

21.11.2019

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

**Cosentyx® 150 mg solution for injection** הנדון:  
המרכיב הפעיל: secukinumab 150 mg/ml

התכשיר שבנדון רשום בישראל להתוויות הבאות:

**- Plaque psoriasis:**

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

**- Psoriatic arthritis:**

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease modifying anti rheumatic drug (DMARD) therapy has been inadequate.

**- Ankylosing spondylitis:**

Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

ברצוננו להודיעכם על עדכון העלון לרופא והעלונים לצרכן של התכשיר בנדון. להלן השינויים מהיבט בטיחות שנעשו (מודגש בכחול – טקסט חדש, מודגש באדום עם קו חוצה – טקסט שהוסר):

עלון לרופא:**4.3 Contraindications**

~~H~~~~Severe~~ hypersensitivity ~~reactions~~ to the active substance or to any of the excipients listed in section 6.1. Clinically important, active infection, ~~(e.g. active tuberculosis;~~ (see section 4.4).

**4.4 Special warnings and precautions for use**Concomitant immunosuppressive therapy

† In psoriasis studies, the safety and efficacy of ~~Secukinumab~~ ~~Cosentyx~~ in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

**4.8 Undesirable effects**



System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
	Uncommon	Oral candidiasis
		Tinea pedis
		Otitis externa
		<b>Lower respiratory tract infections</b>
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	<b>Uncommon</b>	<b>Inflammatory bowel disease</b>
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	<b>Rare</b>	<b>Exfoliative dermatitis<sup>2)</sup></b>
<sup>1)</sup> Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA and AS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA and AS) treatment duration <sup>2)</sup> <b>Cases were reported in patients with psoriasis diagnosis</b>		

#### עלון לצרכן:

**תופעות לוואי לא שכיחות** (עשויות להופיע עד משתמש 1 מתוך 100 משתמשים)

- זיהום פטרייתי בפה (זיהום בקנדידה בפה)
- סימנים של רמות נמוכות של תאי הדם הלבנים, כגון חום, כאב גרון או כיבים בפה בשל זיהומים (נויטרופניה)
- פטרת כף הרגל
- זיהום באוזן החיצונית (אוטיטיס חיצונית)
- הפרשה מהעיניים בליווי גרד, אודם ונפיחות (דלקת הלחמית)
- פריחה המלווה בגרד (סרפדת)
- **זיהומים בדרכי הנשימה התחתונות**
- **התכווצויות וכאבים בבטן, שלשול, אובדן משקל או דם בצואה (סימנים לבעיות במעי)**

**תופעות לוואי נדירות** (עשויות להופיע עד משתמש 1 מתוך 1,000 משתמשים)

- תגובה אלרגית חריפה עם שוק אנפילקטי
- **אדמומיות וקילוף עור על פני אזור גדול בגוף, אשר עלולים להיות מגרדים או כואבים (exfoliative dermatitis)**

קראו את העלונים בעיון ועדכנו את המטופלים במידע הנדרש. בנוסף לשינויים המפורטים מעלה, קיימים תיקונים עריכתיים אשר אינם מפורטים כאן. מצורפים העלון לרופא והעלונים לצרכן לעיונכם. העלונים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על-ידי פניה לבעל הרישום.

בברכה,  
שירן חן גולדשטיין  
רוקחת ממונה

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## **1. NAME OF THE MEDICINAL PRODUCT**

**Cosentyx® 150 mg solution for injection**

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each pre-filled syringe or pre-filled pen contains 150 mg secukinumabin 1ml.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Solution for injection in pre-filled syringe

Solution for injection in pre-filled pen (SensoReady® pen)

The solution is clear and colourless to slightly yellow.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

#### Plaque psoriasis

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

#### Psoriatic arthritis

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

#### Ankylosing spondylitis

Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

### **4.2 Posology and method of administration**

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

#### Posology

### Plaque psoriasis

The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

### Psoriatic arthritis

For patients with concomitant moderate to severe plaque psoriasis or 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 monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg.

### Ankylosing spondylitis

The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4 followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

### Special populations

#### Elderly patients (aged 65 years and over)

No dose adjustment is required (see section 5.2).

#### Renal impairment / hepatic impairment

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

#### Paediatric population

The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.

### Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The solution/the syringe/the pen must not be shaken.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients 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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

### 4.4 Special warnings and precautions for use

#### Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab 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 secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, 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).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

#### Inflammatory bowel disease

Cases of new or exacerbations of Crohn's disease and ulcerative colitis have been reported. Caution should be exercised when prescribing secukinumab to patients with inflammatory bowel disease, including Crohn's disease and ulcerative colitis. Patients should be closely monitored.

#### Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

#### Latex-sensitive individuals

The removable needle cap of the Cosentyx pre-filled syringe/pre-filled pen contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable needle cap. Nevertheless, the use of Cosentyx pre-filled syringes/pre-filled pens in latex-sensitive individuals has not been studied and there is therefore a potential risk of hypersensitivity reactions which cannot be completely ruled out.

#### Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate

immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

#### Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of Secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

### **4.5 Interaction with other medicinal products and other forms of interaction**

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

In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis).

### **4.6 Fertility, pregnancy and lactation**

#### Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

#### Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

#### Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

#### Fertility

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

### **4.7 Effects on ability to drive and use machines**

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

### **4.8 Undesirable effects**

## Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) are upper respiratory tract infections (most frequently nasopharyngitis, rhinitis).

### Tabulated list of adverse reactions

ADRs from clinical studies and post-marketing reports (Table 1) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. 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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ); and not known (cannot be estimated from the available data).

Over 11,900 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and other autoimmune conditions), representing 20,995 patient years of exposure. Of these, over 7,100 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

**Table 1            List of adverse reactions in clinical studies<sup>1)</sup> and post-marketing experience**

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
	Uncommon	Oral candidiasis
		Tinea pedis
		Otitis externa
		Lower respiratory tract infections
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Exfoliative dermatitis <sup>2)</sup>
<sup>1)</sup> Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA and AS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA and AS) treatment duration		
<sup>2)</sup> Cases were reported in patients with psoriasis diagnosis		

#### Description of selected adverse reactions

##### Infections

In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab 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 secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and ankylosing spondylitis clinical studies were similar to those observed in the psoriasis studies.

##### 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  $<1.0-0.5 \times 10^9/l$  (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 secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis and ankylosing spondylitis is similar to psoriasis.

Rare cases of neutropenia  $<0.5 \times 10^9/l$  (CTCAE grade 4) were reported.

#### Hypersensitivity reactions

In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

#### Immunogenicity

In psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il>

### **4.9 Overdose**

Doses up to 30 mg/kg (approximately 2000 to 3000 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.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

#### Mechanism of action

Secukinumab is a fully human IgG1/ $\kappa$  monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). 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.

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, psoriatic arthritis and ankylosing spondylitis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis.

#### Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, 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.

#### Clinical efficacy and safety

##### Plaque psoriasis

The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naïve, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4 followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (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.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab 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 randomised to receive placebo at weeks 0, 1, 2, 3 and 4,

followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 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. Patients randomised to “retreatment as needed” did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

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 (see Table 2 and Table 3). The 300 mg dose provided improved skin clearance particularly for “clear” or “almost clear skin” across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

**Table 2            Summary of PASI 50/75/90/100 & IGA\*   mod 2011 “clear” or “almost clear”  
clinical response in psoriasis studies 1, 3 and 4 (ERASURE , FEATURE and JUNCTURE)**

		Week 12		Week 16		Week 52	
	Placebo	150 mg	300 mg	150 mg	300 mg	150 mg	300 mg
<b>Study 1</b>							
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%)
<b>Study 3</b>							
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%)	-	-	-	-
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%)**	-	-	-	-
<b>Study 4</b>							
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 colouration 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 3** Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	150 mg	300 mg	Etanercept	150 mg	300 mg	Etanercept	150 mg	300 mg	Etanercept
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%)
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

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), 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 to week 52.

**Table 4** 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 (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	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 (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	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 every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

