1 PRODUCT NAME

COSENTYX® 75mg/0.5 mL Solution for Injection
COSENTYX® 150 mg Powder for Injection
COSENTYX® 150 mg/mL Solution for Injection
COSENTYX® 300mg/2 mL Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Secukinumab 150mg
Each vial of powder for injection contains 150 mg of secukinumab

Secukinumab 75mg/0.5mL
Each single-use pre-filled syringe contains 75 mg of secukinumab in 0.5 mL

Secukinumab 150mg/mL
Each single-use pre-filled syringe contains 150 mg of secukinumab in 1 mL
Each single-use prefilled pen contains 150 mg of secukinumab in 1 mL

Secukinumab 300mg/2mL
Each single-use pre-filled syringe contains 300 mg of secukinumab in 2 mL
Each single-use prefilled pen contains 300 mg of secukinumab in 2 mL

Secukinumab is a recombinant fully human monoclonal antibody selective for interleukin-17A.
Secukinumab is composed of one heavy chain containing 457 amino acids and one light chain containing 215 amino acids.
Secukinumab is of the IgG1/κ-class produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Powder for injection
Each vial of powder for injection contains 150 mg of secukinumab as a lyophilized cake in glass vials.

Solution for injection
Solution for injection in a single-use, pre-filled syringe and/or pen (auto-injector). The solution is clear and colourless to slightly yellow. The pH value ranges from 5.5 to 6.1 and Osmolality between 300- 400 mOsmol/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Plaque psoriasis
COSENTYX is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy.

Psoriatic arthritis
COSENTYX is indicated for the treatment of adult patients with active psoriatic arthritis when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.

Axial spondyloarthritis (axSpA) with or without radiographic damage
Ankylosing spondylitis (axSpA with radiographic damage)
COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis.

Non-radiographic axial spondyloarthritis (axSpA without radiographic damage)
COSENTYX is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or MRI change, who have had an inadequate response to, or are intolerant to, NSAIDs.

Juvenile Idiopathic Arthritis (JIA)
Juvenile Psoriatic Arthritis (JPsA)
COSENTYX is indicated for the treatment of active juvenile psoriatic arthritis in patients 2 years and older.

Enthesitis-Related Arthritis (ERA)
COSENTYX is indicated for the treatment of active enthesitis-related arthritis in patients 4 years of age and older.

Hidradenitis Suppurativa (HS)
COSENTYX is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic hidradenitis suppurativa therapy.

4.2 Dose and method of administration

Dosage

Plaque psoriasis
Adult patients
The recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Some patients ≥90 kgs may derive an additional benefit from receiving 300 mg every 2 weeks.

Each 300 mg dose is given as one subcutaneous injection of 300mg or as two subcutaneous injections of 150 mg. When administering two 150 mg doses (i.e., 300 mg dose), two injection sites should be used. New injection sites should be used for each set of injections.

Paediatric patients
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as one subcutaneous injection of 300mg or as two subcutaneous injections of 150 mg.

Table 1 Recommended dose of Cosentyx for paediatric plaque psoriasis

Body weight at time of dosing	Recommended Dose
<25 kg	75 mg
25 to <50 kg	75 mg (*may be increased to 150 mg)

≥50 kg	150 mg (*may be increased to 300 mg)

**Some patients may derive additional benefit from the higher dose.*

Psoriatic arthritis
Adult patients

The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Based on clinical response, the dose can be increased to 300 mg.
For patients with concomitant moderate to severe plaque psoriasis, please refer to adult plaque psoriasis recommendation.
For patients who are anti-TNF-alpha inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

COSENTYX may be administered with or without methotrexate.

Axial spondyloarthritis
Ankylosing spondylitis
The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or two subcutaneous injections of 150 mg.

Non-radiographic axial spondyloarthritis
With a loading dose: The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month.

Without a loading dose: The recommended dose is 150 mg by subcutaneous injection every month.

Juvenile Idiopathic Arthritis
Juvenile Psoriatic Arthritis (JPsA) and Enthesitis-Related Arthritis (ERA)
The recommended dose based on body weight is administered by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month.
- For patients weighing ≥ 15 kg and < 50 kg the recommended dose is 75 mg
- For patients weighing ≥ 50 kg the recommended dose is 150 mg

Paediatric patients requiring 75mg :
Each dose is given as one subcutaneous injection of 75 mg (COSENTYX 75mg/0.5 mL Solution for Injection in pre-filled syringe)

Paediatric patients requiring 150 mg :
Each 150 mg dose is given as one subcutaneous injection of 150 mg (COSENTYX 150 mg Powder for Injection in vial, or COSENTYX 150 mg/mL Solution for Injection in pre-filled syringe or pre-filled pen)

Paediatric patients requiring 300 mg :
Each 300 mg dose is given as one subcutaneous injection of 300mg (COSENTYX 300 mg/2mL Solution for Injection in pre-filled syringe or pre-filled pen) or as two subcutaneous injections of 150 mg (COSENTYX 150 mg/mL Solution for Injection in pre-filled syringe or pre-filled pen).

Hidradenitis Suppurativa
The recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3, and 4 followed by a maintenance dose of 300 mg every 4 weeks. Some patients may derive an additional benefit from receiving 300 mg every 2 weeks. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Assessment Prior to Initiation of COSENTYX

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX (see section 4.4)

Special populations

Patients with renal or hepatic impairment

COSENTYX has not been specifically studied in these patient populations. No dose recommendations can be made.

Paediatric and adolescent patients

Safety and effectiveness in paediatric patients with plaque psoriasis below the age of 6 years have not yet been established.

Safety and effectiveness in paediatric patients with the JIA categories of ERA (below the age of 4 years) and JPsA (below the age of 2 years) have not been established.

Safety and effectiveness in paediatric patients below the age of 18 years in other indications have not yet been established.

Elderly patients (≥ 65 years of age)

No dose adjustment is needed for elderly patients.

Administration

The product is for single use in one patient only. Discard any residue.

Powder for injection

COSENTYX is administered by subcutaneous injection. Each vial of COSENTYX must be reconstituted with 1 mL of sterile water for injections to obtain a 150 mg/mL solution. The powder for injection should be administered by healthcare professionals only.

Prefilled syringe and pre-filled pen

COSENTYX is administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

Before injection, secukinumab may be allowed to reach room temperature (20 minutes) without removing the needle cap during this time.

Prior to administration, the liquid must be checked whether it is clear and colourless. The solution should not be used if discoloured, or cloudy, or if foreign particles are present.

After proper training in subcutaneous injection technique, patients ≥12 years old may self-inject COSENTYX or, for all patients ≥6 years old, the injection may be given by a caregiver if a physician determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients and/or caregivers should be instructed to inject the full amount of COSENTYX according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Severe hypersensitivity reactions to the active substance or to any of the excipients (see sections 2, 4.4, and 6.1).

Clinically important, active infections (see section 4.4).

4.4 Special warnings and precautions for use

Infections

COSENTYX has the potential to increase the risk of infections. In clinical studies, infections have been observed in patients receiving COSENTYX (see section 4.8). Most of these were mild or moderate.

Related to the mechanism of action of COSENTYX, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8). A similar increase in risk of infection was seen in placebo-controlled trials in patients with psoriatic arthritis and axial spondyloarthritis. The incidence of some types of infections appeared to be dose-dependent in clinical studies (see section 4.8).

Caution should be exercised when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and COSENTYX should not be administered until the infection resolves.

Pre-treatment evaluation for tuberculosis

Tuberculosis (active and/or latent reactivation) can occur in patients treated with COSENTYX. Patients should be evaluated for tuberculosis infection prior to initiating treatment with COSENTYX. . COSENTYX should not be given to patients with active tuberculosis. Initiation of treatment for latent tuberculosis should be considered prior to administering COSENTYX. Anti-tuberculosis therapy should be considered prior to initiation of COSENTYX in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed. Patients should be closely monitored for signs and symptoms of active tuberculosis during and after treatment.

Hepatitis B reactivation

Hepatitis B virus reactivation can occur in patients treated with COSENTYX. In accordance with clinical guidelines for immunosuppressants, testing patients for HBV infection is to be considered before

initiating treatment with COSENTYX. COSENTYX should not be given to patients with active hepatitis B. Patients with evidence of positive HBV serology should be monitored for clinical and laboratory signs of HBV reactivation during COSENTYX treatment. If reactivation of HBV occurs while on COSENTYX, discontinuation of the treatment should be considered, and patients should be treated according to clinical guidelines.

Crohn's disease
Caution should be exercised, when prescribing COSENTYX to patients with inflammatory bowel disease. Exacerbations, in some cases serious, occurred in both COSENTYX and placebo groups during clinical trials in plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. In addition, new onset inflammatory bowel disease cases have been reported with post-marketing use.

Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease.

Hypersensitivity reactions
In clinical studies, rare cases of anaphylactic reactions and angioedema have been observed in patients receiving COSENTYX. Angioedema cases have also been reported in the post-marketing setting. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated.

Eczematous eruptions
In post-marketing reports, cases of severe eczematous eruptions, including dermatitis-like eruptions, dyshidrotic eczema, and erythroderma (exfoliative dermatitis), were reported in patients receiving Cosentyx; some cases resulted in hospitalization (see section *4.8 Undesirable Effects*). The onset of eczematous eruptions was variable, ranging from days to months after the first dose of Cosentyx.
Treatment with Cosentyx may need to be discontinued to resolve the eczematous eruption. Some patients were successfully treated for eczematous eruptions while continuing Cosentyx.

Latex-sensitive individuals – prefilled-syringe/pen only
The removable caps of the COSENTYX 1 mL and 2 mL pre-filled syringe/pen contains a derivative of natural rubber latex. Although no natural rubber latex is detected in the cap, the safe use of COSENTYX pre-filled syringe/pen in latex-sensitive individuals has not been studied.

Vaccinations
Live vaccines should not be given concurrently with COSENTYX (see section 4.5).

Patients treated with COSENTYX may receive vaccinations, except for live vaccines. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of COSENTYX-treated and placebo-treated patients were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* or *influenza* ***vaccines***. The data suggest that COSENTYX does not suppress the humoral immune response to the meningococcal and influenza vaccines.

Patients receiving COSENTYX may receive concurrent inactivated or non-live vaccinations.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Use in Patients with Hepatic or Renal Impairment
No data are available in patients with hepatic or renal impairment.

Paediatric Use

Safety and effectiveness in paediatric patients with plaque psoriasis below the age of 6 years have not yet been established.

Safety and effectiveness in paediatric patients with the JIA categories of ERA (below the age of 4 years) and JPsA (below the age of 2 years) have not been established.

Safety and effectiveness in paediatric patients below the age of 18 years in other indications have not yet been established.

Use in the Elderly
Based on population PK analysis, clearance in patients aged 65 and older (n=230) and patients less than 65 years of age was similar.

Carcinogenicity
Secukinumab has not been evaluated for carcinogenic potential.

Genotoxicity
COSENTYX has not been evaluated for genotoxic potential.

Effect on laboratory tests
There is no known interference between COSENTYX and routine laboratory tests.

4.5 Interaction with other medicines and other forms of interaction

Live vaccines should not be given concurrently with COSENTYX (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no clinically relevant pharmacokinetic interaction was observed between secukinumab and midazolam (CYP 3A4 substrate). Following initiation or discontinuation and during ongoing use of secukinumab in patients being treated with CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment as needed.

No interaction was seen when COSENTYX was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Fertility
There are no special recommendations for females of reproductive potential

The effect of COSENTYX on human fertility has not been evaluated.

Fertility was unaffected in mice treated with an anti-murine IL17-A antibody.

Use in Pregnancy (Category C)
There are no adequate data from the use of COSENTYX in pregnant women. Secukinumab was shown to cross the placenta in monkeys. Use of secukinumab during pregnancy may compromise the immunity of the fetus and neonate.

In an embryofetal development study in cynomolgus monkeys, secukinumab showed no maternal toxicity, embryofetal toxicity or teratogenicity when administered throughout organogenesis and late gestation.

No undesirable effects of an anti-murine IL-17A antibody were seen in a pre-and postnatal development study in mice. The high dose used in this study was in excess of the maximally effective dose in terms of IL-17A suppression and activity.

COSENTYX should be used in pregnancy only if the benefits clearly outweigh the potential risks.

If secukinumab has been used during pregnancy, administration of live vaccines to newborns/ infants for 16 weeks after the mother's last dose of secukinumab is generally not recommended.

Use in Lactation
It is not known whether secukinumab is excreted in human milk. Because immunoglobulins are excreted in human milk, caution should be exercised when COSENTYX is administered to a woman who is breast-feeding and a decision on whether to discontinue breast-feeding during treatment should be made.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use of machines have been performed.

4.8 Undesirable effects
Summary of the safety profile
A total of 20,000 patients have been treated with COSENTYX in blinded and open-label clinical studies in various indications (plaque psoriasis and other autoimmune conditions) representing 34,908 patient years of exposure. Of these, over 14,000 patients were exposed to COSENTYX for at least one year.

Adverse reactions in plaque psoriasis
Adult patients
Four placebo-controlled phase III studies in plaque psoriasis were pooled to evaluate the safety of COSENTYX in comparison to placebo up to 12 weeks after treatment initiation. In total, 2,076 patients were evaluated (692 patients on 150 mg, 690 patients on 300 mg and 694 patients on placebo).

The most frequently reported adverse drug reactions (ADRs) were upper respiratory tract infections (most frequently nasopharyngitis, rhinitis). Most of the events were mild or moderate in severity.

In the placebo-controlled period of plaque psoriasis phase III studies the proportion of patients who discontinued treatment due to adverse events was approximately 1.2 % in the COSENTYX arm and 1.2 % in the placebo arm.

The adverse reactions from clinical studies (Table 2) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000) very rare (< 1/10,000).

