOTAL)

ICONIC-TOTAL enrolled adult and pediatric subjects with 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. Additionally, subjects in ICONIC-TOTAL had at least one of the following baseline conditions: ss-IGA score ≥3 (at least moderate psoriasis involving scalp area), static Physician's Global Assessment of Genitalia (sPGA-G) score ≥3 (at least moderate psoriasis involving the genital area), and/or Physician's Global Assessment of Hands and Feet (hf-PGA) score ≥3 (at least moderate psoriasis involving the hands/feet).

In ICONIC-TOTAL, 311 subjects (305 subjects 18 years of age and older and 6 pediatric subjects 12 years of age and older) were randomized to either Icotyde 200 mg orally once daily or placebo for 16 weeks. At Week 16, subjects originally randomized to placebo switched to receive Icotyde 200 mg orally once daily, and subjects randomized to Icotyde at baseline remained on treatment through the end of study.

In ICONIC-TOTAL, 64% of subjects were male, 78% of the subjects were White, 0.6% of the subjects were Black, and 20% of subjects were Asian; 7% identified as Hispanic or Latino. The mean age was 45 (Range: 12 to 87) years, the mean baseline weight was 86 kg, 1.9% were 12 years to less than 18 years of age, and 8% were 65 years of age and older. The proportion of subjects with affected BSA less than 10% was 36% with a median affected BSA of 12%. The proportion of subjects with a baseline IGA score of 2 (mild), 3 (moderate) and 4 (severe) were 5.5%, 73%, and 22%, respectively. The proportion of subjects with ss-IGA score of 3 or greater was 81%. The proportion of subjects with sPGA-G score of 3 or greater was 45%. The proportion of subjects with hf-PGA score of 3 or greater was 23%. Scalp, genital and hand/foot subpopulations are not mutually exclusive. At baseline, 73%

had received prior systemic therapy, 39% of subjects had received prior phototherapy, and 33% had received prior biologic therapy.

Clinical response

In ICONIC-TOTAL, the primary endpoint was the proportion of subjects who achieved an IGA 0/1 response (defined as IGA score of 0 or 1 and a ≥2 grade improvement from baseline) at Week 16. Other key secondary endpoints included proportion of subjects who achieved IGA 0, PSSD symptom score of 0, improvement of itch severity as measured by at least a 4-point reduction in PSSD Itch score, ss-IGA 0 or 1, Psoriasis Scalp Severity Index (PSSI) 90, improvement in scalp itch as measured by Scalp Itch NRS Score, sPGA-G 0 or 1, improvement of genital itch severity as measured by a reduction of at least 4 points in the 11-point Genital Psoriasis Symptoms Scale (GPSS) score Itch Numeric Rating Scale (NRS), and the patient-perceived impact of psoriasis affecting 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, and hf-PGA 0 or 1.

Table 5 presents the efficacy results and patient reported outcomes in adult and pediatric subjects 12 years of age and older from ICONIC-TOTAL.

Table 5: Efficacy Results and Patient Reported Outcomes in Adult and Pediatric Subjects 12 Years and Older With Plaque Psoriasis Involving Special Areas (Scalp, Genitalia and Hand/Foot); (ICONIC-TOTAL)

Endpoint	Icotyde (N=208) n (%)	Placebo (N=103) n (%)
IGA 0 or 1 and a ≥2-grade improvement from baseline		
Week 16 (Primary Endpoint)	118 (57%)	6 (6%)
Difference from placebo, % (95% CI)	51% (42%, 59%)[a]	
Week 52	139 (67%)	
IGA 0		
Week 16	53 (25%)	1 (1.0%)
Difference from placebo, % (95% CI)	25% (17%, 32%)[a]	
Week 52	91 (44%)	
ss-IGA 0/1 (scalp) (N)[b]	167	85
Week 16	110 (66%)	9 (11%)
Difference from placebo, % (95% CI)	56% (45%, 64%)[a]	
Week 52	121 (72%)	
PSSI 90 (scalp) (N)[b]	167	85
Week 16	96 (57%)	5 (6%)
Difference from placebo, % (95% CI)	52% (42%, 60%)[a]	
Week 52	105 (63%)	

