▼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 adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 75 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 75 mg risankizumab in 0.83 ml solution.

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody selective to the interleukin (IL)-23 protein produced in Chinese Hamster Ovary cells using recombinant DNA technology.

Excipients with known effect

This medicinal product contains 68.0 mg sorbitol per 150 mg dose.

This medicinal product contains less than 1 mmol sodium (23 mg) per 150 mg dose, that is to say essentially ‘sodium free’.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

The solution is colourless to slightly yellow and clear to slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Skyrizi is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

4.2 Posology and method of administration

Skyrizi is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.

Posology

The recommended dose is 150 mg (two 75 mg injections) administered by subcutaneous injection at week 0, week 4, and every 12 weeks thereafter.

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

Special populations

Elderly (aged 65 years and over)

No dose adjustment is required (see section 5.2).
There is limited information in subjects aged ≥65 years.

Renal or hepatic impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of Skyrizi. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population

The safety and efficacy of Skyrizi in children and adolescents aged 6 to 18 years have not yet been established. No data are available.

There is no relevant use of Skyrizi in children aged below 6 years for the indication of moderate to severe plaque psoriasis.

Overweight patients

No dose adjustment is required (see section 5.2).

Method of administration

Skyrizi is administered by subcutaneous injection. For each dose, the injections should be administered at different anatomic locations (such as thighs or abdomen), and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. Administration of Skyrizi in the upper, outer arm may only be performed by a healthcare professional or caregiver.

Patients may self-inject Skyrizi after training in subcutaneous injection technique. Patients should be instructed to inject 2 pre-filled syringes for the full 150 mg dose and to read the ‘Instructions for use’ provided in the package leaflet before administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g. active tuberculosis, see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Risankizumab may increase the risk of infection.

In patients with a chronic infection, a history of recurrent infection, or known risk factors for infection, risankizumab should be used with caution. Treatment with risankizumab should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with risankizumab should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops such an infection or is not responding to standard therapy for the infection, the patient should be closely monitored and risankizumab should not be administered until the infection resolves.

Tuberculosis

Prior to initiating treatment with risankizumab, patients should be evaluated for tuberculosis (TB) infection. Patients receiving risankizumab should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating risankizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Immunisations

Prior to initiating therapy with risankizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. If a patient has received live vaccination (viral or bacterial), it is recommended to wait at least 4 weeks prior to starting treatment with risankizumab. Patients treated with risankizumab should not receive live vaccines during treatment and for at least 21 weeks after treatment (see section 5.2).

Hypersensitivity

If a serious hypersensivity reaction occurs, administration of risankizumab should be discontinued immediately and appropriate therapy initiated.

Excipients with known effect

This medicinal product contains 68.0 mg sorbitol per 150 mg dose.
The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

This medicinal product contains less than 1 mmol sodium (23 mg) per 150 mg dose, that is to say essentially ‘sodium free’.

4.5 Interaction with other medicinal products and other forms of interaction

Risankizumab is not expected to undergo metabolism by hepatic enzymes or renal elimination. Drug interactions between risankizumab and inhibitors, inducers, or substrates of drug metabolising enzymes are not expected and no dose adjustment is needed (see section 5.2).

Concomitant immunosuppressive therapy or phototherapy

The safety and efficacy of risankizumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 21 weeks after treatment.

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of risankizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of risankizumab during pregnancy.

Breast-feeding

It is unknown whether risankizumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. A decision should be made whether to discontinue/abstain from risankizumab therapy, taking into account the benefit of breast-feeding to the child and the benefit of risankizumab therapy to the woman.

Fertility

The effect of risankizumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Risankizumab has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were upper respiratory infections, which occurred in 13% of patients.