Table 2 Percentage of patients with adverse drug reactions in psoriasis clinical studies[1]

Adverse drug reactions	Secukinumab 300 mg (N=690) n (%)	Secukinumab 150 mg (N=692) n (%)	Placebo (N=694) n (%)	Frequency category[2]
Infections and infestations				
Upper respiratory tract infections	117 (17.0)	129 (18.6)	72 (10.4)	Very common
• Nasopharyngitis	79 (11.4)	85 (12.3)	60 (8.6)	Very common
• Upper respiratory tract infection	17 (2.5)	22 (3.2)	5 (0.7)	Common
• Rhinitis	10 (1.4)	10 (1.4)	5 (0.7)	Common
• Pharyngitis	8 (1.2)	7 (1.0)	0 (0)	Common
• Sinusitis	3 (0.4)	6 (0.9)	1 (0.1)	Uncommon
• Tonsillitis	4 (0.6)	4 (0.6)	3 (0.4)	Uncommon
Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)	Common
Oral candidiasis	4 (0.6)	1 (0.1)	1 (0.1)	Uncommon
Tinea pedis	5 (0.7)	5 (0.7)	0 (0)	Uncommon
Blood and lymphatic system disorders				
Neutropenia	2 (0.3)	1 (0.1)	0 (0)	Uncommon
Eye disorders				
Conjunctivitis	5 (0.7)	2 (0.3)	1 (0.1)	Uncommon
Respiratory, thoracic and mediastinal disorders				
Rhinorrhoea	8 (1.2)	2 (0.3)	1 (0.1)	Common
Gastrointestinal disorders				
Diarrhoea	28 (4.1)	18 (2.6)	10 (1.4)	Common
Inflammatory bowel disease (including Crohn's disease and ulcerative colitis)[3]	1 (0.1)	1 (0.1)	0 (0)	Uncommon
Skin and subcutaneous tissue disorders				
Urticaria	4 (0.6)	8 (1.2)	1 (0.1)	Common
Dermatitis (including eczema)[3,4]	12 (1.7)	8 (1.2)	3 (0.4)	Common
Dyshidrotic eczema[3]	1 (0.1)	1 (0.1)	0 (0)	Uncommon

1) *placebo-controlled clinical studies (phase III) in plaque psoriasis patients exposed to 300 mg, 150 mg or placebo up to12-weeks treatment duration*
2) *ADR frequencies are based upon the highest percentage rate seen in any of the secukinumab groups*
3) *ADR added based on postmarketing reports. Frequency determined based on placebo-controlled clinical studies (phase III) in plaque psoriasis patients*
4) *These events are related to Eczematous eruptions.*

Paediatric patients

The safety of Cosentyx was assessed in two 52 week phase III studies in paediatric patients from 6 to less than 18 years of age: 162 patients with severe plaque psoriasis. 84 patients with moderate to severe plaque psoriasis. The safety profile reported in these studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Table 3 Most frequent (≥ 4% in any treatment group) treatment emergent adverse events, by preferred term up to Week 12

Preferred term	AIN457 Low dose N=40 n (%)	AIN457 High dose N=40 n (%)	Any AIN457 dose N=80 n (%)	Placebo N=41 n (%)	Etanercept N=41 n (%)
Any preferred term	**23 (57.5)**	**25 (62.5)**	**48 (60.0)**	**22 (53.7)**	**25 (61.0)**

Preferred term	AIN457 Low dose N=40 n (%)	AIN457 High dose N=40 n (%)	Any AIN457 dose N=80 n (%)	Placebo N=41 n (%)	Etanercept N=41 n (%)
Nasopharyngitis	7 (17.5)	6 (15.0)	13 (16.3)	1 (2.4)	4 (9.8)
Headache	2 (5.0)	3 (7.5)	5 (6.3)	4 (9.8)	1 (2.4)
Abdominal pain	2 (5.0)	2 (5.0)	4 (5.0)	0 (0.0)	3 (7.3)
Pharyngitis	2 (5.0)	2 (5.0)	4 (5.0)	4 (9.8)	0 (0.0)
Asthenia	1 (2.5)	2 (5.0)	3 (3.8)	1 (2.4)	0 (0.0)
Conjunctivitis	1 (2.5)	2 (5.0)	3 (3.8)	0 (0.0)	0 (0.0)
Cough	1 (2.5)	2 (5.0)	3 (3.8)	0 (0.0)	0 (0.0)
Diarrhoea	2 (5.0)	1 (2.5)	3 (3.8)	0 (0.0)	1 (2.4)
Abdominal pain upper	0 (0.0)	2 (5.0)	2 (2.5)	1 (2.4)	2 (4.9)
Aspartate aminotransferase increased	1 (2.5)	1 (2.5)	2 (2.5)	0 (0.0)	2 (4.9)
Dry skin	2 (5.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)
Nausea	1 (2.5)	1 (2.5)	2 (2.5)	2 (4.9)	3 (7.3)
Upper respiratory tract infection	2 (5.0)	0 (0.0)	2 (2.5)	3 (7.3)	1 (2.4)
Oral herpes	0 (0.0)	1 (2.5)	1 (1.3)	1 (2.4)	2 (4.9)
Rhinitis	0 (0.0)	1 (2.5)	1 (1.3)	4 (9.8)	1 (2.4)
Arthralgia	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	2 (4.9)
Bronchitis	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)
Conjunctivitis allergic	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)
Influenza	0 (0.0)	0 (0.0)	0 (0.0)	3 (7.3)	1 (2.4)

Preferred terms are sorted in descending order of frequency in the any AIN457 column.
A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.

The safety of Cosentyx was also assessed in a Phase III study in 86 paediatric patients from 2 to less than 18 years of age with the ERA and JPsA categories of JIA. The safety profile reported in this study was consistent with the safety profile reported in adult patients.

Adverse drug reactions from spontaneous reports and literature cases (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with COSENTYX via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. Adverse drug reactions are listed according to system organ classes in MedDRA. Within each system organ class, ADRs are presented in order of decreasing seriousness.

Table 4 Adverse drug reactions from spontaneous reports and literature (frequency not known)

Infections and infestations
Mucosal and cutaneous candidiasis

Skin and subcutaneous tissue disorders
Angioedema
Dermatitis exfoliative generalized
Hypersensitivity vasculitis
Pyoderma grangrenosum

Description of selected adverse drug reactions

Adult patients

Infections

In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with COSENTYX and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7 % of patients treated with COSENTYX compared with 18.9 % of patients treated with placebo. Most of these were mild or moderate. Serious infections occurred in 0.14 % of patients treated with COSENTYX and in 0.3 % of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with COSENTYX for up to 52 weeks for the majority of patients), infections were reported in 47.5 % of patients treated with COSENTYX (0.9 per patient-year of follow-up). Serious infections were reported in 1.2 % of patients treated with COSENTYX (0.015 per patient-year of follow-up).

There was an increase in mucosal or cutaneous candidiasis, related to the mechanism of action. The cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Frequency of candida infection was 1.2% (secukinumab 300 mg) vs 0.3% (placebo and etanercept arms) in the induction period.

Infection rates as observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to what was observed in the psoriasis studies.

Patients with hidradenitis suppurativa are more susceptible to infections. In the placebo-controlled period of clinical studies in hidradenitis suppurativa (a total of 721 patients treated with secukinumab and 363 patients treated with placebo for up to 16 weeks), infections were numerically higher to those observed in the psoriasis studies (30.8% of patients treated with secukinumab compared with 31.7% in patients treated with placebo). Most of these were non-serious, mild or moderate in severity and did not require treatment discontinuation or interruption.

Neutropenia

In psoriasis phase 3 clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5 x 10^9/L (CTCAE Grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of COSENTYX were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) is similar to psoriasis.
Rare cases of neutropenia <0.5x 10^9/L (CTCAE Grade 4) were reported.

Hypersensitivity reactions

In clinical studies, urticaria, one case of anaphylactic reaction and rare case of angioedema were observed in patients receiving Cosentyx. Angioedema cases have also been reported in the post-marketing setting.

Immunogenicity

In psoriasis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa clinical studies less than 1% of patients treated with COSENTYX developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment emergent anti-drug antibodies were neutralizing, but this was not associated with loss of efficacy or PK abnormalities.

Reproductive system related adverse events

In the induction period of psoriasis clinical studies, mild and moderate reproductive system adverse events were reported in females, including dysmenorrhoea (secukinumab 300 mg, 1.9%; placebo, 0.5%; etanercept, 1.1%), menorrhagia (secukinumab 300 mg, 0.9%; placebo, 0%; etanercept, 0%) and metrorrhagia (including menometrorrhagia) (secukinumab 300 mg, 1.4%; placebo, 0%; etanercept, 0%). Women of child-bearing potential were included in studies only if using adequate contraception.

Major adverse cardiovascular events (MACE)

In the secukinumab clinical trials, MACE events were observed in patients receiving secukinumab. In the Phase 3 studies in psoriasis, PsA and AS, the exposure adjusted incidence rates of adjudication-confirmed MACE cases per 100 patient-years was 0.49 (19/3911.6 patient-years, 95% CI 0.29, 0.76) for secukinumab versus 0.00 (0/351.3 patient-years, 95% CI 0.00, 1.05) for placebo. In the Phase 3 study in nr-axSpA, the exposure adjusted incidence rates of adjudicated confirmed MACE cases per 100 patient-years was 0 (0/759.9 patient-years, 95% CI 0.0, 0.5) for secukinumab versus 1.0 (1/108.6 patient-years, 95% CI 0.0, 5.1). In the overall secukinumab program, the exposure adjusted incidence rates of adjudication-confirmed cases per 100 patient-years for secukinumab was 0.40 (25/6259.8 patient-years, 95% CI 0.26, 0.59) versus 0.39 (2/515.1 patient-years, 95% CI 0.05, 1.40) for placebo.

Adverse reactions in psoriatic arthritis

COSENTYX was studied in five placebo-controlled psoriatic arthritis trials with 2,754 patients (1,871 patients on COSENTYX and 883 patients on placebo) for a total exposure of 4,478 patient- years of study exposure on COSENTYX. The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, upper respiratory tract infection, headache, urinary tract infection, and hypercholesterolemia. The safety profile observed in patients with psoriatic arthritis treated with COSENTYX is consistent with the safety profile in psoriasis.

The proportion of patients with infections in the COSENTYX groups (28.5%) is similar to the placebo group (28.1%) (see section 4.4).

There were cases of Crohn's disease and ulcerative colitis that include patients who experienced either exacerbations or the development of new disease. In the psoriatic arthritis program with 2,536 patients exposed to COSENTYX there were 17 cases of inflammatory bowel disease during the entire treatment period (0.4 per 100 patient-years). During the placebo-controlled period 16 week period,

there were seven cases of inflammatory bowel disease, of which five patients received secukinumab and two received placebo (see section 4.4).

Cholesterol and triglycerides

Elevations of blood cholesterol and triglyceride levels were reported in patients receiving either secukinumab or placebo in psoriatic arthritis clinical trials. The elevations of cholesterol levels were limited primarily to CTCAE Grade 1 (28.7% vs. 19.1%, respectively) and Grade 2 (1.6% vs. 0.5%, respectively). No cases of CTCAE Grade 3 and Grade 4 cholesterol levels were observed in either secukinumab or placebo groups during the placebo controlled period.

An increase in blood triglycerides levels was also observed in psoriatic arthritic patients receiving secukinumab compared to placebo (CTCAE Grade 1: 26.7% vs. 19.1%, Grade 2: 4.6% vs. 3.5%, Grade 3: 1.0% vs. 0.7% and Grade 4: 0.2% vs. 0.1%, respectively) up to Week 16.

Elevations (mainly CTCAE Grade 1 and Grade 2) in cholesterol and triglycerides were also observed during long-term treatment with secukinumab.

Hepatic transaminases

During the placebo-controlled period, increased incidence of elevated hepatic transaminases was observed in psoriatic arthritis patients treated with secukinumab compared to placebo. The elevations in hepatic transaminases were seen primarily in CTCAE Grade 1 (ALT: 17.1% vs 14.8%; AST: 12.5% vs. 10.1%, respectively). No difference in the incidence of elevated ALT and AST was seen between secukinumab and placebo in CTCAE Grade 2, Grade 3, and Grade 4. No cases of CTCAE Grade 4 were observed for AST.

Elevations (mainly CTCAE Grade 1 and grade 2) in ALT and AST was also observed during long-term treatment with secukinumab.

Adverse reactions in axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis)

COSENTYX was studied in three placebo-controlled ankylosing spondylitis trials with 816 patients (544 patients on COSENTYX and 272 patients on placebo). The median duration of exposure for secukinumab-treated patients was 469 days in AS1 Study, 460 days in AS2 Study, and 1,142 days in AS3 Study. During the 16-week placebo-controlled period of the trials in patients with ankylosing spondylitis, the overall proportion of patients with adverse events was higher in the secukinumab groups than the placebo-treatment groups (60% and 55%, respectively).

The overall safety profile of COSENTYX in AS3 Study remained in line with the safety profile established in the pivotal AS1 and AS2 studies, which are summarised in the next paragraphs.

The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, nausea, and upper respiratory tract infection.

COSENTYX was also studied in one placebo-controlled non-radiographic axial spondyloarthritis trial with 555 patients (369 patients on COSENTYX and 186 patients on placebo) for a total of 757.9 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 540 days). During the 20-week placebo-controlled period of the trial in patients with non-radiographic axial spondyloarthritis, the overall proportion of patients with adverse events was higher in the secukinumab groups than the placebo-treatment groups (61.2% and 54.3%, respectively). The adverse

events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo group during the 20-week placebo-controlled period were nasopharyngitis, diarrhoea, headache, upper respiratory tract infection, oropharyngeal pain, back pain, nausea, urinary tract infection, abdominal pain upper and tonsillitis.

The safety profile observed in patients with axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) treated with COSENTYX is consistent with the safety profile in psoriasis.

Similar to clinical trials in patients with psoriasis, there was an increased proportion of ankylosing spondylitis patients with infections in the COSENTYX groups (31%) compared to the placebo group (18%). The proportion of non-radiographic axial spondyloarthritis patients with infections is similar in the COSENTYX groups (35.5%) compared to the placebo group (32.8%) (see section 4.4).

In the ankylosing spondylitis program, with 571 patients exposed to COSENTYX there were 8 cases of inflammatory bowel disease during the entire treatment period (5 Crohn's (0.7 per 100 patient-years) and 3 ulcerative colitis (0.4 per 100 patient-years)). During the placebo-controlled 16-week period, there were 2 Crohn's disease exacerbations and 1 new onset ulcerative colitis case that was a serious adverse event in patients treated with COSENTYX compared to none of the patients treated with placebo. During the remainder of the study when all patients received COSENTYX, 1 patient developed Crohn's disease, 2 patients had Crohn's exacerbations, 1 patient developed ulcerative colitis, and 1 patient had an ulcerative colitis exacerbation. In the non-radiographic axial spondyloarthritis program, with 524 patients exposed to COSENTYX there were 7 cases of inflammatory bowel disease during the entire treatment period (5 Crohn's (0.7 per 100 patient-years) and 2 ulcerative colitis (0.3 per 100 patient-years)). During the placebo-controlled 20-week period, there was 1 new onset of Crohn's disease in a patient treated with COSENTYX compared to none of the patients treated with placebo. During the remainder of the study when all patients received COSENTYX, 3 patients developed Crohn's disease, 1 patient had Crohn's disease exacerbations, 1 patient developed ulcerative colitis, and 1 patient had an ulcerative colitis exacerbation (see section 4.4).

Cholesterol and triglycerides

Elevations of blood cholesterol and triglyceride levels were reported in patients receiving either secukinumab or placebo in ankylosing spondylitis clinical trials.

The elevations of cholesterol levels were limited primarily to CTCAE Grade 1 (20.0% vs. 19.8%, respectively) without any clinically meaningful impact on patients. Increase in CTCAE Grade 2 cholesterol levels was uncommon (0.8% vs. 0.0%, respectively) and no cases of CTCAE Grade 3 and Grade 4 cholesterol levels were observed in both secukinumab and placebo groups during the placebo controlled period.