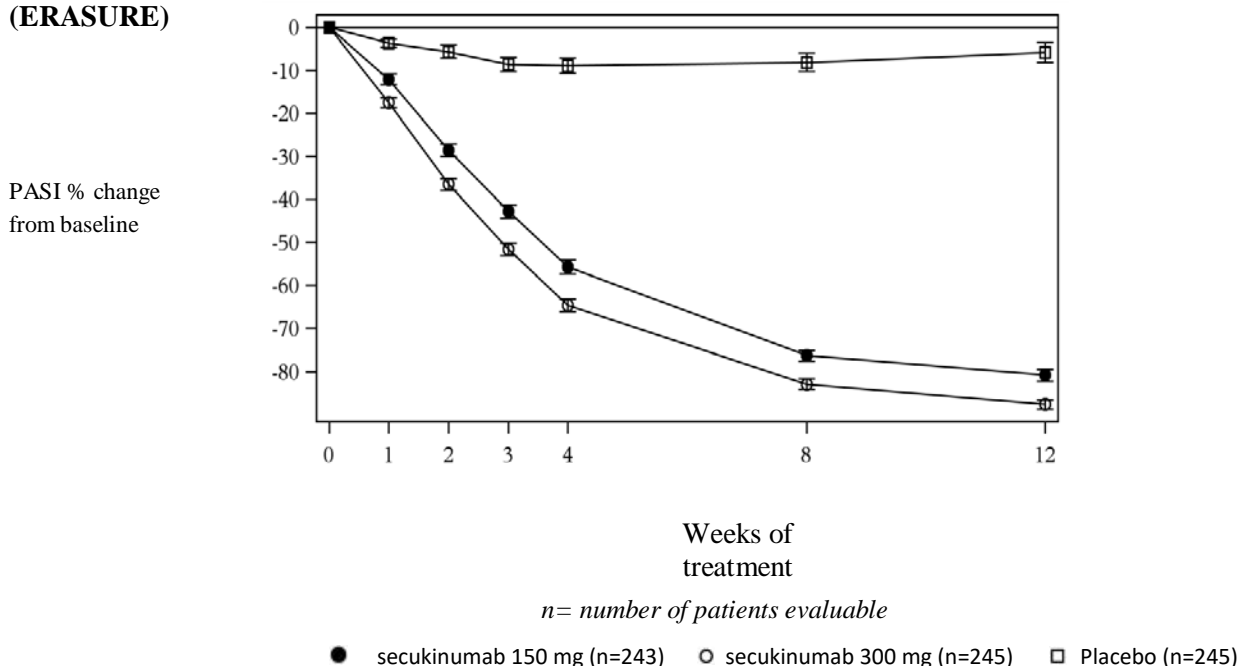
\*\* p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

\*\*\* p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naïve, biologic-naïve, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy, with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

**Figure 1** Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



#### *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 ppIGA 0 or 1 response (“clear” or “almost clear”) for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of  $\geq 12$ , an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the 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% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

#### *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). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary<sup>®</sup>. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

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 and these improvements were maintained for up to 52 weeks.

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 (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

### Psoriatic arthritis

The safety and efficacy of secukinumab were assessed in 1,999 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis ( $\geq 3$  swollen and  $\geq 3$  tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid 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 of at least five years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For all studies, the primary endpoint was American College of Rheumatology (ACR) 20 response. For Psoriatic Arthritis study 1 (PsA study 1) and Psoriatic Arthritis study 2 (PsA study 2), the primary endpoint was at week 24. For Psoriatic Arthritis study 3 (PsA study 3), the primary endpoint was at week 16 with the key secondary endpoint, the change from baseline in modified Total Sharp Score (mTSS), at week 24.

In PsA study 1, PsA study 2 and PsA study 3, 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).

PsA study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to secukinumab received 75 mg, 150 mg or 300 mg subcutaneously 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 crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) 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 secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

PsA study 3 (FUTURE 5) evaluated 996 patients, of whom 50.1% had concomitant MTX. Patients were randomised to receive secukinumab 150 mg, 300 mg or placebo subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month, or a once monthly injection of secukinumab 150 mg (without loading). Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were then crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) 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 secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed

by the same dose every month.

#### *Signs and symptoms*

Treatment with secukinumab resulted in significant improvement in measures of disease activity compared to placebo at weeks 16 and 24 (see Table 5).