Table 5: Efficacy Results and Patient Reported Outcomes in Adult and Pediatric Subjects 12 Years and Older With Plaque Psoriasis Involving Special Areas (Scalp, Genitalia and Hand/Foot); (ICONIC-TOTAL)

Endpoint	Icotyde (N=208) n (%)	Placebo (N=103) n (%)
Scalp Itch (≥4-point improvement) (N)[c]	131	58
Week 16	77 (59%)	5 (9%)
Difference from placebo, % (95% CI)	50% (38%, 61%)[a]	
Week 52	97 (74%)	
sPGA-G 0/1 (genitalia) (N)[d]	98	42
Week 16	75 (77%)	9 (21%)
Difference from placebo, % (95% CI)	55% (39%, 68%)[a]	
Week 52	83 (85%)	
GPSS Genital Itch (≥4-point improvement) (N)[e]	69	31
Week 16	44 (64%)	4 (13%)
Difference from placebo, % (95% CI)	50% (31%, 64%)[a]	
Week 52	54 (78%)	
GenPs-SFQ Item 2 score 0/1 (genitalia) (N)[f]	55	25
Week 16	44 (80%)	9 (36%)
Difference from placebo, % (95% CI)	43% (20%, 62%)[a]	
Week 52	48 (87%)	
hf-PGA 0/1 (hand/foot) (N)[g]	48	23
Week 16	20 (42%)	6 (26%)
Difference from placebo, % (95% CI)	17% (-6%, 37%)[h]	
Week 52	30 (63%)	
PSSD Symptom Score 0 (N)[i]	191	87
Week 16	31 (16%)	3 (3.4%)[b]
Difference from placebo, % (95% CI)	13% (6%, 19%)[j]	
Week 52[k]	64 (39%)	
PSSD Itch NRS (≥4-point improvement) (N)[l]	168	74
Week 16	100 (60%)	10 (14%)[e]
Difference from placebo, % (95% CI)	45% (33%, 55%)[a]	
Week 52	112 (67%)	
DLQI score of 0 or 1 (adults) (N)	202	99
Week 16	91 (45%)	8 (8%)
Difference from placebo, % (95% CI)	37% (28%, 45%) [m]	
Week 52	120 (59%)	

Table 5: Efficacy Results and Patient Reported Outcomes in Adult and Pediatric Subjects 12 Years and Older With Plaque Psoriasis Involving Special Areas (Scalp, Genitalia and Hand/Foot); (ICONIC-TOTAL)

Endpoint	Icotyde (N=208) n (%)	Placebo (N=103) n (%)

Key: IGA = Investigator's Global Assessment; CI = Confidence interval; ss-IGA = Scalp-specific Investigator Global Assessment; PSSI = Psoriasis Scalp Severity Index; sPGA-G = Static Physician's Global Assessment of Genitalia; GPSS = Genital Psoriasis Symptoms Scale; GenPs-SFQ = Genital Psoriasis Sexual Frequency Questionnaire; hf-PGA = Physician's Global Assessment of Hands and Feet; PSSD = Psoriasis Symptoms and Signs Diary (PSSD); DLQI = Dermatology Life Quality Index

[a] p<0.001 for comparison between Icotyde and placebo; under error control and statistically significant.

[b] Includes subjects with baseline ss-IGA score ≥3.

[c] Includes subjects with baseline Scalp Itch NRS Score ≥4 and baseline ss-IGA score ≥3.

[d] Includes subjects with baseline sPGA-G score ≥3.

[e] Includes subjects with baseline GPSS Genital Itch NRS Score ≥4 and baseline sPGA-G score ≥3

[f] Includes subjects with baseline GenPs-SFQ Item 2 score ≥2 and baseline sPGA-G score ≥3

[g] Includes subjects with baseline hf-PGA score ≥3.

[h] p=0.144 for comparison between Icotyde and placebo; under error control and statistically not significant.

[i] Includes subjects with baseline PSSD symptom score > 0.

[j] p=0.003 for comparison between Icotyde and placebo; under error control and statistically not significant.

[k] In ICONIC-TOTAL at Week 52, the Icotyde arm included 163 subjects with baseline PSSD symptom score >0 eligible for analysis.

[l] Includes subjects with baseline PSSD Itch score ≥4.

[m] Includes subjects with baseline DLQI score >1. NOTE: This endpoint was not multiplicity controlled.