An increase in blood triglycerides levels was also observed in ankylosing spondylitis patients receiving secukinumab or placebo (CTCAE Grade 1: 17.8% vs. 17.1%, Grade 2: 2.7% vs. 2.7%, and Grade 3: 0.8% vs. 0.5%, respectively). No cases of CTCAE Grade 4 triglyceride levels were reported during the placebo-controlled period.

CTCAE Grade 1 and Grade 2 elevations of blood cholesterol and triglyceride levels were also reported in patients receiving secukinumab compared to placebo in the non-radiographic axial spondyloarthritis clinical trial.

An increase in cholesterol levels was observed in non-radiographic axial spondyloarthritis patients receiving secukinumab or placebo (CTCAE Grade 1: 16.2% vs. 15.8%, Grade 2: 0.8% vs. 0.6%, and Grade

3: 0.3% vs. 0.0%, respectively). No cases of CTCAE Grade 4 cholesterol levels were reported during the placebo-controlled period.

An increase in blood triglycerides levels was also observed in non-radiographic axial spondyloarthritis patients receiving secukinumab or placebo (CTCAE Grade 1: 18.0% vs. 21.0%, Grade 2: 3.2% vs. 3.4%, and Grade 3: 0.6% vs. 0.5%, respectively). No cases of CTCAE Grade 4 triglyceride levels were reported during the placebo-controlled period.

Elevations (mainly CTCAE Grade 1 and Grade 2) in cholesterol and triglycerides were also observed during long-term treatment with secukinumab.

Hepatic transaminases

During the placebo-controlled period, increased incidence of elevated hepatic transaminases was observed in ankylosing spondylitis patients treated with secukinumab compared to placebo. The elevations in hepatic transaminases were seen primarily in CTCAE Grade 1 (ALT: 16.6% vs 7.1%; AST: 11.3% vs. 7.0%, respectively) without any clinically meaningful impact on patients. Increase in CTCAE Grade 2 and Grade 3 hepatic transaminase levels was uncommon in both secukinumab and placebo groups (Grade 2 ALT: 1.0% vs. 0.5%, AST: 0.5% vs. 0.0%; Grade 3 ALT: 0.8% vs. 0.0%, AST: 0.8% vs.1.6%, respectively). One case of CTCAE Grade 4 ALT levels was reported in the placebo group and no cases of CTCAE Grade 4 ALT and AST levels were reported in the secukinumab group.

Similar pattern in ALT and AST was also observed during the long-term treatment with secukinumab.

During the placebo-controlled period, increased incidence of elevated hepatic transaminases was observed in non-radiographic axial spondyloarthritis patients treated with secukinumab compared to placebo. The elevations in hepatic transaminases were seen primarily in CTCAE Grade 1 (ALT: 12.9% vs 9.5%; AST: 11.1% vs. 2.8%, respectively). Increase in CTCAE Grade 2 and Grade 3 hepatic transaminase levels was uncommon in both secukinumab and placebo groups (Grade 2 ALT: 1.1% vs. 0.5%, AST: 0.5% vs. 0.0%; Grade 3 ALT: 0.0% vs. 0.0%, AST: 0.3% vs.0.5%, respectively). No cases of CTCAE Grade 4 ALT and AST levels were reported during the placebo-controlled period.

Elevations (mainly CTCAE Grade 1 and Grade 2) in ALT and AST was also observed during the long-term treatment with secukinumab.

Adverse reactions in hidradenitis suppurativa

COSENTYX was studied in two placebo-controlled hidradenitis suppurativa trials with 1,084 patients (721 patients on COSENTYX and 363 on placebo) with a total exposure of 825 patient years of study exposure (median duration of exposure for secukinumab-treated patients: 307 days, time on placebo 112 days).

The safety profile observed in trial patients with HS treated with COSENTYX was consistent with the known trial safety profile observed in psoriasis.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions : https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

No case of overdose has been reported in clinical studies.

Doses up to 30 mg/kg (i.e. approximately 2,000 mg to 3,000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity.

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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group**:** interleukin inhibitors; ATC Code**:** L04AC10

Active ingredient:	Secukinumab
Chemical name:	Recombinant human monoclonal anti-human Interleukin-17A (IL-17A, IL-17) antibody of the IgG1/kappa isotype
CAS Numbers:	875356-43-7 (heavy chain), 875356-44-8 (light chain)
Molecular formula:	$C_{6584}H_{10134}N_{1754}O_{2042}S_{44}$
Molecular weight:	Approximately 148 kDa
Structure:	The amino acid sequences of the light chain (215 amino acids) and the heavy chain (457 amino acids) respectively.

Mechanism of action

Secukinumab is a fully human IgG1 antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, hidradenitis suppurativa, psoriatic arthritis, and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis). Increased numbers of IL-17A producing lymphocytes and innate immune cells and increased levels of IL-17A have been found in the blood of patients with plaque psoriasis, psoriatic arthritis, and axial spondyloarthritis, and affected skin of patients with plaque psoriasis. IL-17A is highly up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients. Higher frequency of IL-17- producing cells was detected in the synovial fluid of patients with psoriatic arthritis and in the subchondral bone marrow of facet joints from patients with axial spondyloarthritis. IL-17A is considerably upregulated in hidradenitis suppurativa lesions compared to psoriasis patients and healthy controls, and significantly increased IL-17A serum levels have been observed in affected patients. Inhibition of IL-17A was shown to be effective in the treatment of AS, thus establishing the key role of this cytokine in axial spondyloarthritis (see Clinical efficacy and safety).

IL-17A also promotes tissue inflammation, neutrophil infiltration, bone and tissue destruction, and tissue remodelling including angiogenesis and fibrosis.

Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence, treatment with secukinumab reduces erythema, induration, and desquamation present in plaque psoriasis lesions.

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are increased due to reduced clearance of secukinumab-bound IL-17A within 2 to 7 days in patients receiving secukinumab, indicating that secukinumab selectively captures free IL-17A which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis).

Clinical efficacy and safety

Plaque psoriasis

Adult patients

The safety and efficacy of COSENTYX were evaluated versus placebo or etanercept in four randomised, double-blind, placebo-controlled phase 3 studies in adult patients with moderate to severe chronic plaque-type psoriasis poorly controlled by topical treatments and / or phototherapy and / or previous systemic therapy (ERASURE, FIXTURE, FEATURE, and JUNCTURE). The safety and efficacy of COSENTYX were evaluated versus placebo or etanercept in four randomized, double-blind, placebo-controlled phase 3 studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy (ERASURE, FIXTURE, FEATURE, and JUNCTURE). In addition, one study assessed a chronic treatment regimen versus a 'retreatment as needed' regimen (SCULPTURE). In these studies, each 300 mg dose was given as two subcutaneous injections of 150 mg. The co-primary endpoints in the placebo and active controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' response versus placebo at Week 12.

Key exclusion criteria across pivotal trials were: forms of psoriasis other than chronic plaque-type; drug-induced psoriasis; ongoing use of certain psoriasis treatments, e.g. topical or systemic corticosteroids or UV therapy; patients with active, ongoing inflammatory disease; patients with active, ongoing, chronic or recurrent infectious disease; evidence of tuberculosis infection (enrolment was allowed for patients with latent tuberculosis if appropriate treatment was initiated and maintained according to the local treatment guideline); history of HIV, hepatitis B or hepatitis C; underlying immunocompromising conditions; presence of lymphoproliferative disease, malignancy or history of malignancy within the past 5 years; significant medical problems including uncontrolled hypertension and congestive heart failure (NYHA Class III and IV); patients with serum creatinine >176.8 micromol/L or with white blood cell count <2,500 /microL, platelets <100,000/microL, neutrophils <1,500/microL or haemoglobin <8.5 g/dL; pregnant or nursing women; and women of child-bearing potential not using effective contraception during the study.

Of the 2,403 patients who were included in the placebo-controlled studies, 79 % were biological medicine-naïve, 45 % failed treatment with non-biological medicines, 8% failed treatment with biological medicines, 6 % were anti-TNF failures, and 2 % were anti-p40 failures. Baseline disease characteristics were generally consistent across all treatment groups with a median baseline Psoriasis Area Severity Index (PASI) score from 19 to 20, IGA mod 2011 baseline score ranged from "moderate" (62 %) to "severe" (38 %), median baseline Body Surface Area (BSA) ≥ 27 and median Dermatology Life Quality Index (DLQI) score from 10 to 12. Approximately 15 to 25 % of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

ERASURE Study (A2302)

This trial evaluated 738 patients. Patients were randomised to COSENTYX received 150 mg or 300 mg doses at weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Patients were randomized to receive placebo who were non-responders at week 12 were then crossed over to receive COSENTYX (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

FIXTURE Study (A2303)

This trial evaluated 1,306 patients. Patients were randomised to COSENTYX received 150 mg or 300 mg doses at weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Patients were randomized to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. Patients were randomised to receive placebo who were non-responders at week 12 then crossed over to receive COSENTYX (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

FEATURE Study (A2308)

This trial evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of COSENTYX self-administration via the pre-filled syringe. Patients randomised to COSENTYX received 150 mg or 300 mg doses at weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Patients were also randomized to receive placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every month.

JUNCTURE Study (A2309)

This trial evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of COSENTYX self-administration via the pre-filled pen. Patients were randomised to COSENTYX received 150 mg or 300 mg doses at weeks 0, 1, 2, and 3, followed by the same dose every month starting at week 4. Patients were also randomized to receive placebo at weeks 0, 1, 2, and 3, followed by the same dose every month starting at week 4.

SCULPTURE Study (A2304)

This trial evaluated 966 patients. All patients received COSENTYX 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at Week 12 or a “retreatment as needed” regimen of the same dose.

Results

The 300 mg dose provided improved skin clearance across efficacy endpoints of PASI 75/90/100, and IGA mod 2011 ‘clear’ or ‘almost clear’ responses across all studies with peak effects seen at week 16 (see to Table 5 and Table 6). Therefore the 300 mg dose is recommended.

COSENTYX was efficacious in patients naïve to biological medicines and in patients who had prior exposure to biological medicines, including /anti-TNFs.

COSENTYX was associated with a fast onset of efficacy as shown in Figure 1 with a 50 % reduction in mean PASI by week 3 for 300 mg.

Figure 1 Time course of percentage change from baseline of mean PASI score in ERASURE trial (m = number of patients evaluable)

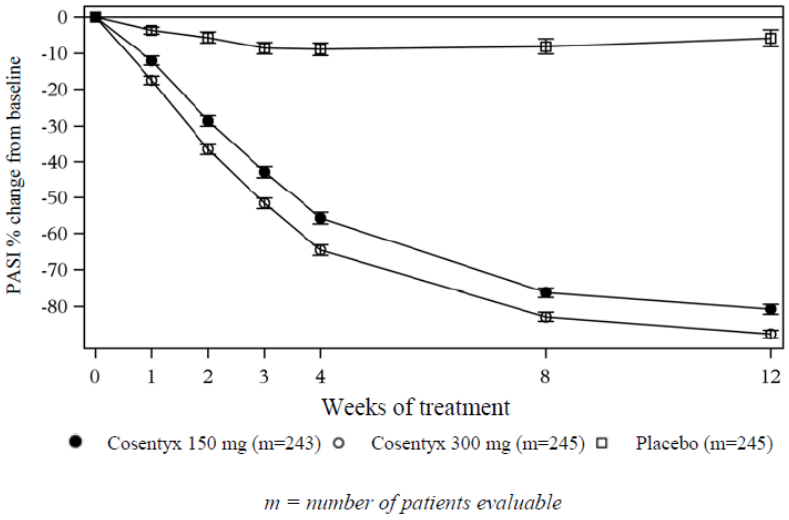


Table 5 Summary of clinical response in ERASURE, FEATURE and JUNCTURE trials

	Week 12			Week 16		Week 52	
	Placebo	150 mg	300 mg	150 mg	300 mg	150 mg	300 mg
ERASURE							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
FEATURE							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-

	Week 12			Week 16		Week 52	
	Placebo	150 mg	300 mg	150 mg	300 mg	150 mg	300 mg
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
JUNCTURE							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

*The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink coloration of lesions, no thickening of the plaque and none to minimal focal scaling.
** p values versus placebo and adjusted for multiplicity: $p<0.0001$

Table 6 Summary of clinical response in FIXTURE trial

		Week 12			Week 16			Week 52		
	Placebo	150 mg	300 mg	Etaner-cept	150 mg	300 mg	Etaner-cept	150 mg	300 mg	Etaner-cept
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)

		Week 12			Week 16			Week 52		
	Placebo	150 mg	300 mg	Etaner-cept	150 mg	300 mg	Etaner-cept	150 mg	300 mg	Etaner-cept
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 "clear" or "almost clear" response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: p=0.0250

An additional psoriasis study (CLEAR) evaluated 676 patients. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at Week 16 and speed of onset of PASI 75 response at Week 4, and long term PASI 90 response at Week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response ("clear" or "almost clear") was observed early and continued through Week 52. In this study, each 300 mg dose was administered as two injections of 150 mg.

Table 7 Summary of clinical response on CLEAR Study

	Week 4		**Week 16**		**Week 52**	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	167 (50.0%)**	69 (20.6%)	311 (93.1%)	277 (82.7%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	193 (57.6%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 "clear" or "almost clear" response n (%)	126 (37.7%)	41 (12.2%)	277 (82.9%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at Weeks 0, 1, 2, 3, and 4 followed by the same dose at Weeks 8 and 12. Patients treated with ustekinumab received 45 mg or 90 mg at Weeks 0 and 4 (dosed by weight as per approved posology)

** p values versus ustekinumab: p<0.0001 for primary endpoint PASI 90 at Week 16 and secondary endpoint PASI 75 at Week 4

*** p value versus ustekinumab: p = 0.0001 for secondary endpoint of PASI 90 at Week 52

All plaque psoriasis phase III studies included approximately 15 to 25% of patients with concurrent psoriatic arthritis at baseline. Improvements in PASI 75 in this patient population were similar to those in the overall plaque psoriasis population.

In the subset of psoriatic arthritis patients in the ERASURE and FIXTURE studies, physical function was assessed using the HAQ Disability Index (HAQ-DI). In these studies, patients treated with 150 mg or 300 mg COSENTYX showed greater improvement from baseline in the HAQ-DI score (mean decreases

of -27.5% and -50.2% at week 12) compared to placebo (-8.9%). This improvement was maintained up to week 52.

Patients in the SCULPTURE study that were randomised after week 12 to a "retreatment as needed" maintenance regimen did not achieve adequate maintenance of response to either dose used. After 52 weeks of treatment patients with 300 mg "retreatment as needed" regimen achieved a PASI 75 of 41.0% and a PASI 90 of 13.8%, whereas patients with a monthly maintenance regimen of 300 mg achieved a PASI 75 of 78.2% and a PASI 90 of 59.7%. Similarly, patients with 150 mg "retreatment as needed" regimen achieved a PASI 75 of 35.0% and a PASI 90 of 11.2%, whereas patients with a monthly maintenance regimen of 150 mg achieved a PASI 75 of 62.1% and a PASI 90 of 45.8% after 52 weeks of treatment. Therefore, a fixed monthly maintenance regimen is recommended.