**Table 5 Clinical response in PsA study 2 and PsA study 3 at week 16 and week 24**

	PsA study 2			PsA study 3		
	Placebo	150 mg <sup>1</sup>	300 mg <sup>1</sup>	Placebo	150 mg <sup>1</sup>	300 mg <sup>1</sup>
<b>Number of patients randomised</b>	98	100	100	332	220	222
<b>ACR20 response n (%)</b>						
<b>Week 16</b>	18 (18.4%)	60 (60.0% ***)	57 (57.0% ***)	91 <sup>◇</sup> (27.4%)	122 <sup>◇</sup> (55.5% ***)	139 <sup>◇</sup> (62.6% ***)
<b>Week 24</b>	15 <sup>◇</sup> (15.3%)	51 <sup>◇</sup> (51.0% ***)	54 <sup>◇</sup> (54.0% ***)	78 (23.5%)	117 (53.2% ***)	141 (63.5% ***)
<b>ACR50 response n (%)</b>						
<b>Week 16</b>	6 (6.1%)	37 (37.0% ***)	35 (35.0% ***)	27 (8.1%)	79 (35.9% *)	88 (39.6% *)
<b>Week 24</b>	7 (7.1%)	35 (35.0%)	35 (35.0% **)	29 (8.7%)	86 (39.1% ***)	97 (43.7% ***)
<b>ACR70 response n (%)</b>						
<b>Week 16</b>	2 (2.0%)	17 (17.0% **)	15 (15.0% **)	14 (4.2%)	40 (18.2% ***)	45 (20.3% ***)
<b>Week 24</b>	1 (1.0%)	21 (21.0% **)	20 (20.0% **)	13 (3.9%)	53 (24.1% ***)	57 (25.7% ***)
<b>DAS28-CRP</b>						
<b>Week 16</b>	-0.50	-1.45***	-1.51***	-0.63	-1.29*	-1.49*
<b>Week 24</b>	-0.96	-1.58**	-1.61**	-0.84	-1.57***	-1.68***
<b>Number of patients with ≥3% BSA psoriasis skin involvement at baseline</b>	43 (43.9%)	58 (58.0%)	41 (41.0%)	162 (48.8%)	125 (56.8%)	110 (49.5%)
<b>PASI 75 response n (%)</b>						
<b>Week 16</b>	3 (7.0%)	33 (56.9% ***)	27 (65.9% ***)	20 (12.3%)	75 (60.0% *)	77 (70.0% *)
<b>Week 24</b>	7 (16.3%)	28 (48.3% **)	26 (63.4% ***)	29 (17.9%)	80 (64.0% ***)	78 (70.9% ***)
<b>PASI 90 response n (%)</b>						
<b>Week 16</b>	3 (7.0%)	22 (37.9% ***)	18 (43.9% ***)	15 (9.3%)	46 (36.8% *)	59 (53.6% *)
<b>Week 24</b>	4 (9.3%)	19 (32.8% **)	20 (48.8% ***)	19 (11.7%)	51 (40.8% ***)	60 (54.5% ***)



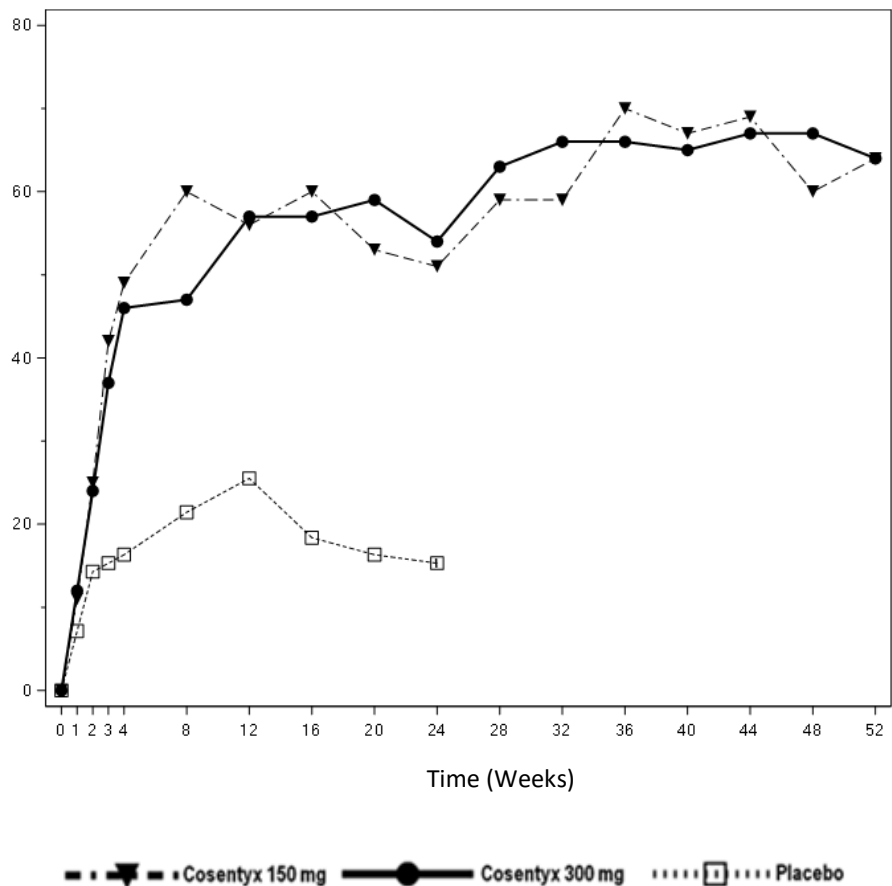
<b>Dactylitis resolution n (%) †</b>						
<b>Week 16</b>	10 (37%)	21 (65.6%*)	26 (56.5%)	40 (32.3%)	46 (57.5%*)	54 (65.9%*)
<b>Week 24</b>	4 (14.8%)	16 (50.0%**)	26 (56.5%**)	42 (33.9%)	51 (63.8%***)	52 (63.4%***)
<b>Enthesitis resolution n (%) ‡</b>						
<b>Week 16</b>	17 (26.2%)	32 (50.0%**)	32 (57.1%***)	68 (35.4%)	77 (54.6%*)	78 (55.7%*)
<b>Week 24</b>	14 (21.5%)	27 (42.2%*)	27 (48.2%**)	66 (34.4%)	77 (54.6%***)	86 (61.4%***)
<p>* p&lt;0.05, ** p&lt;0.01, *** p&lt;0.001; versus placebo</p> <p>All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 24 for PsA study 2, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints and all endpoints at week 16.</p> <p>All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 16 for PsA study 3, except for ACR70 which was an exploratory endpoint and all endpoints at week 24.</p> <p>Non-responder imputation used for missing binary endpoint.</p> <p>ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area</p> <p>◊Primary Endpoint</p> <p><sup>1</sup> Secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month</p> <p>†In patients with dactylitis at baseline (n=27, 32, 46, respectively for PsA study 2 and n=124, 80, 82, respectively for PsA study 3)</p> <p>‡In patients with enthesitis at baseline (n=65, 64, 56, respectively for PsA study 2 and n=192, 141, 140, respectively for PsA study 3)</p>						

