19 June 2025
EMADOC-1700519818-2265245
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Skyrizi

Risankizumab

Procedure no: EMA/PAM/0000265652

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	26 May 2025	23 May 2025
☐	CHMP comments	10 June 2025	n/a
☐	Updated CHMP Rapporteur AR	12 June 2025	n/a
☒	CHMP outcome	19 June 2025	19 June 2025

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1. Introduction

On 8 April 2025, the MAH submitted a completed paediatric study for Skyrizi (risankizumab), in accordance with Article 46 of Regulation (EC) No 1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study M19-977, a randomized, active-controlled, efficacy assessor-blinded study to evaluate pharmacokinetics, safety, and efficacy of risankizumab in patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis (PsO), submitted under Article 46 of Regulation (EC) No1901/2006, as amended, is a standalone study.

No updates to the product information have been proposed by the MAH as part of this Article 46 submission.

The MAH stated that an indication extension for approval of risankizumab in paediatric PsO subjects supported by the data from the submitted M19-977 study is currently planned for 2025.

The MAH confirmed that the indication extension submission will be supported by a line extension which is currently in development.

2.2. Information on the pharmaceutical formulation used in the study

Patients received 150 mg risankizumab SC at Weeks 0, 4, 16, 28, and 40 (part 1 of the study).

Patients in Parts 2, 3, and 4 of the study were treated with weight-based dosing of Risankizumab - subjects who weighed ≥ 40 kg received 150 mg risankizumab, while subjects who weighed < 40 kg received 55 mg risankizumab and doses were administered at Weeks 0, 4, 16 and then every 12 weeks (q12w) thereafter.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for study M19-977, a randomized, active-controlled, efficacy assessor-blinded study to evaluate pharmacokinetics, safety, and efficacy of risankizumab in patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis.

Since this study used risankizumab in PsO patients under the age of 18, the MAH outlined that specific risks for this population have yet to be identified; however, no significant risks were expected as the planned dosing was equivalent to the adult efficacious dose that is considered safe and well tolerated. Children under the age of 6 were not included in this study because it is difficult to perform PsO clinical trials in this population due to rarity of disease.

2.3.2. Clinical study

Clinical study number and title

Study M19-977: *a randomized, active-controlled, efficacy assessor-blinded study to evaluate pharmacokinetics, safety, and efficacy of risankizumab in patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis.*

Description

Study M19-977 was a Phase 3, randomized, active controlled, efficacy assessor-blinded, multicenter, 4-part study to evaluate PK, safety, and efficacy of risankizumab in subjects 6 to <18 years of age with moderate to severe plaque PsO.

The study consisted of 4 parts, each with distinct patient populations.

Part 1 was a sentinel, open-label cohort of 12 adolescents (aged 12 to < 18 years) with severe plaque PsO who had undergone PK sampling for 16 weeks and continued risankizumab treatment until Week 40. Pharmacokinetic data up to Week 16 informed the Risankizumab dosing regimen for Part 2 and Part 3. In Part 1, all subjects received 150 mg risankizumab SC at Weeks 0, 4, 16, 28, and 40.

Part 2 was a randomized, efficacy assessor-blinded cohort comparing risankizumab with ustekinumab in 82 adolescents (aged 12 to < 18 years) with moderate to severe plaque PsO. A 16-week initial treatment period (Period A) was followed by an up to 36-week randomized treatment or withdrawal period (Period B) for risankizumab responders, and in case of disease flare a 16-week retreatment period (Period C). Risankizumab nonresponders and subjects who received ustekinumab in Period A received risankizumab (Period B) until Week 40. In Part 2 Period A, subjects randomized to ustekinumab received ustekinumab SC based on weight (0.75 mg/kg for subjects < 60 kg; 45 mg for subjects 60 to < 100 kg; 90 mg for subjects ≥ 100 kg) at Weeks 0 and 4.