Specific locations/forms of plaque psoriasis

In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at Week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at Week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of the Palmoplantar Investigator's Global Assessment (ppIGA) 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis. In these studies, each 300 mg dose was given as two subcutaneous injections of 150 mg.

The placebo-controlled SCALP study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater, and at least 30% of the scalp affected. In this study, 62% of patients had at least 50% or more of scalp surface area affected. Secukinumab 300 mg was superior to placebo at Week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% vs. 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% vs. 5.9%). Greater efficacy of secukinumab 300 mg over placebo for both endpoints was observed by Week 3. Improvement in both endpoints was sustained for secukinumab patients who continued treatment through Week 24 (PSSI 90 response 58.8% and IGA mod 2011 0 or 1 scalp only response 62.7%). In these studies, each 300 mg dose was given as two subcutaneous injections of 150 mg.

Quality of Life / Patient reported outcomes

Statistically significant improvements at week 12 (Studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index), these improvements were maintained for 52 weeks (Studies 1 and 2).

Statistically significant improvements at week 12 from baseline compared to placebo (ERASURE and FIXTURE Studies) in patient reported signs and symptoms of itching, pain and scaling were demonstrated in the validated Psoriasis Symptom Diary.

Statistically significant improvements at Week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI (Dermatology Life Quality Index), and these improvements were maintained for up to 52 weeks. The Work Productivity and Activity Impairment Questionnaire-Psoriasis outcomes (WPAI-PSO) showed greater improvement in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements in patient reported signs and symptoms of itching, pain and scaling at Week 16 and Week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements at Week 12 from baseline compared to placebo (SCALP) were demonstrated in the HRQoL (Health Related Quality of Life Index) as measured by Scalpdex. These improvements were observed starting at Week 4 and were maintained through 24 weeks.

Statistically significant improvements (decreases) at week 12 from baseline (SCALP) were demonstrated in patient reported signs and symptoms of scalp itching (-59.4%), pain (-45.9%), and scaling (-69.5%), whereas placebo treated patients demonstrated worsening (increases) in scalp itching (7.7%) and pain (38.5%), and less improvement in scalp scaling (-4.7%).

Plaque Psoriasis Dose Flexibility

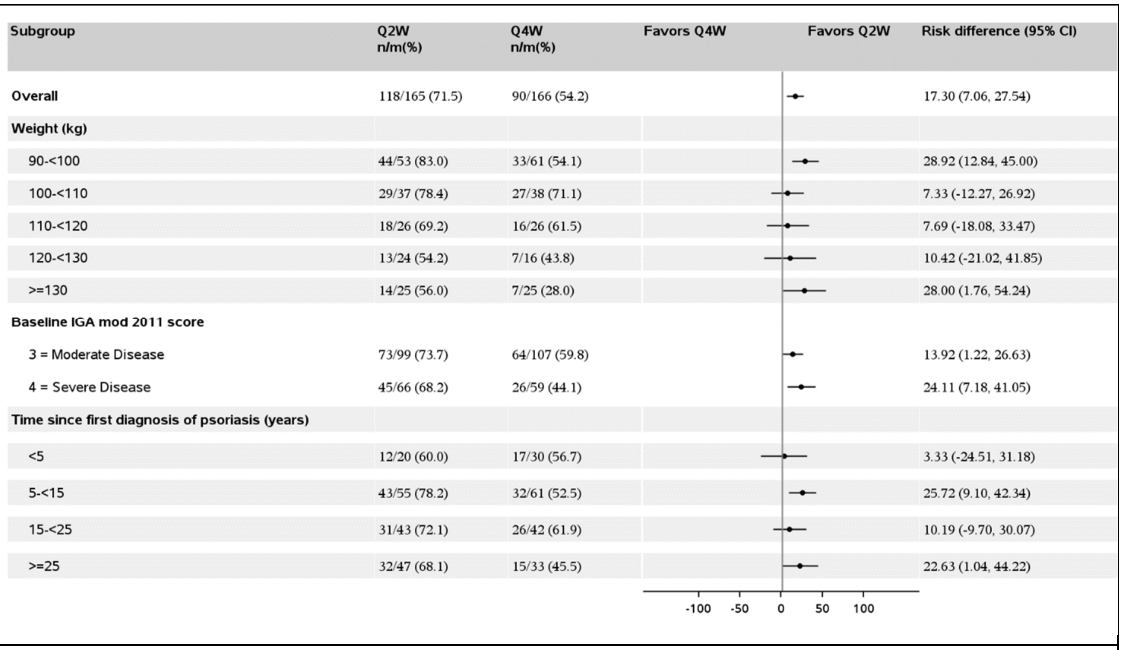
The efficacy, safety, and tolerability of Cosentyx 300 mg administered every 4 weeks vs. Cosentyx 300 mg administered every 2 weeks in adult patients weighing ≥ 90 kg with moderate to severe plaque psoriasis were assessed in a randomised, double-blind, multicentre study of 331 patients. Patients were randomised 1:1 as follows:

- secukinumab 300 mg at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 2 weeks up to Week 52 (n=165).
- secukinumab 300 mg at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks up to Week 16 (n=166).
    - Patients randomised to receive secukinumab 300 mg every 4 weeks who were PASI 90 responders at Week 16 continued to receive the same dosing regimen up to Week 52. Patients randomised to receive Cosentyx 300 mg every 4 weeks who were PASI 90 non-responders at Week 16 either continued on the same dosing regimen, or were reassigned to receive Cosentyx 300 mg every 2 weeks up to Week 52.

The primary and key secondary endpoints were the proportion of patients who achieved a PASI 90 response and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) response at Week 16. At Week 16, the proportion of patients who were PASI 90 responders was higher in the group treated with the every 2 week regimen vs. the every 4 week regimen (73.2% vs. 55.5%, respectively). The treatment difference was clinically relevant and statistically significant (one-sided p-value = 0.0003). The proportion of patients who achieved an IGA mod 2011 ‘clear’ or ‘almost clear’ response was also higher but not statistically different from the group treated with the every 2 week regimen vs. the group treated with the every 4 week regimen (74.2% vs. 65.9%, respectively).

Patients on the every 2 week regimen vs. the every 4 week regimen (Figure 2) showed overall benefit, and benefit for some of the subgroups (weight, IGA, and time since diagnosis). The highest incremental benefit as shown by the calculated risk differences was for patients with severe disease (IGA 4).

Figure 2 Forest plot of risk difference of PASI 90 response at Week 16 with subgroups (modified non-responders imputation) – Full Analysis set* *Post hoc*



* Figure 2 Forest plot presents risk difference of every 2 week regimen (Q2W) vs. every 4 week regimen (Q4W)

The safety profiles of the two dosing regimens, Cosentyx 300 mg administered every 4 weeks and Cosentyx 300 mg administered every 2 weeks, in patients weighing ≥ 90 kg were comparable and consistent with the safety profile reported in psoriasis patients.

In the PASI 90 non-responders at week 16 who were up-titrated to secukinumab 300 mg Q2W, the PASI 90 response rates improved compared to those who remained on the secukinumab 300 mg Q4W dosing regimen, while the IGA mod 2011 0/1 response rates remained stable over time in both treatment groups.

Paediatric patients

Severe plaque psoriasis

A 52-week, randomised, double-blind, placebo and etanercept-controlled phase III study enrolled 162 paediatric patients 6 to less than 18 years of age, with severe plaque psoriasis (as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and involving ≥10% of the body surface area) who were candidates for systemic therapy. Approximately 43% had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biological medicines, and 9% had concomitant psoriatic arthritis.

Patients were randomised to receive one of the following four treatments:

- low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks,
- high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks,
- placebo at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks

- etanercept (0.8 mg/kg) weekly (up to a maximum of 50 mg)

Patients randomised to receive placebo who were non-responders at Week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at Weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at Week 16.

The co-primary endpoints were the proportion of patients who achieved a reduction in PASI score of at least 75% (PASI 75) and IGA mod 2011 'clear' or 'almost clear' (0 or 1) with at least a 2 point improvement from baseline to Week 12. The key secondary endpoint was the proportion of patients who achieved a reduction in PASI score of at least 90% (PASI 90) from baseline to Week 12. Other secondary endpoints included PASI 50, 100 responder rates at Week 12, PASI 50, 75, 90, 100 and IGA 0/1 responder rates at Week 16 and over time up to and including Week 52, change in PASI score over time up to and including Week 52 and IGA score over time up to and including Week 52, the proportion of patients with a Children's Dermatology Life Quality Index (CDLQI) score of 0 or 1 at Week 12 and over time up to and including Week 52, and change from baseline in CDLQI compared to placebo at Week 12 and over time up to and including Week 52.

At Week 12 the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were clinically relevant and statistically significant for both the PASI 75 and IGA mod 2011 'clear' or 'almost clear' (0 or 1) responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 'clear' or 'almost clear' (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at Week 4, the difference becoming more prominent at Week 12. The response was maintained throughout the 52 week time period. Improvement in PASI 50, 90, 100 responder rates and CDLQI 0 or 1 scores were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at Weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept.

Beyond Week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable.

The efficacy results at Weeks 12 are presented in Table 8.

Table 8 Summary of clinical response in severe paediatric psoriasis at Weeks 12*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n/m** (%)	'control' n/m** (%)	odds ratio estimate (95% CI)	p-value
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08,114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31,98.93)	<0.0001
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02,538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48,329.52)	<0.0001
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83,6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22,4850.13)	<0.0001

** non-responder imputation was used to handle missing values*

*** n is the number of responders, m = number of patients evaluable*

**** extended visit-window at week 12*

Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at Week 12 (low dose 44.7%, high dose 50%, placebo 15%). This improvement was further maintained through Week 52.

Moderate to severe plaque psoriasis

An open-label, two-arm, parallel-group, multicentre phase III study enrolled 84 paediatric patients 6 to less than 18 years of age with moderate to severe plaque psoriasis (as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and involving ≥10% of the body surface area) who were candidates for systemic therapy.

Patients were randomised to receive secukinumab at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks as follows:

- low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg),
- high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg).

The co-primary endpoints were the proportion of patients who achieved a reduction in PASI score of at least 75% (PASI 75) and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) with at least a 2 point improvement from baseline to Week 12. Secondary endpoints included PASI 90 response at Week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically and clinically meaningful improvement compared to historical placebo for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were clinically relevant and statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses versus historical placebo. The estimated posterior probability of a positive treatment effect was 100%.

The efficacy results at Weeks 12 are presented in Table 9.

Table 9 Summary of clinical response in moderate to severe paediatric psoriasis at Weeks 12* (paediatric psoriasis)

	Week 12	
	Secukinumab low dose	**Secukinumab high dose**
Number of patients	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)
PASI 90 response n (%)	29 (69.0%)	32 (76.2%)

** non-responder imputation was used to handle missing values*

300 mg/2 mL pre-filled syringe and 300 mg/2 mL pre-filled pen

The results of the studies ALLURE and MATURE showed similar safety, efficacy, and overall patient experience in patients that received one injection of 300 mg and those that received 2 injections of 150 mg, with both the PFS and AI device.

Adult Psoriatic Arthritis

The safety and efficacy of COSENTYX were assessed in 1,999 patients in three randomised, double-blind, placebo-controlled phase III studies in adult patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroids or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA for a median of 3.9 to 5.3 years. The majority of patients also have active psoriasis skin lesions or a documented history of psoriasis. Approximately half of all enrolled patients had at least 3% BSA involvement with skin psoriasis at baseline. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively.

In FUTURE 1 Study (PsA1 Study), FUTURE 2 Study (PsA2 Study), and FUTURE 5 Study (PSA3 Study), 29%, 35%, and 30% of patients, respectively, were previously treated with an anti-TNF-alpha agent and discontinued the anti-TNF-alpha agent for either lack of efficacy or intolerance (anti-TNF-alpha-IR patients). For FUTURE 1 and FUTURE 2, the primary endpoint was American College of Rheumatology (ACR) 20 response at Week 24. The primary endpoint for FUTURE 5 was ACR20 response at Week 16, and the key secondary endpoint was the change from baseline in modified Total Sharp Score (mTSS) at Week 24.

Key exclusion criteria across pivotal trials were: use of high potency opioid analgesics; ongoing use of certain psoriasis treatments, e.g. topical or systemic corticosteroids or UV therapy; previous exposure to secukinumab or any other biological medicines for psoriasis and PsA except for those targeting TNFα, patients with active, ongoing inflammatory disease other than PsA; patients with active, ongoing, chronic or recurrent infectious disease; evidence of tuberculosis infection (enrolment was allowed for patients with latent tuberculosis if appropriate treatment was initiated and maintained according to the local treatment guideline); history of HIV, hepatitis B or hepatitis C; underlying immunocompromising conditions; presence of lymphoproliferative disease, malignancy or history of malignancy within the past 5 years; significant medical problems including uncontrolled hypertension and congestive heart failure (NYHA Class III and IV); patients with serum creatinine >132.6 micromol/L

or with white blood cell count <3,000 /microL,, platelets <100,000/microL, neutrophils <1,500/microL or haemoglobin <8.5 g/dL; pregnant or nursing women; and women of child-bearing potential not using effective contraception during the study.

FUTURE 1 Study (F2306)
PsA1 Study evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to receive placebo who were non-responders at Week 16 (early rescue) and other placebo patients at Week 24 were crossed over to receive COSENTYX (either 75 mg or 150 mg) at Week 16 followed by the same dose every month.

FUTURE 2 Study (F2312)
PsA2 Study evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to COSENTYX received 75 mg, 150 mg or 300 mg s.c. at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. Patients randomised to receive placebo who were non-responders at Week 16 (early rescue) were then crossed over to receive COSENTYX (either 150 mg or 300 mg, s.c.) at Week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at Week 16 were crossed over to receive COSENTYX (either 150 mg or 300 mg) at Week 24 followed by the same dose every month.

FUTURE 5 Study (F2342)
PsA3 Study evaluated 996 patients, of whom 50.1% had concomitant MTX treatment. Patients were randomised to receive COSENTYX 150 mg, 300 mg, or placebo s.c. at Weeks 0, 1, 2, 3 and 4 followed by the same dose every month, or a once monthly injection of COSENTYX 150 mg (without loading). Patients randomised to receive placebo who were non-responders at Week 16 were then crossed over to receive COSENTYX (either 150 mg or 300 mg, s.c.) at Week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at Week 16 were crossed over to receive COSENTYX (either 150 mg or 300 mg) at Week 24 followed by the same dose every month. The total combined duration of treatment for PsA3 Study is 2 years.

Signs and symptoms
Treatment with COSENTYX resulted in significant improvement in the measure of disease activity compared to placebo at Weeks 16 and 24 (see Table 10).