The onset of action of secukinumab occurred as early as week 2. Statistically significant difference in ACR 20 versus placebo was reached at week 3.

The percentage of patients achieving ACR 20 response by visit is shown in **Figure 2**.

**Figure 2 ACR20 response in PsA study 2 over time up to week 52**

Percentage  
of  
responders



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. In PsA study 2, at week 24, secukinumab -treated patients with concomitant MTX use had a higher ACR 20 response (47.7% and 54.4% for 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (31.8% and 38.6% for 150 mg and 300 mg, respectively, compared to placebo 8.0%). Secukinumab -treated patients without concomitant MTX use had a higher ACR 20 response (53.6% and 53.6% for 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (37.5% and 32.1% for 150 mg and 300 mg, respectively, compared to placebo 6.3%).

In PsA study 2, both anti-TNF $\alpha$ -naïve and anti-TNF $\alpha$ -IR secukinumab -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 (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%). In the anti-TNF $\alpha$ -IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo ( $p < 0.05$ ) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNF $\alpha$ -IR patients.

The number of PsA patients with axial involvement was too small to allow meaningful assessment.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. In PsA study 2, the proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the secukinumab -treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at week 24.

In PsA study 1 and PsA study 2, efficacy was maintained up to week 104. In PsA study 2, among 200 patients initially randomised to secukinumab 150 mg and 300 mg, 178 (89%) patients were still on

treatment at week 52. Of the 100 patients randomised to secukinumab 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to secukinumab 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

#### *Radiographic response*

In PsA study 3, 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. secukinumab 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 6).

Inhibition of progression of structural damage was also assessed in PsA study 1 at weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 6.

**Table 6** Change in modified Total Sharp Score in psoriatic arthritis

	PsA study 3			PsA study 1	
	Placebo n=296	secukinumab 150 mg <sup>1</sup> n=213	secukinumab 300 mg <sup>1</sup> n=217	Placebo n=179	secukinumab 150 mg <sup>2</sup> n=185
<b>Total score</b>					
<b>Baseline (SD)</b>	15.0 (38.2)	13.5 (25.6)	12.9 (23.8)	28.4 (63.5)	22.3 (48.0)
<b>Mean change at Week 24</b>	0.50	0.13*	0.02*	0.57	0.13*
*p<0.05 based on nominal, but non adjusted, p-value					
<sup>1</sup> secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month					
<sup>2</sup> 10 mg/kg at weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg					

In PsA study 1, inhibition of structural damage was maintained with secukinumab treatment up to week 52.

In PsA study 3, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of  $\leq 0.5$ ) from randomisation to week 24 was 80.3%, 88.5% and 73.6% for secukinumab 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed in anti-TNF $\alpha$ -naïve and anti-TNF $\alpha$ -IR patients and in patients treated with and without concomitant MTX.