Tabulated list of adverse reactions

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

Table 1: List of adverse reactions in clinical studies

System Organ Class	Frequency	Adverse Reactions
Infections and infestations	Very common	Upper respiratory infections[a]
	Common	Tinea infections[b]
	Uncommon	Folliculitis
Nervous system disorders	Common	Headache[c]
Skin and subcutaneous tissue disorders	Common	Pruritus
General disorders and administration site conditions	Common	Fatigue[d] Injection site reactions[e]

[a] Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis
[b] Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, onychomycosis
[c] Includes: headache, tension headache, sinus headache
[d] Includes: fatigue, asthenia
[e] Includes: injection site bruising, erythema, haematoma, haemorrhage, irritation, pain, pruritus, reaction, swelling

Description of selected adverse reactions

Infections

Over the entire psoriasis programme including long-term exposure to risankizumab, the rate of infections was 75.5 events per 100 subject-years. The majority of cases were non-serious and mild to moderate in severity and did not lead to discontinuation of risankizumab. The rate of serious infections was 1.7 events per 100 subject-years (see section 4.4).

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity with risankizumab. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

For subjects treated with risankizumab at the recommended clinical dose for up to 52 weeks in psoriasis clinical trials, treatment-emergent anti-drug antibodies and neutralising antibodies were detected in 24% (263/1,079) and 14% (150/1,079) of evaluated subjects, respectively.

For most subjects, antibodies to risankizumab including neutralising antibodies were not associated with changes in clinical response or safety. Among the few subjects (approximately 1%; 7/1,000 at week 16 and 6/598 at week 52) with high antibody titers (>128), clinical response appeared to be reduced. The incidence of injection site reactions is numerically higher in the anti-drug antibody-positive compared with anti-drug antibody-negative groups over short-term (16 weeks: 2.7% vs 1.3%) and longer term treatment (>52 weeks: 5.0% vs 3.3%). The injection site reactions were all mild to moderate in severity, none were serious, and none led to discontinuation of risankizumab.

Elderly

There is limited safety information in subjects aged ≥65 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC18

Mechanism of action

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.

Pharmacodynamic effects

In a study of subjects with psoriasis, expression of genes associated with the IL-23/IL-17 axis was decreased in the skin after single doses of risankizumab. Reductions in epidermal thickness, infiltration of inflammatory cells, and expression of psoriatic disease markers were also observed in psoriatic lesions.

Clinical efficacy and safety

The efficacy and safety of risankizumab was assessed in 2,109 subjects with moderate to severe plaque psoriasis in four multicentre, randomised, double-blind studies (ULTIMMA-1, ULTIMMA-2, IMMHANCE, and IMMVENT). Enrolled subjects were 18 years of age and older with plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, a static Physician Global Assessment (sPGA) score of ≥3 in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 4, a Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for systemic therapy or phototherapy.

Overall, subjects had a median baseline PASI score of 17.8, a median BSA of 20.0%, and a median baseline DLQI score of 13.0. Baseline sPGA score was severe in 19.3% of subjects and moderate in 80.7% of subjects. A total of 9.8% of study subjects had a history of diagnosed psoriatic arthritis.

Across all studies, 30.9% of subjects were naïve to any systemic therapy (including non-biologic and biologic), 38.1% had received prior phototherapy or photochemotherapy, 48.3% had received prior non-biologic systemic therapy, 42.1% had received prior biologic therapy, and 23.7% had received at least one anti-TNF alpha agent for the treatment of psoriasis.

ULTIMMA-1 and ULTIMMA-2

ULTIMMA-1 and ULTIMMA-2 enrolled 997 subjects (598 randomised to risankizumab 150 mg, 199 to ustekinumab 45 mg or 90 mg [according to baseline weight], and 200 to placebo). Subjects received treatment at week 0, week 4, and every 12 weeks thereafter. The two co-primary endpoints in ULTIMMA-1 and ULTIMMA-2 were the proportion of subjects who achieved 1) PASI 90 response and 2) sPGA score of clear or almost clear (sPGA 0 or 1) at week 16 versus placebo. The results for the co-primary and other endpoints are presented in Table 2 and Figure 1.