Table 10 Clinical response in PsA2 and PSA3 Studies at Week 16 and Week 24

	PsA2			PsA3		
	Placebo	150 mg[1]	300 mg[1]	Placebo	150 mg[1]	300 mg[1]
Number of patients randomised	98	100	100	332	220	222
ACR 20 response n (%)						
Week 16				**91**◊ (27.4%)	**122**◊ (55.5%***)	**139**◊ (62.6%***)
Week 24	**15**◊ (15.3%)	**51**◊ (51.0%***)	**54**◊ (54.0%***)			
ACR 50 response n (%)						
Week 16				**27** (8.1%)	**79** (35.9%*)	**88** (39.6%*)
Week 24	**7** (7.1%)	**35** (35.0%)	**35** (35.0%**)			
ACR 70 response n (%)						
Week 16				**14** (4.2%)	**40** (18.2%)	**45** (20.3%)

Week 24	**1** (1.0%)	**21** (21.0%)	**20** (20.0%)			
DAS28-CRP **Week 16** **Week 24**	-0.96	-1.58**	-1.61**	-0.63	-1.29*	-1.49*
Number of patients with ≥ 3% BSA psoriasis skin involvement at baseline	**43** (43.9%)	**58 (58.0%)**	**41 (41.0%)**	**162** (48.8%)	**125** (56.8%)	**110** (49.5%)
PASI 75 response n (%) **Week 16** **Week 24**	**7** (16.3%)	**28** (48.3%**)	**26** (63.4%***)	**20** (12.3%)	**75 (60.0%*)**	**77** (70.0%*)
PASI 90 response n (%) **Week 16** **Week 24**	**4** (9.3%)	**19** (32.8%**)	**20** (48.8%***)	**15** (9.3%)	**46** (36.8%*)	**59** (53.6%*)
Dactylitis Resolution n (%) † **Week 16** **Week 24**	**4** (14.8%)	**16 (50.0%)**	**26 (56.5%)**	**40** (32.3%)	**46** (57.5%*)	**54** (65.9%*)
Enthesitis Resolution n (%) ‡ **Week 16** **Week 24**	**14** (21.5%)	**27 (42.2%)**	**27 (48.2%)**	**68** (35.4%)	**77** (54.6%*)	**78** (55.7%*)

* p<0.05, ** p<0.01, *** p<0.001; versus placebo

All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at Week 24 for PsA Study 2, except for all endpoints at Week 16. ACR70, Dactylitis and Enthesitis, were exploratory endpoints.

All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at Week 16 for PsA Study 3. ACR70 was an exploratory endpoint.

Non-responder imputation used for missing binary endpoint.

NA: Not Available; ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area

◊Primary Endpoint

[1]Cosentyx 150 mg or 300 mg s.c. at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month

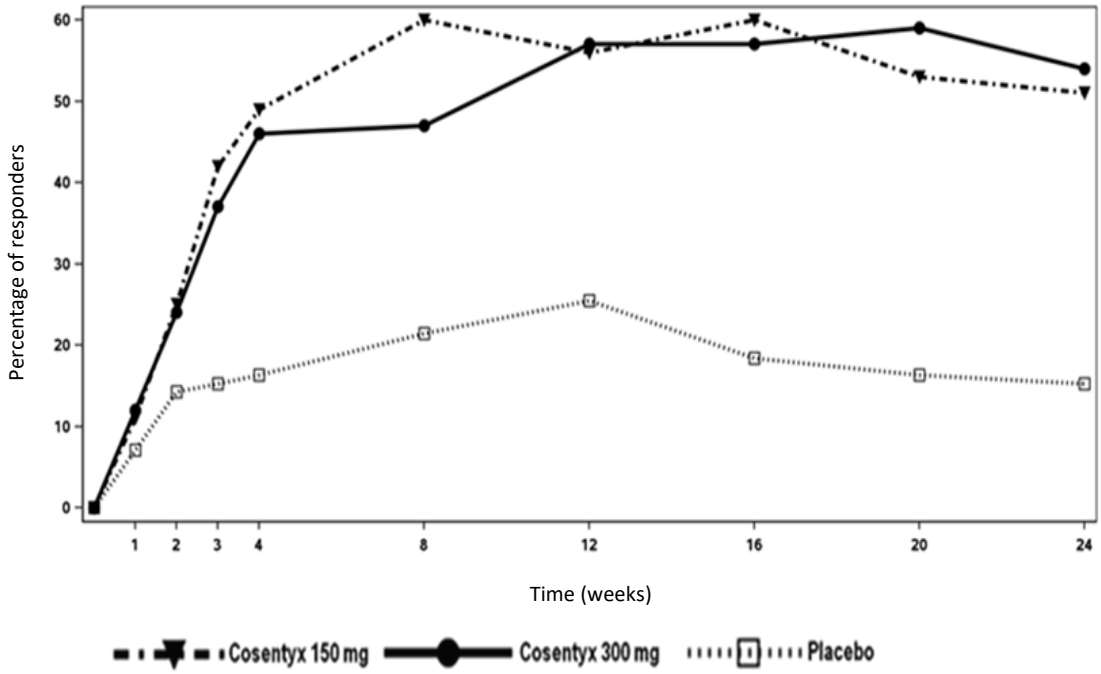
†In patients with dactylitis at baseline (n=27, 32, 46 respectively for PsA2 and n=124, 80, 82 respectively for PsA3)

‡In patients with enthesitis at baseline (n=65, 64, 56 respectively for PsA2 and n=192, 141, 140, respectively for PsA3)

The onset of action of COSENTYX occurred as early as Week 2. Statistically significant difference in ACR 20 vs placebo was reached at Week 3. In PSA2 efficacy responses were maintained up to Week 104. At Week 16, COSENTYX-treated patients demonstrated significant improvements in signs and symptoms among which significantly higher responses in ACR 20 (60.0% and 57.0% for 150 mg and 300 mg, respectively) compared to placebo (18.4%).

The percentage of patients achieving ACR20 response by visit is shown in Figure 3.

Figure 3 ACR 20 response in PsA 2 Study over time up to Week 24



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not.

Both, anti-TNF-alpha-naïve and anti-TNF-alpha-–IR COSENTYX-treated patients, had a significantly higher ACR 20 response compared to placebo at Week 24, with a slightly higher response in the anti-TNF-alpha- naïve group in the PsA2 study (anti-TNF-alpha-naïve: 64% and 58% for 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNF-alpha-IR: 30% and 46% for 150 mg and 300 mg, respectively, compared to placebo 14.3%). Anti-TNF-alpha–IR patients on 300 mg showed higher response rates on ACR20 compared to placebo patients ($p<0.05$) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNF-alpha-IR patients.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. The proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the COSENTYX-treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at Week 24.

In PsA1 Study and PsA2 Study, efficacy was maintained up to Week 52. In PsA2 Study, among 200 patients initially randomised to COSENTYX 150 mg and 300 mg, 178 (89%) patients were still on treatment at Week 52. Of the 100 patients randomised to COSENTYX 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to COSENTYX 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

Radiographic response

In PsA3 Study, inhibition of progression of structural damage was assessed radiographically and expressed by the modified Total Sharp Score (mTSS) and its components, the Erosion Score (ES) and

the Joint Space Narrowing Score (JSN). Radiographs of hands, wrists, and feet were obtained at baseline Week 16 and/or Week 24 and scored independently by at least two readers who were blinded to treatment group and visit number.

COSENTYX 150 mg and 300 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at Week 24 (Table 11).

The percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to Week 24 was 80.3%, 88.5% and 73.6% for COSENTYX 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed irrespective of concomitant MTX use or TNF status.

Structural damage was also assessed in the PsA1 Study. Radiographs of hands, wrists, and feet were obtained at baseline and Week 24 during the double-blind period when patients were on COSENTYX or placebo and at Week 52 when all patients were on open-label COSENTYX.

By Week 24, COSENTYX 150 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS (see Table 11). Inhibition of structural damage was maintained with COSENTYX treatment up to Week 52.

In PsA1 Study, the inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at Weeks 24 and 52, compared to baseline Week 24 data presented in Table 11.

Table 11 Change in modified Total Sharp Score in psoriatic arthritis

	PsA3			**PsA1**	
	Placebo n=296	**150 mg[1] n=213**	**300 mg[1] n=217**	**Placebo n= 179**	**150 mg[2] n= 185**
Total Score					
Baseline	**15.0**	**13.6**	**12.9**	**28.4**	**22.3**
(SD)	**(38.2)**	**(25.6)**	**(23.8)**	**(63.5)**	**(48.0)**
Mean Change at Week 24	**0.5**	**0.13***	**0.02***	**0.57**	**0.13***

** p<0.05 based on nominal, but not adjusted, p-value*

[1] Cosentyx 150 mg or 300 mg s.c. at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month

[2]10 mg/kg at Weeks 0, 2 and 4 followed s.c. doses of 75 mg or 150 mg

Inhibition of structural damage was maintained with COSENTYX 150 mg treatment up to Week 104 in PsA2 Study and with COSENTYX 300 mg treatment up to Week 52 in PsA3 Study.

The percentage of patients with no-disease progression (defined as a change from baseline inmTSS of ≤0.5) from randomisation to Week 24 was 82.3% in secukinumab 10 mg/kg i.v. load – 150 mg s.c. maintenance and 75.7% in placebo. The percentage of patients with no-disease progression, from Week 24 to Week 52, for the same above described regimen, was 85.7% and 86.8%, respectively.

Axial manifestations in PsA

A randomised, double-blind, placebo-controlled study (MAXIMISE) assessed the efficacy of secukinumab in 485 PsA patients with axial manifestations who were naive to biological medicine and responded inadequately to NSAIDs. The primary variable of at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at Week 12 was met. Treatment with secukinumab 300 mg and 150 mg compared to placebo also resulted in greater improvement in signs and symptoms (including decreases from baseline in spinal pain) and improvement in physical function (see Table 12).

Table 12 Clinical response on MAXIMISE Study at Week 12

	Placebo (n=164)	150 mg (n=157)	300 mg (n=164)
ASAS 20 response, % ***(95% CI)***	31.2 ***(24.6, 38.7)***	66.3 ***(58.4, 73.3)****	62.9 ***(55.2, 70.0)****
ASAS 40 response, % ***(95% CI)***	12.2 ***(7.8, 18.4)***	39.5 ***(32.1, 47.4)*** **	43.6 ***(36.2, 51.3)*** **
BASDAI 50, % ***(95% CI)***	9.8 ***(5.9, 15.6)***	32.7 ***(25.8, 40.5)*** **	37.4 ***(30.1, 45.4)*** **
Spinal pain, VAS ***(95% CI)***	-13.6 ***(-17.2, -10.0)***	-28.5 ***(-32.2, -24.8)*** **	-26.5 ***(-30.1, -22.9)*** **
Physical function, HAQDI ***(95% CI)***	-0.155 ***(-0.224, -0.086)***	-0.330 ***(-0.401, -0.259)*** **	-0.389 ***(-0.458, -0.320)*** **

** p<0.0001; ~~** p=0.0005;~~ versus placebo **using multiple imputation.***

***** Comparison versus placebo was not adjusted for multiplicity.***

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: Visual Analog Scale; HAQDI: Health Assessment Questionnaire – Disability Index.

Improvement in ASAS 20 and ASAS 40 for both secukinumab doses were observed by Week 4 and were maintained up to 52 weeks.

Physical function and health related quality of life

In PsA2 and PsA3 studies, patients treated with COSENTYX 150 mg and 300 mg showed improvement in physical function compared to patients treated with placebo as assessed by change from baseline in Heath Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24 and Week 16, respectively. In PsA3 study, the change from baseline in HAQ-DI was -0.44 and -0.55 for COSENTYX 150 mg and 300 mg, respectively, versus -0.21 for placebo (<0.0001). Improvements in HAQ-DI scores were seen regardless of previous anti-TNF-alpha exposure.

COSENTYX-treated patients reported significant improvements in health-related quality of life as measured by the Short Form (36) Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001) and these improvements were maintained up to Week 104 in PsA2.

Axial spondyloarthritis (axSpA) with or without radiographic damage

Ankylosing spondylitis (axSpA with radiographic damage)

The safety and efficacy of COSENTYX were assessed in 816 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory

drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in the AS1 Study and AS2 Study had a diagnosis of AS for a median of 2.7 to 5.8 years.

In MEASURE 1 Study (AS1 Study), MEASURE 2 Study (AS2 Study), and MEASURE 3 Study (AS3 Study), 27.0%, 38.8%, and 23.5% of patients, respectively, were previously treated with an anti-TNF-alpha agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNF-alpha-IR patients).

Key exclusion criteria across pivotal trials were: patients with total ankylosis of the spine; use of high potency opioid analgesics; previous exposure to secukinumab or any other biological medicine except for those targeting TNF-alpha, patients with active, ongoing inflammatory disease, other than AS; patients with active, ongoing, chronic or recurrent infectious disease; evidence of tuberculosis infection (enrolment was allowed for patients with latent tuberculosis if appropriate treatment was initiated and maintained according to the local treatment guideline); history of HIV, hepatitis B or hepatitis C; underlying immunocompromising conditions; presence of lymphoproliferative disease, malignancy or history of malignancy within the past 5 years; significant medical problems including uncontrolled hypertension and congestive heart failure (NYHA Class III and IV); patients with serum creatinine >132.6 micromol/L or with white blood cell count <3,000 /microL, platelets <100,000/microL, neutrophils <1,500/microL or haemoglobin <8.5 g/dL; pregnant or nursing women; and women of child-bearing potential not using effective contraception during the study.

AS1 Study evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to COSENTYX received 10 mg/kg, i.v. at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg s.c. every month starting at week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and all other placebo patients at Week 24 were crossed over to receive COSENTYX (either 75 mg or 150 mg s.c.), followed by the same dose every month. The primary endpoint was at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at Week 16.

AS2 Study evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to COSENTYX received 75 mg or 150 mg s.c. at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month. At Week 16, patients who were randomised to placebo at baseline were re-randomised to receive COSENTYX (either 75 mg or 150 mg) s.c. every month. The primary endpoint was ASAS20 at Week 16.

AS3 Study evaluated 226 patients, of whom 13.3% and 23.5% used concomitant MTX or sulfasalazine, respectively. Patients randomised to COSENTYX received 10 mg/kg, i.v. at Weeks 0, 2, and 4, followed by either 150 mg or 300 mg s.c. every month. At Week 16, patients who were randomised to placebo at baseline were re-randomised to receive COSENTYX (either 150 mg or 300 mg) s.c. every month. The primary end point was ASAS20 at Week 16. Patients were blinded to the treatment regimen up to Week 52, and the study continued to Week 156.

Signs and symptoms

In AS2 Study, treatment with COSENTYX 150 mg resulted in greater improvement in measures of disease activity compared with placebo at Week 16 (see Table 13).