In PsA study 1, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of  $\leq 0.5$ ) from randomisation to week 24 was 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from week 24 to Week 52 for secukinumab 10 mg/kg intravenous load – followed by 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at week 16 or week 24 was 85.7% and 86.8%, respectively.

#### *Physical function and health-related quality of life*

In PsA Study 2 and PsA study 3, patients treated with secukinumab 150 mg (p=0.0555 and p<0.0001) and 300 mg (p=0.0040 and p<0.0001) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24 and week 16, respectively. Improvements in HAQ-DI scores were seen regardless of previous anti-TNF $\alpha$

exposure. Similar responses were seen in PsA study 1.

Secukinumab -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 ( $p < 0.001$ ). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively) and these improvements were maintained up to week 104 in PsA study 2.

Similar responses were seen in PsA study 1 and efficacy was maintained up to week 52.

#### Ankylosing spondylitis

The safety and efficacy of secukinumab were assessed in 590 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)  $\geq 4$  despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in these studies had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at week 16.

In Ankylosing Spondylitis study 1 (AS study 1) and Ankylosing Spondylitis study 2 (AS study 2) 27.0% and 38.8% 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).

AS study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously 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 secukinumab (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 75 mg or 150 mg subcutaneously 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 secukinumab (either 75 mg or 150 mg subcutaneously) every month.

#### *Signs and symptoms*

In AS study 2, treatment with secukinumab 150 mg resulted in greater improvement in measures of disease activity compared with placebo at week 16 (see Table 7).

**Table 7                      Clinical response in AS study 2 at week 16**

<b>Outcome (p-value versus placebo)</b>	<b>Placebo (n = 74)</b>	<b>75 mg (n = 73)</b>	<b>150 mg (n = 72)</b>
ASAS 20 response, %	28.4	41.1	61.1***
ASAS 40 response, %	10.8	26.0	36.1***
hsCRP, (post-BSL/BSL ratio)	1.13	0.61	0.55***
ASAS 5/6, %	8.1	34.2	43.1***
ASAS partial remission, %	4.1	15.1	13.9
BASDAI 50, %	10.8	24.7*	30.6**
ASDAS-CRP major improvement	4.1	15.1*	25.0***
<p>* p&lt;0.05, ** p&lt;0.01, *** p&lt;0.001; versus placebo  All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP  Non-responder imputation used for missing binary endpoint</p> <p>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</p>			

The onset of action of secukinumab 150 mg occurred as early as week 1 for ASAS 20 and week 2 for ASAS 40 (superior to placebo) in AS study 2.

ASAS 20 responses were improved at week 16 in both anti-TNF $\alpha$ -naïve patients (68.2% versus 31.1%; p<0.05) and anti-TNF $\alpha$ -IR patients (50.0% versus 24.1%; p<0.05) for secukinumab 150 mg compared with placebo, respectively.

In both AS studies, secukinumab -treated patients (150 mg in AS study 2 and both regimens in AS study 1) demonstrated significantly improved signs and symptoms at week 16, with comparable magnitude of response and efficacy maintained up to week 52 in both anti-TNF $\alpha$ -naïve and anti-TNF $\alpha$ -IR patients. In AS study 2, among 72 patients initially randomised to secukinumab 150 mg, 61 (84.7%) patients were still on treatment at week 52. Of the 72 patients randomised to secukinumab 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

#### *Spinal mobility*

Patients treated with secukinumab 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at week 16 for both AS study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to week 52.

#### *Physical function and health-related quality of life*

In AS study 1 and study 2, patients treated with secukinumab 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with secukinumab 150 mg also showed statistically significant 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), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to week 52.

#### *Paediatric population*

The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.

## 5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoraitic arthritis and ankylosing spondylitis were similar.

### Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of  $43.2 \pm 10.4$  µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of  $13.7 \pm 4.8$  µg/ml or  $27.3 \pm 9.5$  µg/ml, respectively, between 5 and 6 days post dose.

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

On the basis of simulated data, peak concentrations at steady-state ( $C_{\max,ss}$ ) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

### Distribution

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

### Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

### Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

### Linearity/non-linearity

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

### Special populations

#### Elderly patients

Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age  $\geq 65$  years and n=7 for age  $\geq 75$  years), clearance in elderly patients and patients less than 65 years of age was similar.

#### Patients with renal or hepatic impairment

No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

#### 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 hazard for humans based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

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

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Water for injections  
Trehalose dihydrate  
L-histidine/ L-histidine hydrochloride monohydrate  
L-methionine  
Polysorbate 80, low peroxide quality

### **6.2 Incompatibilities**

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

### **6.3 Shelf life**

The expiry date of the product is printed on the package materials.