Part 3 was a sentinel, open-label cohort of 13 children (aged 6 to < 12 years) with severe plaque PsO with PK sampling through Week 16 who then continued risankizumab treatment until Week 40. PK data from Week 16 informed the risankizumab dosing regimen for Part 4.

Part 4 was a single-arm, 52-week, open-label safety cohort of 30 children (aged 6 to < 12 years) with moderate to severe plaque PsO. In Japan, 2 adolescents aged 12 to < 18 years were included in the study but were not included in the analysis because they were not from the same age cohort as the population studied in Part 4 (children) but were added to Part 4 for administrative reasons (closure of Part 2 enrolment). Enrolment was triggered by Week 16 data from Part 3.

In Parts 2, 3, and 4, risankizumab doses were based on weight; subjects who weighed ≥ 40 kg received 150 mg risankizumab, while subjects who weighed < 40 kg received 55 mg risankizumab and doses were administered at Weeks 0, 4, 16 and then every 12 weeks (q12w) thereafter.

Subjects who completed the Week 52 visit in Part 1, Part 2 Period B, Part 3, or Part 4 and those who completed 16 weeks of the retreatment in Part 2 Period C had the option to enrol into Study M19-973, the open-label extension (OLE) study.

Methods

Treatments

Test Product, Dose/Strength/Concentration, Mode of Administration:

Risankizumab (ABBV-066) 150 mg/1.0 mL solution for injection in prefilled syringe.

Risankizumab (ABBV-066) 55 mg/0.37 mL solution for injection in prefilled syringe.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration :

Ustekinumab 45 mg/0.5 mL solution for injection in prefilled syringe.

Ustekinumab 45 mg/0.5 mL solution for injection in vial.

Objective(s)

The objective of this study was to evaluate the pharmacokinetics (PK), safety, and efficacy of risankizumab in subjects from 6 to less than 18 years of age with moderate to severe plaque PsO.

Study participants

A total of 139 subjects were enrolled (12 subjects in Part 1, 82 subjects in Part 2, 13 subjects in Part 3, and 30 subjects (aged 6 to < 12 years) plus 2 adolescent subjects from Japan in Part 4) from 41 sites across 7 countries (Canada, Germany, Japan, Poland, Spain, the United Kingdom, and the US). The 2 adolescent subjects from Japan in Part 4 were not part of the current analysis because they were not from the same age cohort as the population studied in Part 4 (children) but were added to Part 4 for administrative reasons (closure of Part 2 enrolment). Data for these 2 subjects were analysed separately outside of the study report.

In Part 1, Part 2, Part 3, and Part 4 over a third of the subjects were male. Most subjects were white and not Hispanic or Latino, with a mean (SD) age of 14.7 (1.67) years and 9.1 (1.72) years for Part 1 and 2 combined and Part 3 and 4 combined, respectively. Demographic characteristics were generally balanced between ustekinumab and risankizumab arms in Part 2.

The mean (standard deviation [SD]) duration of study drug exposure was comparable in Parts 1, 3, and 4 with 364.0 (4.20), 363.0 (3.63), and 351.9 (53.07) days, respectively. The duration of study drug exposure in Part 2 was shorter for both ustekinumab and risankizumab with 255.0 (9.50) and 278.1 (111.88) days, respectively.

In Part 1, due to the small sample sizes and the uncontrolled design, no efficacy subgroup analyses were performed.

In Part 2, efficacy subgroup analyses were performed to evaluate the consistency of risankizumab efficacy for categories of demographic and other baseline characteristics for the co-primary efficacy endpoints. Analyses within subgroups were conducted providing descriptive statistics and 95% CI.

In Part 3 and Part 4, subgroup analyses by baseline weight category (< 40 kg, ≥ 40 kg) of the co-primary efficacy endpoints. Due to the small sample sizes and the uncontrolled design of Part 3 and Part 4, no other efficacy subgroup analyses were performed.