Table 13 Clinical response in AS2 Study at Week 16

Outcome (p-value vs placebo)	Placebo (n = 74)	75 mg (n = 73)	150 mg (n = 72)
Efficacy at Week 16			
ASAS20 response, %	**28.4**	**41.1**	**61.1*****
ASAS40 response, %	**10.8**	**26.0**	**36.1*****
hsCRP, (post-BSL/BSL ratio)	**1.13**	**0.61**	**0.55*****
ASAS5/6, %	**8.1**	**34.2**	**43.1*****
BASDAI, LS mean change from baseline score	**–0.85**	**–1.92**	**–2.19*****
ASAS partial remission, %	**4.1**	**15.1**	**13.9**
BASDAI50, %	**10.8**	**24.7***	**30.6****
ASDAS-CRP major improvement	**4.1**	**15.1***	**25.0*****

*p<0.05; **p<0.01; ***p< 0.001 vs. placebo

All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI50 and ASDAS-CRP

Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline; LS: least square

The results of the main components of the ASAS20 response criteria are shown in Table 14.

Table 14 Main components of the ASAS20 response criteria at baseline and Week 16 in AS 2 Study

	Placebo (N = 74)		75 mg (N = 73)		150 mg (N = 72)	
	Baseline	Week16	Baseline	Week16	Baseline	Week16
ASAS20 Response criteria						
-Patient global assessment (0-10)	7.0	5.5	6.5	4.5	6.7	3.8
-Total spinal pain (0-10)	6.9	5.7	6.5	4.6	6.6	3.7
-BASFI (0-10)	6.1	5.3	6.0	4.1	6.2	3.8
-Inflammation (0-10)	6.5	5.7	6.9	4.4	6.5	4.0

The onset of action of COSENTYX 150 mg occurred as early as Week 1 for ASAS20 and Week 2 for ASAS40 (superior to placebo) in AS2 Study. The percentage of patients achieving an ASAS20 response by visit is shown in Figure 4.

Figure 4 ASAS20 responses in AS 2 Study over time up to Week 16

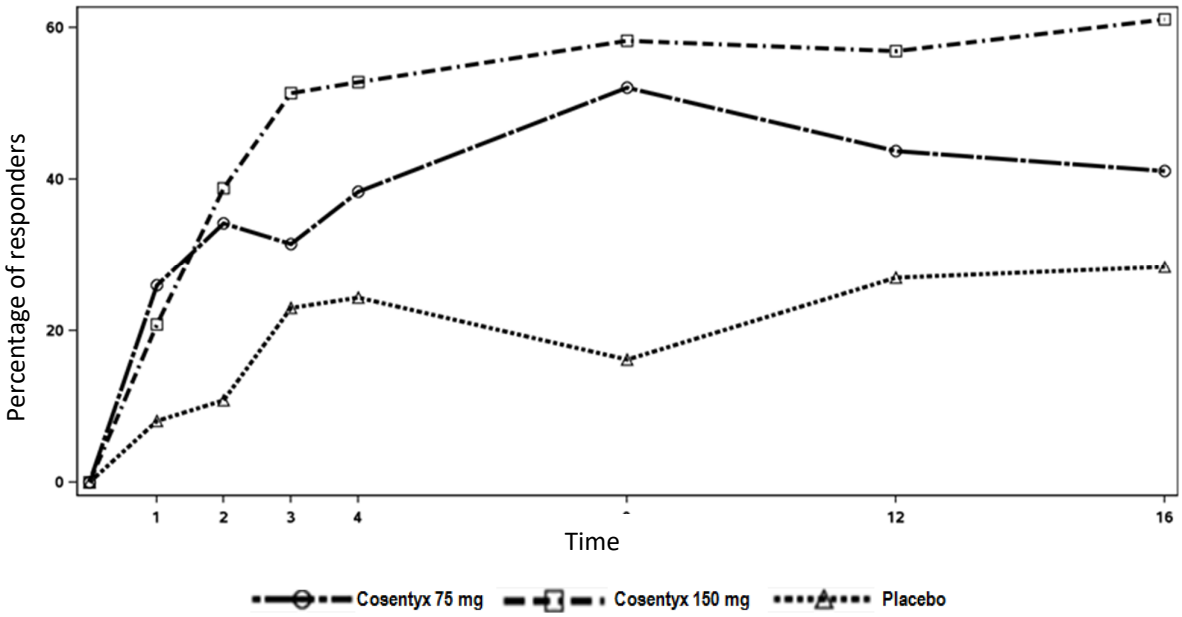
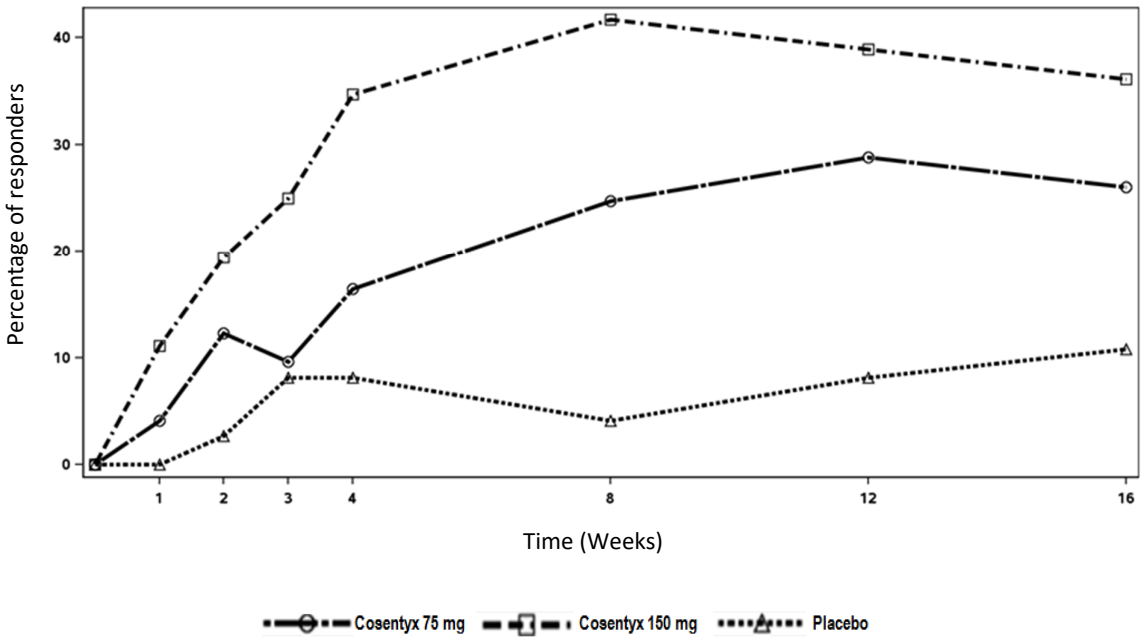


Figure 5 ASAS40 responses in AS 2 Study over time up to Week 16



ASAS20 responses were improved at Week 16 in both antiTNFα-naïve patients (68.2% vs. 31.1%; p<0.05) and anti-TNFα-IR patients (50.0% vs. 24.1%; p<0.05) for COSENTYX 150 mg compared with placebo, respectively.

In AS1 Study and AS2 Study, COSENTYX -treated patients (150 mg in AS2 Study and both regimens in AS1 Study) demonstrated significantly improved signs and symptoms at Week 16, with comparable magnitude of response and efficacy was maintained up to Week 52. The magnitude of response (treatment difference versus placebo) with regards to signs and symptoms at Week 16 was similar in anti-TNF-alpha-naïve and anti-TNF-alpha-IR patients in both studies, with higher absolute response rates in anti-TNF-alpha-naïve patients. Efficacy was maintained in anti-TNF-alpha-naïve and anti-TNF-alpha-IR patients up to Week 52 in both studies.

In AS3 Study, COSENTYX treated patients (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses regardless of dose that were superior to placebo at Week 16 for the primary endpoint (ASAS20). Greater response rates favouring 300 mg were also observed for ASAS partial remission (ASAS PR) response at week 16. During the blinded period, the ASAS20 and ASAS40 responses were 69.7% and 47.6% for 150 mg and 74.3% and 57.4% for 300 mg at Week 52, respectively. The ASAS20 and ASAS40 responses were maintained through Week 156 (69.5% and 47.6% for 150 mg vs. 74.8% and 55.6% for 300 mg). The ASAS partial remission (ASAS PR) responses were 9.5% and 21.1% for 150 mg and 300 mg respectively, compared to 1.3% for placebo at Week 16. The ASAS PR responses were 18.1% and 24.3% for 150 mg and 300 mg at Week 52, respectively. These responses were maintained through Week 156 (15.1% for 150 mg and 27.2% for 300 mg).

Spinal mobility
Spinal mobility was assessed by BASMI up to Week 52. In AS2 Study (150 mg) and in AS1 Study (75 mg and 150 mg), numerically greater improvements in each BASMI component were demonstrated in COSENTYX-treated patients compared with placebo-treated patients at Weeks 4, 8, 12, and 16 (except for lateral lumbar flexion in patients on 75 mg following the IV load at Weeks 4, 8, and 12).

Physical function and health-related quality of life
In AS Study 1 and 2, patients treated with COSENTYX 150 mg showed improvements in health-related quality of life as measured by ASQoL (LS mean change: -4.00 vs -1.37, p = 0.001) and SF-36 PCS (LS mean change: 6.06 vs 1.92, p< 0.001). COSENTYX 150 mg had numerically larger mean improvements than placebo for three of the four Work Productivity and Activity Impairment-General Health (WPAI-GH) outcomes at Week 16. These improvements were sustained up to Week 52.

Patients treated with COSENTYX 150 mg also showed improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68).

Inhibition of inflammation in magnetic resonance imaging (MRI)

In an imaging sub-study including 105 anti-TNF-alpha-naïve patients in AS1 Study, signs of inflammation were assessed by MRI at baseline and Week 16 and expressed as change from baseline in Berlin SI-joint edema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in secukinumab-treated patients.

Non-radiographic axial spondyloarthritis (axSpA without radiographic damage)

The safety and efficacy of COSENTYX were assessed in 555 patients in one randomised, double-blind, placebo-controlled phase III study in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) fulfilling the Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for ankylosing spondylitis (AS). Patients enrolled had

active disease, defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, a Visual Analogue Scale (VAS) for total back pain of ≥40 (on a scale of 0-100 mm), despite current or previous non-steroidal anti-inflammatory drug (NSAID) therapy and increased C-reactive protein (CRP) and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Patients in this study had a diagnosis of axSpA for a mean of 2.1 to 3.0 years and 54% of the study participants were female.

In nr-axSpA 1 Study, 57.6% of patients had increased CRP, 72.2% had evidence of sacroiliitis on MRI and 29.9% had both increased CRP and evidence of sacroiliitis on MRI. In addition, 9.7% of patients were previously treated with an anti-TNF-alpha agent and discontinued the anti-TNF-alpha agent for either lack of efficacy or intolerance (anti-TNF-alpha-IR patients).

Nr-axSpA 1 Study (PREVENT) evaluated 555 patients, of whom 9.9% and 14.8% used concomitant MTX or sulfasalazine, respectively. In the double-blind period, patients received either placebo or COSENTYX for 52 weeks. Patients randomised to COSENTYX received 150 mg s.c. at Weeks 0, 1, 2, 3 and 4 followed by the same dose every four weeks, or COSENTYX 150 mg s.c. every four weeks without a loading dose. The primary endpoint was at least 40% improvement in ASAS 40 at Week 16 in TNF-naive patients.

Clinical response

Signs and symptoms

In nr-axSpA1 Study, treatment with COSENTYX 150 mg resulted in significant improvements in the measures of disease activity compared to placebo at Week 16. These measures include ASAS 40, ASAS 5/6, BASDAI score, BASDAI 50, high-sensitivity CRP (hsCRP), ASAS 20 and ASAS partial remission response compared to placebo at Week 16 (Table 15).

Table 15 Clinical response in nr-axSpA1 Study at Week 16

Outcome (p-value vs placebo)	**Placebo**	**150 mg with load[1]**	**150 mg without load**
Number of TNF-naive patients randomised	**171**	**164**	**166**
ASAS 40 response, %	**29.2%**	**41.5%***	**42.2%***
Total number of patients randomised	**186**	**185**	**184**
ASAS 40 response, %	**28.0%**	**40.0%***	**40.8%***
ASAS 5/6, %	**23.7%**	**40.0%***	**35.9%***
BASDAI, LS mean change from baseline score	**-1.46**	**-2.35***	**-2.43****
BASDAI 50, %	**21.0%**	**37.3%***	**37.5%****
hsCRP, (post-BSL/BSL ratio)	**0.91**	**0.64***	**0.64****
ASAS 20 response, %	**45.7%**	**56.8%***	**58.2%***
ASAS partial remission, %	**7.0%**	**21.6%***	**21.2%****

**p<0.05; **p< 0.001 vs. placebo*

All p-values adjusted for multiplicity of testing based on pre-defined hierarchy

Non-responder imputation used for missing binary endpoint

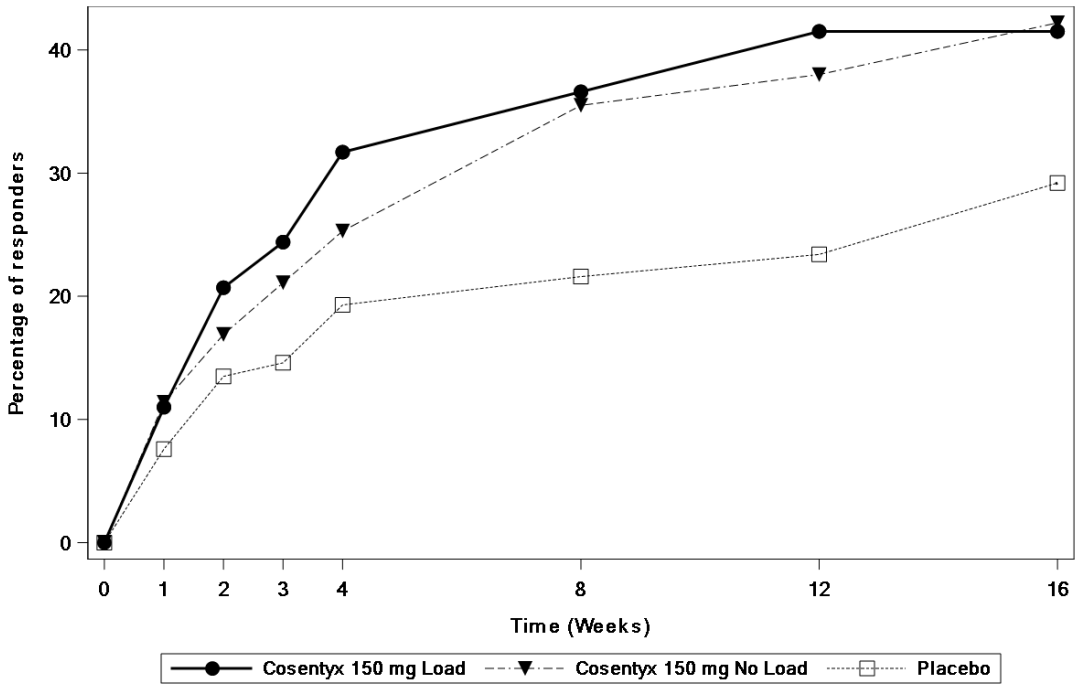
1Cosentyx 150 mg s.c. at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; BSL: baseline; LS: least square

The onset of action of COSENTYX 150 mg occurred as early as Week 3 for ASAS 40 in anti-TNF-alpha naive patients (superior to placebo) in nr-axSpA1 Study. The percentage of patients achieving an ASAS

40 response in anti-TNF-alpha naive patients by visit is shown in Figure 6. Patients treated with COSENTYX maintained their response compared to placebo up to Week 52.