### **6.4 Special precautions for storage**

Store in a refrigerator (2°C - 8°C).. If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C. Do not freeze  
Store the syringes and pens in the original package in order to protect from light.

## **6.5 Nature and contents of container**

### *Cosentyx 150 mg solution for injection in pre-filled syringe*

Cosentyx 150 mg solution for injection is supplied in a pre-filled 1 ml long glass syringe with a rubber plunger stopper, staked needle and rigid needle shield

Cosentyx is available in unit packs containing 1 or 2 pre-filled syringes.  
Not all pack sizes may be marketed.

### *Cosentyx 150 mg solution for injection in pre-filled pen (SensoReady pen)*

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled syringe assembled into a auto-injector (SensoReady pen). The pre-filled syringe inside the pen is a 1 ml glass syringe with a rubber plunger stopper, staked needle and rigid needle shield.

Cosentyx is available in unit pack containing 1 or 2 pre-filled pens.  
Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal and other handling**

### *Cosentyx 150 mg solution for injection in pre-filled syringe and pre-filled pen*

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled syringe/pen for individual use. The syringe or the pen 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/ pre-filled pen 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. MANUFACTURER:**

Novartis Pharma Stein, AG, Stein Switzerland  
For Novartis Pharma AG, Basel, Switzerland

## **8. REGISTRATION HOLDER:**

Novartis Israel Ltd.  
P.O.B 7126, Tel Aviv



**9. REGISTRATION NUMBER: 154-20-34342**

The content of this leaflet was approved by the Ministry of Health in May 2019 and updated on 10 October 2019 according to the guidelines of the Ministry of Health

**עלון לצרכן לפי תקנות הרוקחים (תכשירים) התשמ"ו-1986**

התרופה משווקת על פי מרשם רופא בלבד

## קוסנטיקס 150 מ"ג תמיסה להזרקה תמיסה להזרקה בעט מוכן לשימוש (עט-סנסורדי) להזרקה תת-עורית

**חומר פעיל:**

כל עט קוסנטיקס מוכן לשימוש (עט-סנסורדי) מכיל 150 מ"ג/מ"ל סקוקינומאב (secukinumab).

חומרים בלתי פעילים ואלרגניים: ראה פרק 6 "מידע נוסף".

**קרא בעיון את העלון עד סופו בטרם תשתמש בתרופה.**
עלון זה מכיל מידע תמציתי על התרופה. אם יש לך שאלות נוספות, פנה אל הרופא או אל הרוקח.

תרופה זו נרשמה לטיפול במחלתך. אל תעביר אותה לאחרים. היא עלולה להזיק להם אפילו אם נראה לך כי מחלתם דומה.

### 1.למה מיועדת התרופה?

קוסנטיקס מיועדת לטיפול במחלות הדלקתיות הבאות:

- ספחת רובידית (פסוריאזיס רובידית - plaque psoriasis):

קוסנטיקס מיועדת לטיפול בספחת רובידית ברמה בינונית עד חמורה במבוגרים המועמדים לטיפול מערמתי.

- דלקת מפרקים ספחתית (פסוריאטיק ארטריטיס - psoriatic arthritis):

טיפול בקוסנטיקס או טיפול משולב בקוסנטיקס יחד עם תרופה בשם מתותרקסט (MTX) methotrexate מיועדי לטיפול בדלקת מפרקים ספחתית פעילה במבוגרים כשהתגובה לטיפול קודם בתרופה מסוג DMARD הייתה לא מספקת.

- דלקת חוליות מקשחת (אנקילוזינג ספונדיליטיס - ankylosing spondylitis):

קוסנטיקס מיועדת לטיפול בדלקת חוליות מקשחת פעילה במבוגרים כשהתגובה לטיפול קונבנציונאלי (שגרת) קודם הייתה לא מספקת.

**קבוצה תרופוית:** מעכבי אינטרלוקין (IL) Inhibitors (Interleukin).

החומר הפעיל בקוסנטיקס הינו סקוקינומאב, נוגדן חד שבטי (monoclonal antibody) השייך לקבוצה של תכשירים הנקראים מעכבי אינטרלוקין (IL). התרופה פועלת באמצעות נטרול פעילותו של חלבון המכונה IL-17A, אשר נמצא ברמות מוגברות במחלות כגון ספחת, דלקת מפרקים ספחתית ודלקת חוליות מקשחת.