Table 2: Efficacy and quality of life results in adults with plaque psoriasis in ULTIMMA-1 and ULTIMMA-2

	ULTIMMA-1			ULTIMMA-2		
	Risankizumab (N=304) n (%)	**Ustekinumab (N=100) n (%)**	**Placebo (N=102) n (%)**	**Risankizumab (N=294) n (%)**	**Ustekinumab (N=99) n (%)**	**Placebo (N=98) n (%)**
sPGA of clear or almost clear (0 or 1)						
Week 16[a]	267 (87.8)	63 (63.0)	8 (7.8)	246 (83.7)	61 (61.6)	5 (5.1)
Week 52	262 (86.2)	54 (54.0)	--	245 (83.3)	54 (54.5)	--
sPGA of clear (0)						
Week 16	112 (36.8)	14 (14.0)	2 (2.0)	150 (51.0)	25 (25.3)	3 (3.1)
Week 52	175 (57.6)	21 (21.0)	--	175 (59.5)	30 (30.3)	--
PASI 75						
Week 12	264 (86.8)	70 (70.0)	10 (9.8)	261 (88.8)	69 (69.7)	8 (8.2)
Week 52	279 (91.8)	70 (70.0)	--	269 (91.5)	76 (76.8)	--
PASI 90						
Week 16[a]	229 (75.3)	42 (42.0)	5 (4.9)	220 (74.8)	47 (47.5)	2 (2.0)
Week 52	249 (81.9)	44 (44.0)	--	237 (80.6)	50 (50.5)	--
PASI 100						
Week 16	109 (35.9)	12 (12.0)	0 (0.0)	149 (50.7)	24 (24.2)	2 (2.0)
Week 52	171 (56.3)	21 (21.0)	--	175 (59.5)	30 (30.3)	--
DLQI 0 or 1[b]						
Week 16	200 (65.8)	43 (43.0)	8 (7.8)	196 (66.7)	46 (46.5)	4 (4.1)
Week 52	229 (75.3)	47 (47.0)	--	208 (70.7)	44 (44.4)	--
PSS 0 (symptom-free)[c]						
Week 16	89 (29.3)	15 (15.0)	2 (2.0)	92 (31.3)	15 (15.2)	0 (0.0)
Week 52	173 (56.9)	30 (30.0)	--	160 (54.4)	30 (30.3)	--

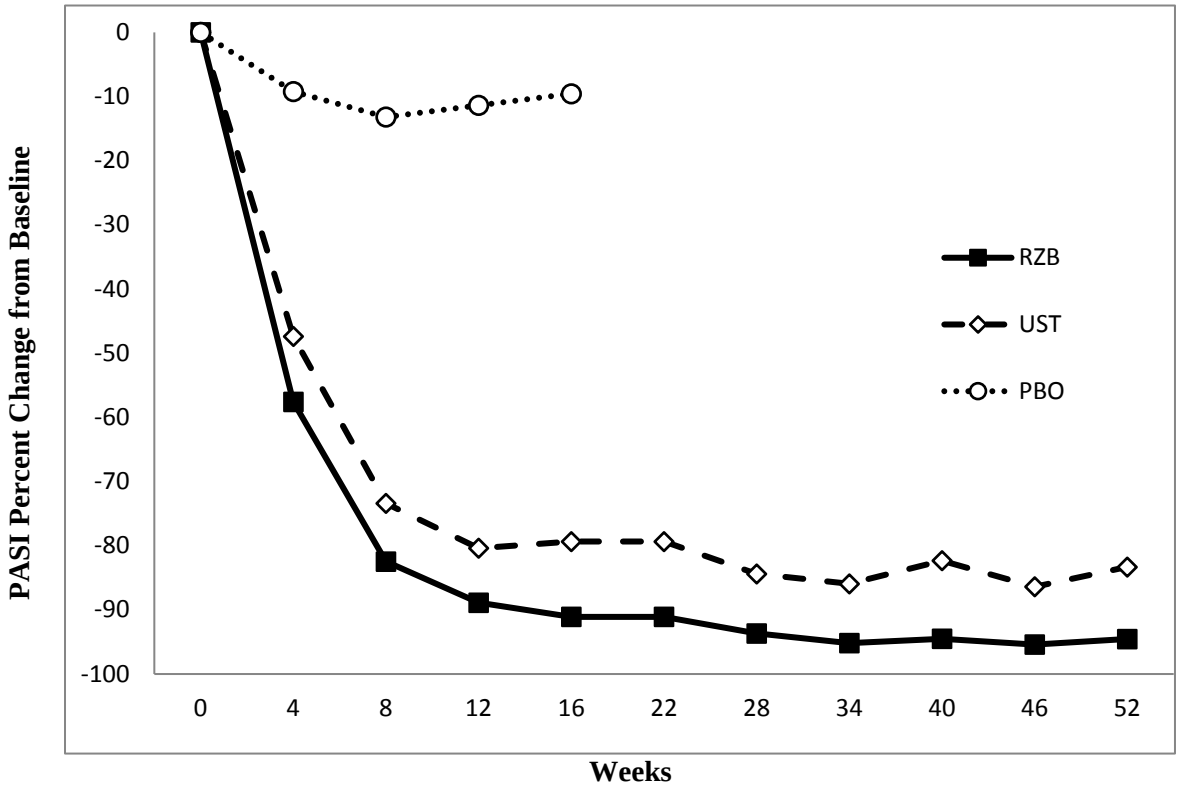
All comparisons of risankizumab versus ustekinumab and placebo achieved $p<0.001$ except for PASI 75 at week 52 in ULTIMMA-2 where $p=0.001$