Maintenance of response

In ICONIC-TOTAL, among subjects who received Icotyde and achieved IGA 0/1 response at Week 16, 87% (103/118) maintained an IGA 0/1 response at Week 52. Among subjects with at least moderate scalp psoriasis at baseline (ss-IGA ≥3) who received Icotyde and achieved ss-IGA 0/1 response at Week 16, 88% (97/110) maintained ss-IGA 0/1 response at Week 52. Among subjects with at least moderate genital psoriasis at baseline (sPGA-G ≥3) who received Icotyde and achieved sPGA-G 0/1 response at Week 16, 89% (67/75) maintained sPGA-G 0/1 response at Week 52.

Adult subjects with plaque psoriasis (ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, ICONIC-LEAD, and ICONIC-TOTAL)

In each of the individual studies (ICONIC-LEAD, ICONIC-TOTAL, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2), greater improvements in general health-related quality of life were observed in summary scores of overall physical health and mental health as measured by Patient-reported Outcomes Measurement Information System-29 (PROMIS-29) in adult subjects treated with Icotyde compared with placebo at Week 16.

Subgroup analysis in subjects with plaque psoriasis (ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, ICONIC-LEAD, and ICONIC-TOTAL)

An examination of age, gender, race, body weight, baseline disease severity, and previous treatment with systemic or biologic agents did not identify differences in response to Icotyde among these subgroups.

Pediatric subjects 12 years to less than 18 years of age (ICONIC-LEAD and ICONIC-TOTAL)

The efficacy of Icotyde was evaluated in 72 pediatric subjects 12 years of age and older and weighing at least 40 kg.

The same disease severity criteria were used for adult and pediatric subjects in ICONIC-LEAD (N=66) and ICONIC-TOTAL (N=6). Pediatric subjects in both trials were randomized to either Icotyde 200 mg orally once daily or placebo for 16 weeks. After 16 weeks, subjects on placebo received Icotyde 200 mg orally daily thereafter.

In ICONIC-LEAD, 44% were male, 73% were White, 3% were Black, 23% were Asian; 14% were Hispanic or Latino. The mean age of pediatric subjects was 15 (Range: 12 to 17) years, and the mean baseline weight was 73 kg. The pediatric subjects had a median baseline PASI score of 18, and a median affected BSA of 23%. The proportion of pediatric subjects with a baseline IGA score of 4 [severe] was 26%, and the proportion of pediatric subjects with ss-IGA score of 2 or greater was 97%. At baseline, 52% had received prior systemic therapy, 20% of pediatric subjects had received prior phototherapy, and 23% had received prior biologic therapy.

Clinical response

Table 6 presents the efficacy results and patient reported outcomes in pediatric subjects 12 years to less than 18 years of age from ICONIC-LEAD.

Table 6: Efficacy Results and Patient Reported Outcomes in Pediatric Subjects 12 Years to Less Than 18 Years of Age With Moderate to Severe Plaque Psoriasis at Week 16; (ICONIC-LEAD)

Endpoint	Icotyde (N=44) n (%)	Placebo (N=22) n (%)
IGA 0 or 1 and a ≥2-grade improvement from baseline		
Week 16	37 (84%)	6 (27%)
Difference from placebo, % (95% CI)	56% (33%, 74%)	
Week 52	36 (82%)	
PASI 90		
Week 16	31 (70%)	3 (14%)
Difference from placebo, % (95% CI)	56% (33%, 73%)	
Week 52	38 (86%)	
IGA 0		
Week 16	18 (41%)	1 (4.5%)
Difference from placebo, % (95% CI)	36% (15%, 52%)	
Week 52	27 (61%)	
PASI 75		
Week 16	38 (86%)	5 (23%)
Difference from placebo, % (95% CI)	63% (40%, 80%)	
Week 52	42 (95%)	
PASI 100		
Week 16	13 (30%)	1 (4.5%)
Difference from placebo, % (95% CI)	24% (4.9%, 41%)	
Week 52	25 (57%)	
ss-IGA 0/1 and a ≥2-grade improvement from baseline (scalp) (N)[a]	43	21
Week 16	35 (81%)	3 (14%)
Difference from placebo, % (95% CI)	65% (43%, 81%)	
Week 52	37 (86%)	
PSSD Symptom Score 0 (N)[b]	37	20
Week 16	13 (35%)	0
Difference from placebo, % (95% CI)	35% (14%, 51%)	
Week 52[c]	19 (59%)	
PSSD Itch NRS (≥4-point improvement) (N)[d]	27	17
Week 16	15 (56%)	2 (12%)
Difference from placebo, % (95% CI)	48% (20%, 68%)	
Week 52	22 (81%)	
CDLQI score of 0 or 1 (N)[e]	40	19