Figure 6 ASAS 40 responses in anti-TNF-alpha naive patients in nr-axSpA1 Study over time up to Week 16



ASAS 40 responses were also improved at Week 16 in anti-TNF-alpha-IR patients (28.6% vs. 13.3%) for COSENTYX 150 mg compared with placebo. The magnitude of response (treatment difference versus placebo) with respect to signs and symptoms at Week 16 was similar in anti-TNF-alpha-naïve and anti-TNF-alpha-IR patients, with higher absolute response rates in anti-TNF-alpha-naïve patients. Efficacy versus placebo was maintained in anti-TNF-alpha-naïve and anti-TNF-alpha-IR patients up to Week 52.

Physical function and health-related quality of life

Patients treated with COSENTYX 150 mg showed statistically significant improvements by Week 16 compared to placebo-treated patients in physical function as assessed by the BASFI (Week 16: -1.75 vs -1.01, $p<0.05$). Patients treated with COSENTYX reported significant improvements compared to placebo-treated patients by Week 16 in health-related quality of life as measured by ASQoL (LS mean change: Week 16: -3.45 vs -1.84, $p<0.05$) and SF-36 Physical Component Summary (SF-36 PCS) (LS mean change: Week 16: 5.71 vs 2.93, $p<0.05$). These improvements were sustained up to Week 52.

Spinal mobility

Spinal mobility was assessed by BASMI up to Week 16. Numerically greater improvements were demonstrated in patients treated with COSENTYX compared with placebo-treated patients at Weeks 4, 8, 12 and 16.

Inhibition of inflammation in magnetic resonance imaging (MRI)

Signs of inflammation were assessed by MRI at baseline and Week 16 and expressed as change from baseline in Berlin SI-joint oedema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with secukinumab. Mean change from baseline in Berlin SI-joint oedema score was -1.68 for patients treated with COSENTYX 150 mg (n=180) versus -0.39 for the placebo-treated patients (n=174) ($p<0.05$).

Juvenile Idiopathic Arthritis (JIA)

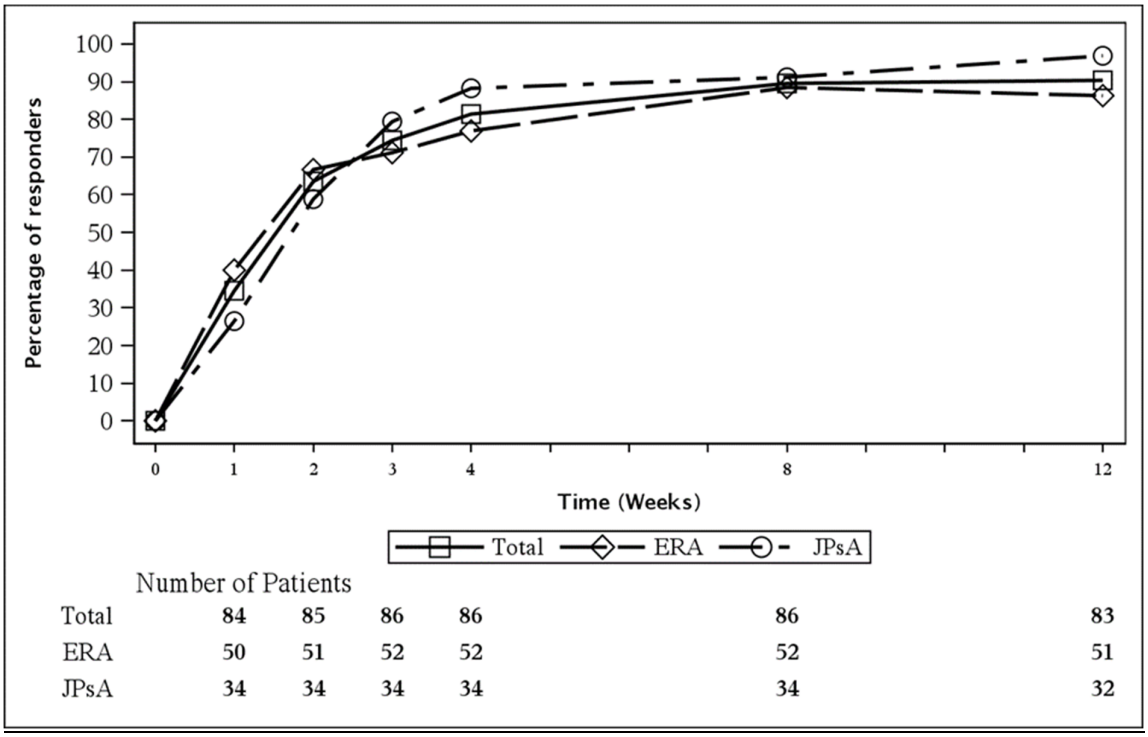
Enthesitis-Related Arthritis (ERA) and Juvenile Psoriatic Arthritis (JPsA)

The efficacy and safety of secukinumab were assessed in 86 patients in a 3-part, double-blind, placebo-controlled, event-driven, randomised, Phase III study in patients 2 to < 18 years of age with active ERA or JPsA as diagnosed based on a modified International League of Associations for Rheumatology (ILAR) JIA classification criteria. The study consisted of an open-label portion (Part 1), followed by randomised withdrawal (Part 2), followed by open-label treatment (Part 3). The JIA patient subtypes at study entry were: 60.5% ERA and 39.5% JPsA. In the study 54.7% of patients were treated concomitantly with MTX. Patients were given a dose of 75 mg if weighing < 50 kg, or 150 mg if weighing ≥ 50 kg.

The primary endpoint was time to flare in Part 2. Disease flare was defined as a ≥ 30% worsening in at least three of the six JIA ACR response criteria and ≥ 30% improvement in not more than one of the six JIA ACR response criteria and a minimum of two active joints.

In open-label Part 1, all patients received secukinumab until Week 12. Patients classified as responders at Week 12 entered into the Part 2 double-blind phase and were randomised 1:1 to continue treatment with secukinumab or begin treatment with placebo. At the end of Part 1, 75 out of 86 patients (90.4%) demonstrated a JIA ACR 30 response and entered into Part 2. Similar responses were seen in each JIA subtype (JPsA and ERA) (Figure 7). At Week 12, 86.7%, 69.9%, and 39.8% of patients were JIA ACR 50, 70, and 90 responders, respectively. Also at Week 12, 36.1% of children had inactive disease based on ACR criteria. The onset of action of secukinumab occurred as early as Week 1. The mean decrease from baseline in Juvenile Arthritis Disease Activity Score (JADAS)-27 was -10.487 (SD: 6.20).

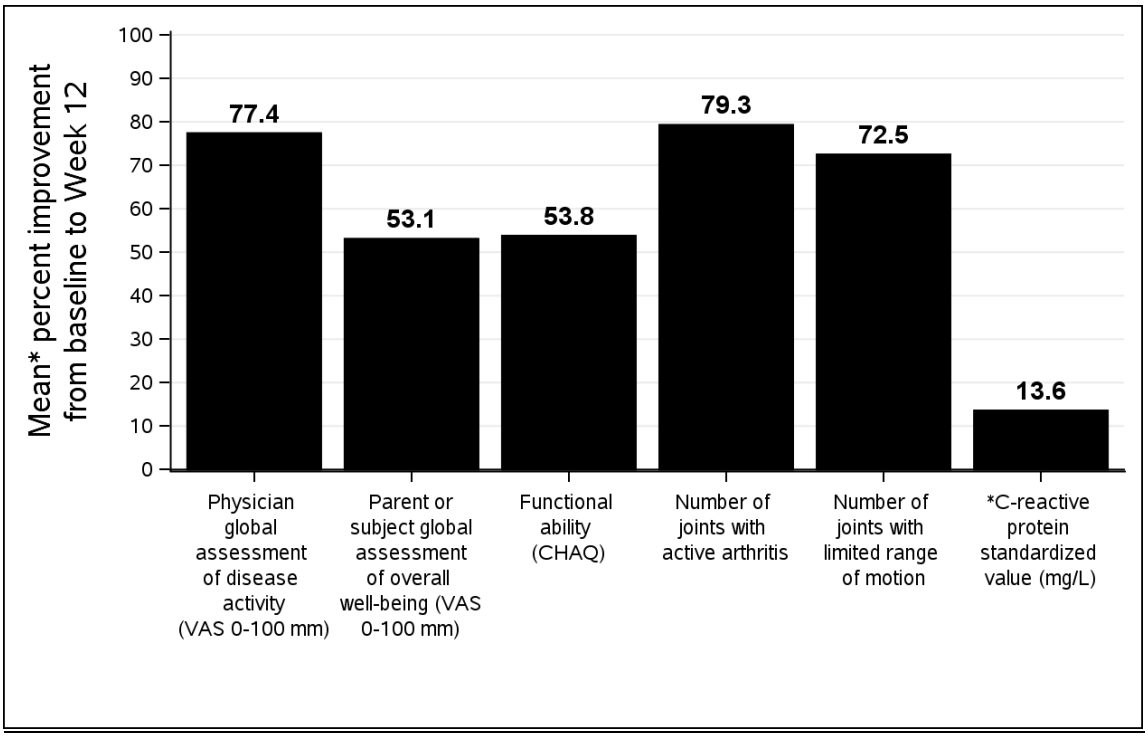
Figure 7 JIA ACR 30 response for all patients and each JIA category up to Week 12 – Part 1



Number of Patients						
Total	84	85	86	86	86	83
ERA	50	51	52	52	52	51
JPsA	34	34	34	34	34	32

Up to Week 12, all JIA ACR components demonstrated clinically relevant improvement from baseline (see Figure 8).

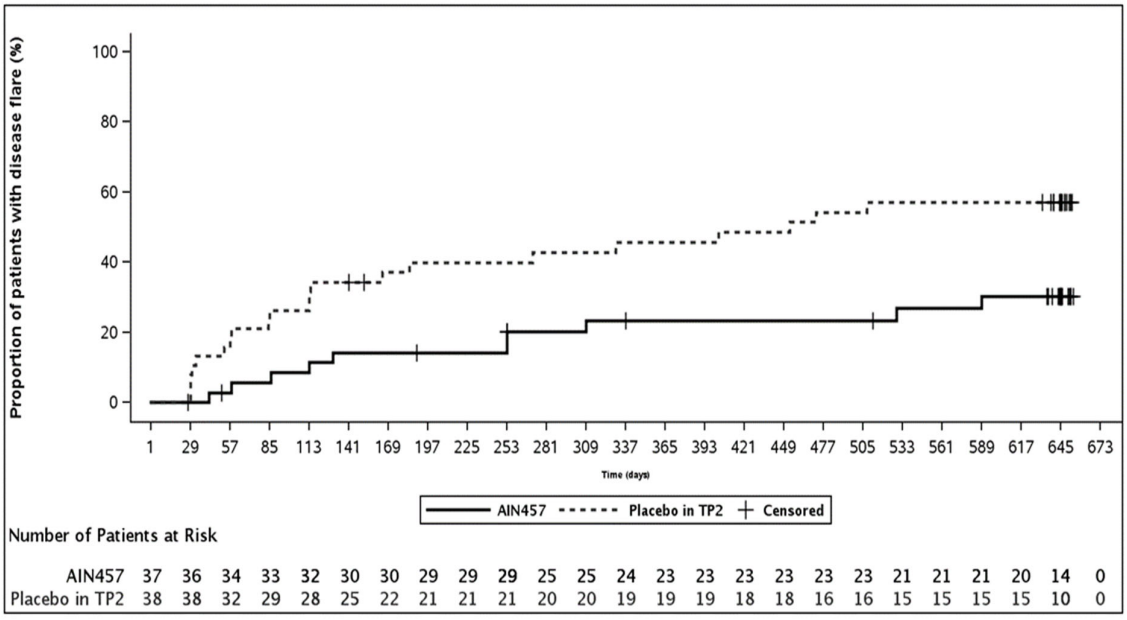
Figure 8 Improvement from baseline for JIA ACR components up to Week 12 in Part 1



**C-reactive protein is shown as median percent improvement from baseline, due to outliers of C-reactive protein values*

The study met its primary endpoint by demonstrating a statistically significant prolongation in the time to disease flare in patients treated with secukinumab compared to placebo. The risk of flare was reduced by 72% for patients on secukinumab compared with patients on placebo (Hazard Ratio of flare events=0.28, 95% CI: 0.13 to 0.63, p<0.001) (Figure 9). During Part 2, a total of 21 patients in the placebo group experienced a flare event (11 JPsA and 10 ERA) compared with 10 patients in the secukinumab group (4 JPsA and 6 ERA). Each component of the JIA ACR core components remained stable or improved for patients that continued on secukinumab.

Figure 9 Kaplan-Meier estimates of the time to disease flare in Part 2



Hidradenitis suppurativa

The safety and efficacy of secukinumab were assessed in 1,084 patients in two similar randomised, double-blind, placebo-controlled phase III studies in adult patients with moderate to severe hidradenitis suppurativa (HS) who were candidates for systemic therapy with biological medicines. Patients enrolled in HS study 1 (SUNSHINE) and HS study 2 (SUNRISE) had Hurley stage I (4.6% and 2.8%, respectively), II (61.4% and 56.7%, respectively) or III (34.0% and 40.5%, respectively) disease at baseline with at least five inflammatory lesions affecting two anatomical areas. The proportion of patients weighing ≥90 kg was 54.7% in HS study 1 and 50.8% in HS study 2. Patients in these studies had a diagnosis of moderate to severe HS for a mean of 7.3 years and 56.3% of the study participants were female. In HS study 1 and HS study 2, 23.8% and 23.2% of patients, respectively, were previously treated with a biological medicine and discontinued the biological agent for either lack of efficacy or intolerance (bio-exposed patients).

HS study 1 (SUNSHINE) evaluated 541 patients and HS study 2 (SUNRISE) evaluated 543 patients, of whom 12.8% and 10.7%, respectively, received concomitant stable dose of antibiotics. In both studies, patients randomised to secukinumab received 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by 300 mg every 2 weeks (Q2W) or every 4 weeks (Q4W). At week 16, patients who were randomised to placebo were reassigned to receive secukinumab 300 mg at weeks 16, 17, 18, 19 and 20 followed by either secukinumab 300 mg every 2 weeks (Q2W) or secukinumab 300 mg every 4 weeks (Q4W).