[a] Co-primary endpoints versus placebo

[b] No impact on health-related quality of life

[c] Psoriasis Symptom Scale (PSS) of 0 means no symptoms of pain, itching, redness, and burning during the last 24 hours

Figure 1: Time course of mean percent change from baseline of PASI in ULTIMMA-1 and ULTIMMA-2



RZB = risankizumab
UST = ustekinumab
PBO = placebo
$p<0.001$ at each time point

Examination of age, gender, race, body weight ≤130 kg, baseline PASI score, concurrent psoriatic arthritis, previous non-biologic systemic treatment, previous biologic treatment, and previous failure of a biologic did not identify differences in response to risankizumab among these subgroups.

Improvements were observed in psoriasis involving the scalp, the nails, and the palms and soles at week 16 and week 52 in subjects treated with risankizumab.

Table 3: Mean changes from baseline in NAPSI, PPASI, and PSSI

	ULTIMMA-1		ULTIMMA-2		IMMHANCE	
	Risankizumab	**Placebo**	**Risankizumab**	**Placebo**	**Risankizumab**	**Placebo**
NAPSI: Change at Week 16 (SE)	N=178; -9.0 (1.17)	N=56; 2.1 (1.86) ***	N=177; -7.5 (1.03)	N=49; 3.0 (1.76) ***	N=235; -7.5 (0.89)	N=58; 2.5 (1.70) ***
PPASI: Change at Week 16 (SE)	N=95; -5.93 (0.324)	N=34; -3.17 (0.445) ***	N=86; -7.24 (0.558)	N=23; -3.74 (1.025) **	N=113; -7.39 (0.654)	N=26; -0.27 (1.339) ***
PSSI: Change at Week 16 (SE)	N=267; -17.6 (0.47)	N=92; -2.9 (0.69) ***	N=252; -18.4 (0.52)	N=83; -4.6 (0.82) ***	N=357; -20.1 (0.40)	N=88; -5.5 (0.77) ***
NAPSI: Change at Week 52 (SE)	N=178; -15.7 (0.94)	-	N=183; -16.7 (0.85)	-	-	-
PPASI: Change at Week 52 (SE)	N=95; -6.16 (0.296)	-	N=89; -8.35 (0.274)	-	-	-
PSSI: Change at Week 52 (SE)	N=269; -17.9 (0.34)	-	N=259; -18.8 (0.24)	-	-	-

Nail Psoriasis Severity Index (NAPSI), Palmoplantar Psoriasis Severity Index (PPASI), Psoriasis Scalp Severity Index (PSSI), and Standard Error (SE)
** $P < 0.01$ comparing to risankizumab
*** $P < 0.001$ comparing to risankizumab

Anxiety and depression, as measured by the Hospital Anxiety and Depression Scale (HADS), improved in the risankizumab group at week 16 compared with the placebo group.