Table 6: Efficacy Results and Patient Reported Outcomes in Pediatric Subjects 12 Years to Less Than 18 Years of Age With Moderate to Severe Plaque Psoriasis at Week 16; (ICONIC-LEAD)

Endpoint	Icotyde (N=44) n (%)	Placebo (N=22) n (%)
Week 16	27 (68%)	2 (11%)
Difference from placebo, % (95% CI)	54% (31%, 72%)	
Week 52	34 (85%)	

Key: IGA = Investigator's Global Assessment; CI = Confidence interval; PASI = Psoriasis Area and Severity Index; ss-IGA = Scalp Specific Investigator's Global Assessment; PSSD = Psoriasis Symptoms and Signs Diary; CDLQI = Children's Dermatology Life Quality Index

[a] Includes subjects with baseline ss-IGA score of ≥2.

[b] Includes subjects with baseline PSSD symptom score >0.

[c] In ICONIC-LEAD at Week 24 and Week 52, the Icotyde arm included 32 subjects with baseline PSSD symptom score >0 eligible for analysis.

[d] Includes subjects with baseline PSSD Itch score ≥4.

[e] Includes subjects with baseline CDLQI score >1.

NOTE: At Week 16, none of the endpoints were multiplicity controlled.

In ICONIC-TOTAL, a greater proportion of pediatric subjects 12 years of age and older treated with Icotyde compared to placebo achieved an IGA score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16 (67% in Icotyde [N=3] vs. 0 in placebo[N=3]).

Maintenance of response

In ICONIC-LEAD, among pediatric subjects 12 years of age and older who received Icotyde and had PASI 75 response at Week 24, 100% (40/40) had a PASI 75 response at Week 52.

Among pediatric subjects 12 years of age and older who received Icotyde and had PASI 90 response at Week 24, 92% (36/39) had a PASI 90 response at Week 52.

Among pediatric subjects 12 years of age and older who received Icotyde and had IGA 0/1 response at Week 24, 89% (34/38) had IGA 0/1 response at Week 52.

Pharmacokinetics

Following oral administration, icotrokinra C_{max} and AUC increased in a dose-proportional manner over a dose range of 10 to 1000 mg (approximately 0.05 to 5 times the recommended dose) in healthy subjects. After repeat once daily dosing of Icotyde, icotrokinra steady state is expected within 3 days with minimal drug accumulation, consistent with its terminal half-life.

Among icotrokinra-treated subjects who developed anti-drug antibodies, population pharmacokinetic analysis using pooled data through Week 52 showed that C_{max} and AUC increased by 1.2- and 1.3-fold, respectively, compared with subjects who did not develop anti-drug antibodies.
There was no identified clinically meaningful effect of anti-drug antibodies on pharmacokinetics, safety, or effectiveness of icotrokinra through Week 52.

Absorption

The median (range) T_{max} of icotrokinra after oral administration of Icotyde 200 mg film-coated tablet is 2.00 (0.25-8.00) hours in healthy subjects. The mean C_{max} and mean AUC_{∞} were 3.62 ng/mL and 44.8 ng*h/mL, respectively.

Based on nonclinical data, the absolute bioavailability of icotrokinra was <1%.

Food Effect

In healthy subjects, coadministration of a single icotrokinra 200 mg film-coated tablet with a high-calorie, high-fat meal decreased icotrokinra AUC_{∞} and C_{max} by 43% and 59%, respectively, relative to fasted state. Icotrokinra should be taken upon waking at least 30 minutes before eating food.

Administration of a single Icotyde 200 mg film-coated tablet with caffeine resulted in no difference in exposure. Co-administration of a single icotrokinra 200 mg tablet with whole milk and a sucrose solution decreased C_{max} by 33% and 22% and AUC_{∞} by 24% and 18%, respectively.