Results

Pharmacokinetic Results

In Study Part 1, following administration of 150 mg SC risankizumab at Weeks 0, 4, and q12w thereafter in subjects with severe plaque PsO, serum concentrations reached geometric mean concentrations of 7.467 µg/mL, 3.011 µg/mL, and 1.640 µg/mL at Weeks 4, 16, and 52, respectively.

In Study Part 2, Periods A and C, following administration of 150 mg SC risankizumab, the geometric mean serum concentrations at Week 4 and Week 16 were similar to those observed in Study Part 1. During Period B, risankizumab geometric mean serum concentrations remained consistent between Week 28 and Week 52.

In Study Part 3, subjects receiving 150 mg SC risankizumab had geometric mean serum concentrations of 10.515 µg/mL at Week 4, 3.065 µg/mL at Week 16, and 1.760 µg/mL at Week 52. For subjects receiving 55 mg SC risankizumab, the concentrations were 6.480 µg/mL at Week 4, 2.247 µg/mL at Week 16, and 1.699 µg/mL at Week 52.

In Study Part 4, subjects receiving 150 mg SC risankizumab had geometric mean serum concentrations of 10.952 µg/mL at Week 4, 3.071 µg/mL at Week 16, and 1.952 µg/mL at Week 52. For subjects receiving 55 mg SC risankizumab, the concentrations were 6.691 µg/mL at Week 4, 1.860 µg/mL at Week 16, and 1.329 µg/mL at Week 52.

Immunogenicity Results

Overall, the incidence of immunogenicity was low in the study. In Study Part 1, no treatment emergent immunogenicity was observed. In Study Part 2, the incidence of treatment emergent ADAs to 150 mg risankizumab ranged from 7.8% to 20% across different periods, with no subjects positive for NAbs. In Study Part 3, the incidence of treatment-emergent ADAs to 150 mg risankizumab was 12.5% (1/8) with no subjects positive for NAbs; the incidence of treatment-emergent ADAs to 55 mg risankizumab was 20% (1/5) and the single subject who developed ADA also tested positive for NAbs. In Study Part 4, the incidence of treatment-emergent ADAs to 150 mg risankizumab was 50% (3/6) with no subjects positive for NAbs; the incidence of treatment-emergent ADAs to 55 mg risankizumab was 8.7% (2/23), with 4.3% (1/23) testing positive for NAbs.

Risankizumab serum exposures were similar in subjects who developed ADAs compared to those who were ADA-negative, suggesting no apparent impact of ADA on risankizumab exposure. Immunogenicity to risankizumab was not considered clinically relevant to either safety or efficacy.

Efficacy results

In this descriptive study of paediatric subjects, risankizumab provided clinical improvement in PsO extent and severity by Week 16, with a high rate of response that was maintained through Week 52 as measured by PASI and sPGA clear or almost clear in Parts 1, 2, 3, and 4.

In Part 2, comparable proportions of subjects randomized to risankizumab and ustekinumab achieved the co-primary endpoints of PASI 75 and sPGA clear or almost clear at Week 16, with a higher number achieving complete skin clearance (PASI 100) in the risankizumab arm. Among Week 16 risankizumab responders (sPGA clear or almost clear) in Part 2 Period A who were rerandomized to withdrawal in

Part 2 Period B, 38% received retreatment by Week 52 and subsequently, the majority regained clinical response by Week 16 of retreatment.

Safety results

There were no SAEs or severe TEAEs during Part 1.

In Part 2 Period A, the proportion of subjects in the ustekinumab arm with TEAEs was higher than that of subjects in the risankizumab arm. TEAEs on Part 2 Period B were generally comparable between subjects on ustekinumab who were switched to risankizumab and those who were rerandomized either to continue on risankizumab or receive no treatment. Overall, in combined Part 1 and Part 2, Part 3, and Part 4 there were 2 subjects with SAEs and 3 subjects with severe TEAEs. There were no TEAEs leading to discontinuation of study drug or deaths reported in subjects from Part 1, Part 2, Part 3, or Part 4.