Maintenance of response

In an integrated analysis of subjects receiving risankizumab in ULTIMMA-1 and ULTIMMA-2 for PASI 100 responders at week 16, 79.8% (206/258) of the subjects who continued on risankizumab maintained the response at week 52. For PASI 90 responders at week 16, 88.4% (398/450) of subjects maintained the response at week 52.

The safety profile of risankizumab with up to 77 weeks of exposure was consistent with the profile observed up to 16 weeks.

IMMHANCE

IMMHANCE enrolled 507 subjects (407 randomised to risankizumab 150 mg and 100 to placebo). Subjects received treatment at week 0, week 4 and every 12 weeks thereafter. Subjects who were originally on risankizumab and had a sPGA response of clear or almost clear at week 28 were re-randomised to continue risankizumab every 12 weeks or have treatment withdrawn.

At week 16, risankizumab was superior to placebo on the co-primary endpoints of sPGA of clear or almost clear (83.5% risankizumab vs 7.0% placebo) and PASI 90 (73.2% risankizumab vs 2.0% placebo).

Of the 31 subjects from the IMMHANCE study with latent tuberculosis (TB) who did not receive prophylaxis during the study, none developed active TB during the mean follow-up of 55 weeks on risankizumab.

Among subjects with sPGA of clear or almost clear at week 28 in IMMHANCE, 81.1% (90/111) of subjects re-randomised to continued treatment with risankizumab maintained this response at week 104 compared to 7.1% (16/225) who were re-randomised to withdrawal from risankizumab. Of these subjects, 63.1% (70/111) of subjects re-randomised to continued treatment with risankizumab achieved a sPGA clear response at week 104 compared to 2.2% (5/225) who were re-randomised to withdrawal from risankizumab.

IMMVENT

IMMVENT enrolled 605 subjects (301 randomised to risankizumab and 304 to adalimumab). Subjects randomised to risankizumab received 150 mg of treatment at week 0, week 4 and every 12 weeks thereafter. Subjects randomised to adalimumab received 80 mg at week 0, 40 mg at week 1 and 40 mg every other week through week 15. Starting at week 16, subjects who were receiving adalimumab continued or switched treatment based on response:

- <PASI 50 were switched to risankizumab
- PASI 50 to <PASI 90 were re-randomised to either continue adalimumab or switch to risankizumab
- PASI 90 continued to receive adalimumab

Results are presented in Table 4.

Table 4: Efficacy and quality of life results at week 16 in adults with plaque psoriasis in IMMVENT

	Risankizumab (N=301) n (%)	**Adalimumab (N=304) n (%)**
sPGA of clear or almost clear[a]	252 (83.7)	183 (60.2)
PASI 75	273 (90.7)	218 (71.7)
PASI 90[a]	218 (72.4)	144 (47.4)
PASI 100	120 (39.9)	70 (23.0)
DLQI 0 or 1[b]	198 (65.8)	148 (48.7)
All comparisons achieved p<0.001 [a] Co-primary endpoints [b] No impact on health-related quality of life		