Distribution

Icotrokinra is 52% bound to plasma protein. Blood to plasma partition ratio was 0.53. The volume of distribution (V/F) at steady state is 92800 L.

Metabolism

Icotrokinra is a peptide, and intact drug is the main species in plasma. Icotrokinra is metabolized by peptide catabolism into smaller peptides and is not metabolized by CYP enzymes.

Elimination

The median terminal half-life (t1/2) of icotrokinra is 12 hours. Clearance following oral dosing (CL/F) is 6550 L/h.
The majority of the drug is not absorbed with 37% to 81% of the intact drug recovered unchanged in feces up to 24 hours after oral dosing. Less than 0.001% of administered dose was recovered as intact drug in urine.
Renal clearance is the main route of elimination for the absorbed drug. Most of the absorbed drug is filtered and excreted in the urine as intact drug or smaller peptides.

Kinetics in specific patient groups

Based on population pharmacokinetic analysis, age, sex, race and ethnicity do not have a clinically meaningful effect on the pharmacokinetics of icotrokinra.

Body weight

Clearance and volume of distribution of icotrokinra after oral dosing increased with increasing body weight. These differences are not clinically meaningful, and no dose adjustment is warranted.

Pediatrics (Less than 18 years of age)

No meaningful difference in the systemic exposure of icotrokinra was observed in pediatric patients with plaque psoriasis 12 years of age and older weighing at least 40 kg compared to adults.

Elderly (65 years of age and older)

No apparent differences in clearance were observed in subjects ≥ 65 years of age compared to subjects < 65 years of age, suggesting no dose adjustment is needed for elderly subjects.

Renal impairment

Icotrokinra AUC∞ was 147% higher and 178% higher in subjects with moderate renal impairment (eGFR ≥30 to <60 mL/min/1.73 m^2) and severe renal impairment (eGFR ≥15 to <30 mL/min/1.73 m^2), respectively, compared to subjects with normal renal function (eGFR ≥ 90 mL/min/1.73 m^2). Mild renal impairment (eGFR ≥60 to <90 mL/min/1.73 m^2) had no effect on icotrokinra exposure based on population pharmacokinetic analysis. Subjects with end-stage renal disease (eGFR <15 mL/min/1.73 m^2) or subjects on dialysis were not studied.

No dose adjustment is recommended in patients with mild, moderate or severe renal impairment (see “Dosage/Administration”).
Patients with end-stage renal disease (eGFR <15 mL/min/1.73 m^2), on dialysis, or with a current diagnosis or signs/symptoms of progressive or uncontrolled renal disease were excluded from study participation. Therefore, no treatment recommendation can be made for these patients.

Hepatic impairment

No formal pharmacokinetic studies with Icotyde were conducted in patients with hepatic impairment. Changes in hepatic function are unlikely to have any effect on the elimination of icotrokinra as icotrokinra is not metabolized through hepatic pathways. Patients with severe hepatic impairment were excluded from clinical trials.

Preclinical data

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity, and toxicity to fertility, and pre- and post-natal development.

Reproductive Toxicology

Icotrokinra did not cause embryo-fetal toxicity in rats or rabbits at maternal exposures at least 157 times the MRHD, respectively based on AUC. In rabbits, maternal body weight loss, low food consumption, as well as pregnancy losses were observed at maternal exposures 157 times the MRHD based on AUC.
Icotrokinra had no effects on prenatal and post-natal development including sexual maturation and reproductive performance at maternal exposures 127 times the MRHD based on AUC in rats. Although not directly measured in rat milk, icotrokinra was detected in the plasma of nursing rat pups.

Fertility

Icotrokinra had no effects on fertility or early embryonic development in male and female rats at exposures up to approximately 114 and 335 times the MHRD, respectively based on AUC.

Other information

Incompatibilities

Not applicable

Shelf life

Do not use this medicine after the expiry date marked as "EXP" on the pack.

Special precautions for storage

Do not store above 30°C.
Store in original package to protect the contents from moisture.
Keep out of the reach of children.

Authorisation number

70373 (Swissmedic).

Packs

Icotyde is available in an aluminum blister pack of 28 film-coated tablets (4 blister cards of 7 film-coated tablets each) [B].

Marketing authorisation holder

Janssen-Cilag AG, Zug, ZG.

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