In Part 1, a treatment-emergent hepatic event ASI was reported in one subject (8.3%).

In Part 2, the following treatment-emergent ASIs were reported in risankizumab-treated subjects: hypersensitivity events (3 subjects [3.7%]), hepatic events (5 subjects [6.1%]), injection site reactions (1 subject [1.2%]) and suicidal ideation behavior (1 subject [1.2%]). In Part 3, no treatment-emergent ASIs were reported. In Part 4, with the exception of hypersensitivity events (6 subjects [20.0%]), no treatment-emergent ASIs were reported.

Across all adolescents (combined Part 1 and Part 2) and children (combined Part 3 and Part 4), no subjects experienced potentially clinically significant (PCS) hematology values. During Part 1, 2 subjects experienced Grade 4 creatine kinase abnormalities, with one of the same subjects also experiencing a Grade 3 creatine kinase abnormality and a Grade 3 aspartate aminotransferase (AST) abnormality.

In Part 2, 1 subject experienced a Grade 3 alanine aminotransferase (ALT) abnormality and 2 subjects experienced Grade 3 triglycerides. Across children (combined Part 3 and Part 4) with potentially clinically significant (PCS) values, 1 subject (Part 3) with Grade 3 PCS potassium (hyper) experienced an AE of blood potassium increased. No subjects reported SAEs or discontinued study drug due to AEs associated with PCS chemistry values during the study period. During Part 2 Period A, the proportions of subjects who had liver test elevations that met PCS criteria were similar between the risankizumab and ustekinumab arms. Overall, across adolescents (combined Part 1 and Part 2), few risankizumab-treated subjects had PCS ALT, AST, total bilirubin, or alanine aminotransferase (ALP) values. Overall, across children (combined Part 3 and Part 4), 2 subjects had PCS elevations (increased ALP and total bilirubin in 1 subject each). There were few PCS blood pressure values during risankizumab exposure.

Overall, the safety profile of risankizumab in pediatric subjects with PsO was considered to be consistent with the known safety profile in adults with PsO.

2.3.3. Discussion on clinical aspects

The overview of data provided in Study M19-977 suggests that treatment with risankizumab 150 mg SC for subjects who weigh ≥ 40 kg and 55 mg SC for subjects who weigh < 40 kg q12w can be considered to provide clinical disease improvements measured by PASI and sPGA at Week 16. Treatment with risankizumab 150 mg and 55 mg SC at Week 0, Week 4, and q12w thereafter was considered safe and well tolerated in subjects with moderate to severe plaque PsO 6 years of age and older who were candidates for systemic therapy.

The MAH states that submission of an indication extension for approval of risankizumab in paediatric PsO subjects supported by the Study M19-977 data is planned for 2025. The MAH confirmed that the indication extension submission will be supported by a line extension which is currently in development.

In this context, a full assessment of Study M19-977 will be conducted as part of the impending variation (expected in 2025). Therefore, no queries on the data submitted or recommendations for updates to the SmPC are made at this time.

3. CHMP's overall conclusion and recommendation

It is acknowledged that the MAH has provided the completed study report for this paediatric study (Study M19-977) in accordance with Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation'). The study report for Study M19-977 is submitted as a stand-alone post authorisation measure. The MAH is planning to submit a Type II variation application in 2025 to extend the indication for use of risankizumab to paediatric PsO subjects supported by the Study M19-977, hence, a full assessment of the study results will be conducted as part of the impending variation. In this context, no queries on the data submitted or recommendations for updates to the SmPC are proposed at this time.

☒ **Fulfilled:**

No regulatory action required, however, a full assessment of the results for Study M19-977 will be performed with the Type II variation application to extend the indication for use of risankizumab to paediatric PsO subjects supported by the Study M19-977. The MAH is intending to submit this variation application in 2025.