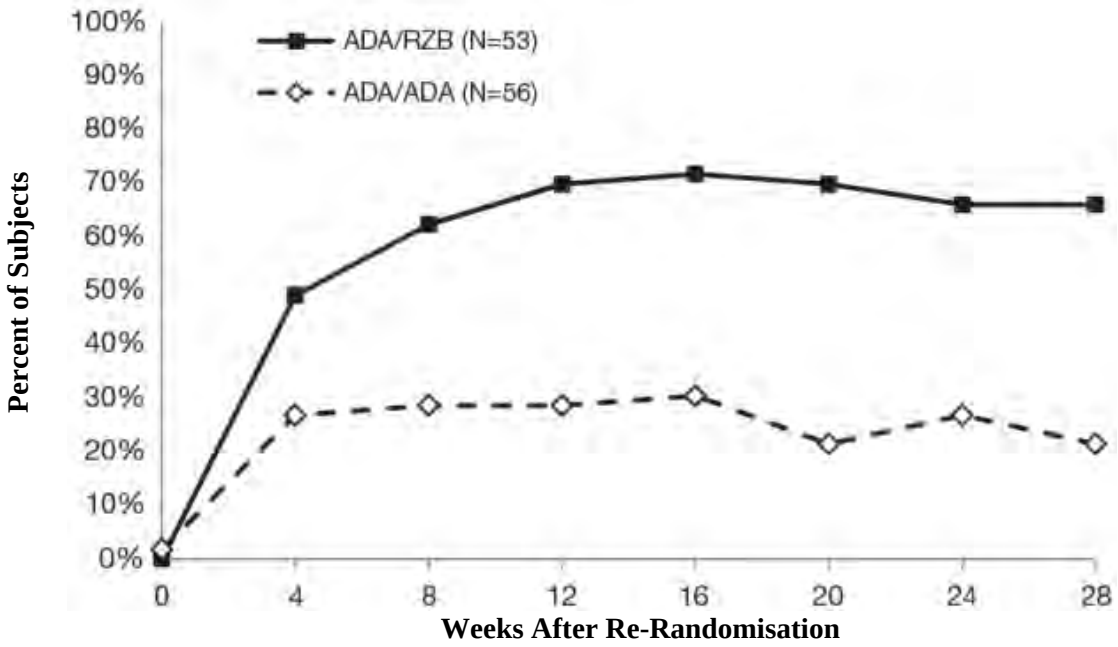
For subjects who had PASI 50 to <PASI 90 with adalimumab at week 16 and were re-randomised, differences in PASI 90 response rates between switching to risankizumab and continuing adalimumab were noted 4 weeks after re-randomisation (49.1% vs 26.8%, respectively).

Results 28 weeks after re-randomisation are presented in Table 5 and Figure 2.

Table 5: Efficacy results 28 weeks after re-randomisation in IMMVENT

	Switched to Risankizumab (N=53) n (%)	Continued on Adalimumab (N=56) n (%)
PASI 90	35 (66.0)	12 (21.4)
PASI 100	21 (39.6)	4 (7.1)
All comparisons achieved p<0.001		

Figure 2: Time course of PASI 90 after re-randomisation in IMMVENT



ADA/ADA: Subjects randomised to adalimumab and continued on adalimumab
ADA/RZB: Subjects randomised to adalimumab and switched to risankizumab
p<0.05 at week 4 and p<0.001 at each time point beginning at week 8

In 270 patients who switched from adalimumab to risankizumab without a washout period, the safety profile of risankizumab was similar to that in patients who initiated risankizumab after wash out of any prior systemic therapies.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with risankizumab in one or more subsets of the paediatric population in the treatment of plaque psoriasis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Risankizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure across dose ranges of 18 to 300 mg and 0.25 to 1 mg/kg administered subcutaneously, and 200 to 1,200 mg and 0.01 to 5 mg/kg administered intravenously.

Following subcutaneous dosing of risankizumab, peak plasma concentrations were achieved between 3-14 days after dosing with an estimated absolute bioavailability of 89%. With dosing of 150 mg at week 0, week 4 and every 12 weeks thereafter, estimated steady-state peak and trough plasma concentrations are 12 and 2 µg/mL, respectively.

Distribution

The mean (±standard deviation) steady-state volume of distribution (V_{ss}) of risankizumab was 11.4 (±2.7) L in Phase 3 studies in subjects with psoriasis, indicating that the distribution of risankizumab is primarily confined to the vascular and interstitial spaces.

Biotransformation

Therapeutic IgG monoclonal antibodies are typically degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs. Risankizumab is not expected to be metabolised by cytochrome P450 enzymes.

Elimination

The mean (±standard deviation) systemic clearance (CL) of risankizumab was 0.3 (±0.1) L/day in Phase 3 studies in subjects with psoriasis. The mean terminal elimination half-life of risankizumab ranged from 28 to 29 days in Phase 3 studies in subjects with psoriasis.