The primary endpoint in both studies (HS study 1 and HS study 2) was the proportion of patients achieving a Hidradenitis Suppurativa Clinical Response defined as at least a 50% decrease in abscesses and inflammatory nodules count with no increase in the number of abscesses and/or in the number of draining fistulae relative to baseline (HiSCR50) at week 16. Reduction in HS-related skin pain was assessed as a secondary endpoint on the pooled data of HS study 1 and HS study 2 using a Numerical Rating Scale (NRS) in patients who entered the studies with an initial baseline score of 3 or greater.

In HS study 1 and HS study 2, a higher proportion of patients treated with secukinumab 300 mg Q2W or 300 mg Q4W achieved a HiSCR50 response and a decrease in abscesses and inflammatory nodules (AN) count compared to placebo at week 16. In both studies, a lower proportion of patients experienced flares up to week 16 with secukinumab 300 mg Q2W or 300 mg Q4W. A higher proportion of patients treated with secukinumab at either dose (pooled data) experienced a clinically relevant decrease in HS-related skin pain compared to placebo at week 16 (Table 16).

Table 16 Clinical response in HS study 1 and HS study 2 at week 16[1]

	HS study 1 (SUNSHINE)			**HS study 2 (SUNRISE)**		
	Placebo	300 mg Q4W	300 mg Q2W	Placebo	300 mg Q4W	300 mg Q2W
Number of patients randomised	180	180	181	183	180	180
HiSCR50, %	33.7	41.8	45.0*	31.2	46.1*	42.3*
AN count, LS mean change from baseline	-24.3	-42.4	-46.8*	-22.4	-45.5*	-39.3*
Flares, %	29.0	23.2	15.4*	27.0	15.6*	20.1
	Pooled data (HS study 1 and HS study 2)					
	Placebo		300 mg Q4W		300 mg Q2W	
Number of patients with NRS ≥3 at baseline	251		252		266	
NRS30 response, %	23.0		33.5		36.6*	

[1] Multiple imputation was implemented for missing data

* Statistically significant versus placebo based on the pre-defined hierarchy with overall alpha = 0.05

AN: Abscesses and inflammatory Nodules; HiSCR: Hidradenitis Suppurativa Clinical Response; NRS: Numerical Rating Scale

Table 17 Clinical response in HS pooled data study 1 and study 2 at week 16

Treatment comparison	**Odds ratio estimate (95% CI)**	**LS mean difference estimate (95% CI)**
HiSCR50 response		
AIN457 Q2W vs. Placebo	**1.69 (1.24, 2.31)**	
AIN457 Q4W vs. Placebo	**1.67 (1.22, 2.29)**	
Percentage change from baseline in AN count		
AIN457 Q2W vs. Placebo		**-19.98 (-28.27, -11.69)**
AIN457 Q4W vs. Placebo		**-20.82 (-29.02, -12.62)**
Analysis of flares		
AIN457 Q2W vs. Placebo	**0.54 (0.37, 0.77)**	
AIN457 Q4W vs. Placebo	**0.60 (0.42, 0.87)**	
NRS30 response (skin pain)		
AIN457 Q2W vs. Placebo	**2.08 (1.37, 3.16)**	
AIN457 Q4W vs. Placebo	**1.77 (1.15, 2.70)**	

In both studies, the onset of action of secukinumab occurred as early as week 2, the efficacy progressively increased to week 16 and was maintained up to week 52.

Improvements were seen for the primary and key secondary endpoints in HS patients regardless of previous or concomitant antibiotic treatment.

HiSCR50 responses were numerically similar at week 16 in trial participants who had previous exposure to biological medicines and those who were naive to biological medicines.

Greater improvements at week 16 from baseline compared to placebo were demonstrated in health-related quality of life as measured by the Dermatology Life Quality Index.

5.2 Pharmacokinetic properties

The mean pharmacokinetic parameters of secukinumab following single and multiple subcutaneous administration in adult patients with psoriasis, resulting from population pharmacokinetic analysis, are shown in Table 18. C_{max} and AUC were dose-proportional at 150 mg and 300 mg subcutaneous doses.

Table 18 Summary of pharmacokinetic parameters of COSENTYX at steady – state following 150 or 300 mg s.c. administration in adult patients with psoriasis

	COSENTYX 4-weekly dose			
	150 mg		300 mg	
Parameter	Mean (SD)	Range	Mean (SD)	Range
Cmax,ss (µg/mL)	27.6 (10.7)	(13.7, 47.4)	55.2 (21.5)	(27.5, 94.8)
Cav,ss (µg/mL)	22.2 (9.2)	(10.5, 39.0	44.5 (18.4)	(21.1, 77.9)
Tmax,ss (day)	6.0	(4.0, 8.0)	6.0	(4.0, 8.0)
AUCss (day.µg/mL)	622 (257)	(295, 1090)	1245 (515)	(590, 2180)

Absorption

Following a single subcutaneous dose of either 150 mg or 300 mg administered as two injections of 150 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7 ± 4.8 ug/mL or 27.3 ± 9.5 ug/mL, respectively, between 5 to 6 days post dose.

After the initial weekly dosing during the first month, the time to reach the maximum concentration was between 31 and 34 days.

Peak concentrations at steady-state (Cmax,ss) following subcutaneous administration of 150 mg or 300 mg were 27.6 ug/mL and 55.2 ug/mL, respectively. Steady-state is reached after 20 weeks with monthly dosing regimens.
Compared with exposure after a single dose, patients exhibited a 2-fold increase in peak serum concentrations and AUC following repeated monthly dosing during maintenance.

Secukinumab is absorbed with an average absolute bioavailability of 73%.

Following multiple subcutaneous doses of 300 mg administered via the 300 mg/2 mL pen and/or pre-filled syringe in plaque psoriasis patients, the mean serum trough concentrations of secukinumab were consistent with those observed in the previous 150 mg/1 mL studies used to deliver 300 mg.
Following subcutaneous administrations of 300 mg at weeks 0, 1, 2, 3, and 4 followed by 300 mg every 2 weeks, the mean ± SD steady-state secukinumab trough concentration at week 16 was approximately 55.1±26.7 µg/ml and 58.1±30.1 µg/ml in HS study 1 and HS study 2, respectively.

Distribution

The mean volume of distribution during the terminal phase (V_z) following a single intravenous administration ranged from 7.10 to 8.60 L in plaque psoriasis patients suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Secukinumab concentrations in interstitial fluid in the skin of plaque psoriasis patients ranged from 28 % to 39 % of those in serum at 1 and 2 weeks after a single subcutaneous dose of 300 mg secukinumab (administered as two injections of 150 mg).

Metabolism

The metabolic pathway of secukinumab has not been characterized. As a human IgG1κ monoclonal antibody secukinumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

Mean systemic clearance (CL) was 0.19 L/d in plaque psoriasis patients. Clearance was dose- and time-independent, as expected for a therapeutic IgG1 monoclonal antibody interacting with a soluble cytokine target, such as IL-17A.

The mean elimination half-life was estimated to be 27 days in plaque psoriasis patients. Estimated half-lives in individual plaque psoriasis patients range from 17 to 41 days.

In a population pharmacokinetic analysis, the mean systemic CL following subcutaneous administrations of 300 mg at weeks 0, 1, 2, 3, and 4 followed by 300 mg every 2 weeks to patients with hidradenitis suppurativa was 0.26 l/day.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 23 days in hidradenitis suppurativa patients.

Dose linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1 x 0.3 mg/kg to 3 x 10 mg/kg and with subcutaneous doses ranging from 1 x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

The pharmacokinetics properties of secukinumab observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) patients were similar to those displayed in plaque psoriasis patients. The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Pharmacokinetics in special patient groups
Paediatrics
Plaque psoriasis

In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At Week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough

concentration of 19.8 ± 6.96 microgram/mL (n=24) after 75 mg of secukinumab, and patients weighing ≥50 kg had a mean ± SD steady-state trough concentration of 27.3 ± 10.1 microgram/mL (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6 ± 10.8 microgram/mL at Week 24 after 75 mg dose.

Juvenile Idiopathic Arthritis (JIA): Enthesitis-Related Arthritis (ERA) and Juvenile Psoriatic Arthritis (JPsA)

In a paediatric study, ERA and JPsA patients (2 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At Week 24, patients weighing < 50 kg, and patients weighing ≥ 50 kg had a mean ± SD steady-state trough concentration of 25.2 ± 5.45 microgram/mL (n = 10) and 27.9 ± 9.57 microgram/mL (n = 19), respectively.

Elderly patients
Of the 3,430 plaque psoriasis patients exposed to COSENTYX in clinical studies, a total of 230 were 65 years of age or older and 32 patients were 75 years of age or older.

Of the 2,536 psoriatic arthritis patients exposed to COSENTYX in clinical studies, a total of 236 patients were 65 years of age or older and 25 patients were 75 years of age or older.

Of the 794 ankylosing spondylitis patients exposed to COSENTYX in clinical studies, a total of 29 patients were 65 years of age or older and 3 patients were 75 years of age or older.

Of the 524 non-radiographic axial spondyloarthritis patients exposed to COSENTYX in clinical studies, a total of 9 patients were 65 years of age or older and 2 patients were 75 years of age of older.

Of the 721 hidradenitis suppurativa patients exposed to COSENTYX in clinical studies, a total of 11 patients were 65 years of age or older and no patient was 75 years of age or older.

Based on population PK analysis, clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal and hepatic impairment
No pharmacokinetic data are available in patients with hepatic or renal impairment.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

5.3 Preclinical safety data

Non-clinical data revealed no special risks for humans based on tissue cross-reactivity testing, safety pharmacology, repeated dose and reproductive toxicity studies performed with secukinumab or a murine anti-murine IL-17A antibody.

Since secukinumab binds to cynomolgus monkey and human IL-17A, its safety was studied in the cynomolgus monkey. No undesirable effects of secukinumab were seen following subcutaneous administration to cynomolgus monkeys for up to 13 weeks and intravenous administration up to 26 weeks (including pharmacokinetic, pharmacodynamic, immunogenicity and immunotoxicity (e.g. T-cell dependent antibody response and NK cell activity) evaluations). The average serum concentrations observed in monkeys after 13 weekly subcutaneous doses of 150 mg/kg were considerably higher than the predicted average serum concentration expected in psoriatic patients at the highest clinical dose. Antibodies to secukinumab were detected in only one of the exposed

animals. No non-specific tissue cross-reactivity was observed when secukinumab was applied to normal human tissue.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

In an embryofoetal development study in cynomolgus monkeys, secukinumab showed no maternal toxicity, embryotoxicity or teratogenicity when administered throughout organogenesis and late gestation.

No undesirable effects of a murine anti-murine IL-17A antibody were seen in fertility and early embryonic development and pre-and postnatal development studies in mice. The high dose used in these studies was in excess of the maximum effective dose in terms of IL-17A suppression and activity (see section 4.6).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder for injection: water for injections, sucrose, histidine, histidine hydrochloride monohydrate, polysorbate 80**.**

Solution for injection (prefilled syringe and prefilled pen): trehalose dihydrate, histidine, histidine hydrochloride monohydrate, polysorbate 80, methionine, 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

24 months.

6.4 Special precautions for storage

Powder for Solution: Store at 2-8°C. Store in the original package.

Prefilled syringe and prefilled pen: Store at 2-8°C. Do not freeze. Protect from light. Store in the original package. May be stored unrefrigerated (out of fridge) at room temperature for a single period up to a maximum of 4 days at a temperature not above 30°C. Do not put back in the refrigerator after it has reached room temperature. Discard any unused product.

6.5 Nature and contents of container

Powder for Solution: Cosentyx 150 mg	Colourless glass vial with a grey coated rubber stopper and aluminium cap with a white flip-off component. COSENTYX is available in unit packs containing 1* or 2* single-use vials.
Prefilled syringe: Cosentyx 75 mg/ 0.5 mL in Pre-filled	Single use pre-filled 1 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½" needle and rigid needle shield of styrene butadiene rubber assembled in a passive safety device of polycarbonate.

syringe	COSENTYX is available in unit packs containing 1* pre-filled syringe.
Cosentyx 150 mg/ 1 mL in Pre-filled syringe	Single use pre-filled 1 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½" needle and rigid needle shield of styrene butadiene rubber assembled in a passive safety device of polycarbonate. COSENTYX is available in unit packs containing 1* or 2* pre-filled syringes.
Cosentyx 300 mg/ 2mL in Pre-filled syringe	Single use pre-filled 2 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½" needle and rigid needle shield of synthetic polyisoprene rubber assembled in a passive safety device of polycarbonate. COSENTYX is available in unit packs containing 1* pre-filled syringe.
Prefilled pen: Cosentyx 150 mg/ 1 mL in Pre-filled Pen	Single-use pre-filled syringe assembled into a triangular-shaped pen with transparent window and label (SensoReady pen). The pre-filled syringe inside the pen is a 1 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½" needle and rigid needle shield of styrene butadiene rubber. COSENTYX is available in unit packs containing 1* or 2* pre-filled pens.
Cosentyx 300 mg/ 2mL in Pre-filled Pen	Single use pre-filled syringe assembled into a squared-shape pen with transparent window and label (YpsoMate auto-injector). The pre-filled syringe inside the pen is a 2 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½" needle and rigid needle shield of synthetic polyisoprene rubber. COSENTYX is available in unit packs containing 1* pre-filled pens.

**Not all pack sizes or presentations may be marketed.*

6.6 Special precautions for disposal and handling

COSENTYX 150 mg powder for solution is supplied in a single-use vial containing 150 mg secukinumab for reconstitution with sterile water for injections. The resulting solution should be clear and colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

COSENTYX 75 mg/0.5mL, 150 mg/mL and 300 mg/ 2 mL solution for injection is supplied in a single-use pre-filled syringe or prefilled pen for individual use. Do not shake or freeze the syringe. The syringe should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature. Prior to use, a visual inspection of the pre-filled syringe is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Detailed instructions for use are provided in the package leaflet.

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

7 MEDICINE SCHEDULE

Prescription medicine

8 SPONSOR

Novartis New Zealand Limited

PO Box 99102 Newmarket
Auckland 1149
New Zealand
Telephone: 0800 354 335
® = Registered Trademark

9 DATE OF FIRST APPROVAL

14 January 2016	COSENTYX® 150 mg Powder for Injection COSENTYX® 150 mg/mL Solution for Injection
30 March 2023	COSENTYX® 300mg/2 mL Solution for Injection
30 March 2023	COSENTYX® 75mg/0.5 mL Solution for Injection

10 DATE OF REVISION OF THE TEXT

31 January 2025

SUMMARY TABLE OF CHANGES

The overview of the last changes made to the data sheet are as follows:

Section changed	Summary of new information
4.4	Addition of warning for Pre-treatment evaluation for tuberculosis
4.4	Addition of warning for Hepatitis B reactivation
4.8	Addition of Hypersensitivity vasculitis as post marketing adverse drug reaction

Internal document code: cos260225NZi_V2 based on CDS 4.0 dated 9 Dec 2024.