As an IgG1 monoclonal antibody, risankizumab is not expected to be filtered by glomerular filtration in the kidneys or to be excreted as an intact molecule in the urine.

Linearity/non-linearity

Risankizumab exhibited linear pharmacokinetics with approximately dose-proportional increases in systemic exposure (C_{max} and AUC) in the evaluated dose ranges of 18 to 300 mg or 0.25 to 1 mg/kg subcutaneous administration in healthy subjects or subjects with psoriasis.

Drug interactions

A drug interaction study was conducted in subjects with plaque psoriasis to assess the effect of repeated administration of risankizumab on the pharmacokinetics of cytochrome P450 (CYP) sensitive probe substrates. The exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate) and midazolam (CYP3A substrate) following risankizumab treatment were comparable to their exposures prior to risankizumab treatment, indicating no clinically meaningful drug interactions through these enzymes.

Population pharmacokinetic analyses indicated that risankizumab exposure was not impacted by concomitant medications (metformin, atorvastatin, lisinopril, amlodipine, ibuprofen, acetylsalicylate and levothyroxine) used by some subjects with plaque psoriasis during the clinical studies.

Special populations

Paediatric patients

The pharmacokinetics of risankizumab in paediatric subjects has not been established.

Elderly patients

Of the 2,234 subjects with plaque psoriasis exposed to risankizumab, 243 were 65 years or older and 24 subjects were 75 years or older. No overall differences in risankizumab exposure were observed between older and younger subjects who received risankizumab.

Patients with renal or hepatic impairment

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab. Based on population pharmacokinetic analyses, serum creatinine

levels, creatinine clearance, or hepatic function markers (ALT/AST/bilirubin) did not have a meaningful impact on risankizumab clearance in subjects with psoriasis.

As an IgG1 monoclonal antibody, risankizumab is mainly eliminated via intracellular catabolism and is not expected to undergo metabolism via hepatic cytochrome P450 enzymes or renal elimination.

Body weight

Risankizumab clearance and volume of distribution increase as body weight increases which may result in reduced efficacy in subjects with high body weight (>130 kg). However, this observation is based on a limited number of subjects. No dose adjustment based on body weight is currently recommended.

Gender or race

The clearance of risankizumab was not significantly influenced by gender or race in adult subjects with plaque psoriasis. No clinically meaningful differences in risankizumab exposure were observed in Chinese or Japanese subjects compared to Caucasian subjects in a clinical pharmacokinetic study.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on repeat-dose toxicity studies including safety pharmacology evaluations, and a reproductive and developmental toxicity study in cynomolgus monkeys at doses of up to 50 mg/kg/week (producing exposures of about 70 times the clinical exposure at maximum recommended human dose [MRHD]).

Mutagenicity and carcinogenicity studies have not been conducted with risankizumab. In a 26-week chronic toxicology study in cynomolgus monkeys at doses of up to 50 mg/kg/week (about 70 times the clinical exposure at the MRHD), there were no pre-neoplastic or neoplastic lesions observed and no adverse immunotoxicity or cardiovascular effects were noted .

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium succinate hexahydrate
Succinic acid
Sorbitol
Polysorbate 20
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

6.5 Nature and contents of container

Pre-filled glass syringe with a fixed needle and needle cover, assembled in an automatic needle guard. Each pre-filled syringe contains 75 mg risankizumab in 0.83 ml.

Skyrizi is available in packs containing 2 pre-filled syringes and 2 alcohol pads.

6.6 Special precautions for disposal and other handling

Before injecting, patients may remove the carton from the refrigerator and allow to reach room temperature out of direct sunlight (15 to 30 minutes) without removing the pre-filled syringes from the carton.

Prior to use, a visual inspection of each pre-filled syringe is recommended. The solution should be colourless to slightly yellow and clear to slightly opalescent. It may contain a few translucent to white product-related particles. Skyrizi should not be used if the solution is cloudy or discoloured, or contains large particles.

Two pre-filled syringes should be injected for the full 150 mg dose. Comprehensive instructions for use are provided in the package leaflet.

Each pre-filled syringe is for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 April 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.