**ספחת רובידית**

קוסנטיקס הינה תרופה המשמשת לטיפול בעור במצב של ספחת רובידית שגורמת לדלקת הפוגעת בעור. קוסנטיקס מפחיתה את הדלקת ותסמינים אחרים של המחלה. קוסנטיקס משמשת לטיפול במבוגרים הסובלים מפסוריאזיס רובידית בינונית עד חמורה.

התועלת שתפיק מהשימוש בקוסנטיקס בספחת רובידית תתבטא בשופור שיוביל לניקוי העור ולהפחתת התסמינים שלך כגון היווצרות קשקשים, גרד וכאב.

**דלקת מפרקים ספחתית**

קוסנטיקס הינה תרופה המשמשת לטיפול במצב שנקרא "דלקת מפרקים ספחתית". זוהי מחלה דלקתית של המפרקים שלעיתים קרובות מלווה בספחת. אם יש לך דלקת מפרקים ספחתית פעילה, תקבל תחילה תרופות אחרות. אם לא תגיב מספיק טוב לתרופות אלו, תקבל קוסנטיקס כדי להפחית את הסימנים והתסמינים של דלקת מפרקים ספחתית פעילה, לשיפור התיפקוד הגופני, ולהאטה בנזק שנגרם לסחוס ולעצם של אותם המפרקים המעורבים במחלה. קוסנטיקס משמשת לטיפול במבוגרים עם דלקת מפרקים ספחתית פעילה ויכולה להינתן לבד או עם תרופה אחרת הנקראת מתותרקסט. התועלת שתפיק מהשימוש בקוסנטיקס בדלקת מפרקים ספחתית תהיה הפחתת סימנים ותסמינים של המחלה, האטה בנזק לסחוס ולעצם שבמפרקים ותשפר את יכולתך בפעילויות יומיות רגילות.

**דלקת חוליות מקשחת**

קוסנטיקס הינה תרופה המשמשת לטיפול במבוגרים עם דלקת חוליות מקשחת פעילה. מחלה דלקתית שמשפיעה בעיקר על עמוד השדרה כיוון שהיא גורמת לדלקת במפרקי עמוד השדרה. אם יש לך דלקת חוליות מקשחת תקבל תחילה תרופות אחרות. אם לא תגיב מספיק טוב לתרופות אלו, תקבל קוסנטיקס כדי להפחית את הסימנים והתסמינים של המחלה, להפחתה בדלקת ולשיפור התיפקוד הגופני.

קוסנטיקס משמשת לטיפול במבוגרים עם דלקת חוליות מקשחת פעילה. התועלת שתפיק מהשימוש בקוסנטיקס לדלקת חוליות מקשחת תהיה הפחתה בסימנים ובתסמינים של המחלה שלך ושיפור בתיפקוד הגופני.

#### 2.לפני השימוש בתרופה

**⚠ אין להשתמש בתרופה אם:**

- אתה רגיש (אלרגי) לסקוקינומאב או לכל אחד מהמרכיבים הנוספים בקוסנטיקס (המופיעים בפרק 6). אם אתה חושב שאתה עלול להיות אלרגי, פנה לרופא לצורך ייעוץ לפני השימוש בקוסנטיקס. יש לך זיהום פעיל שלדעת הרופא שלך הינו משמעותי.

**⚠ אזרות מיוחדות הנוגעות לשימוש בתרופה:**

**⚠ לפני הטיפול בקוסנטיקס, ספר לרופא אם אחד המצבים שלהלן רלוונטי לגביך:**

- אם עכשיו יש לך זיהום.
- אם אתה סובל מזיהומים ממושכים או חוזרים.
- אם יש לך שחפת.
- אם אי פעם הייתה לך תגובה אלרגית ללטקס.
- אם יש לך מחלת קרוהן.
- אם יש לך דלקת כיבית של המעי הגס.
- אם קיבלת חיסון לאחרונה או אם אתה אמור לקבל חיסון במהלך הטיפול בקוסנטיקס.
- אם הינך מקבל טיפול אחר לפסוריאזיס, כמו מדכא מערכת חיסון (אימונוסופרסור) אחר או פוטותרפיה עם אור אולטרה-סגול (UV).

**⚠ שים לב לזיהומים ותגובות אלרגיות**

קוסנטיקס עלולה לגרום לתופעות לוואי חמורות, כולל זיהומים ותגובות אלרגיות. עליך לעקוב אחרי סימנים למצבים אלו אם אתה מטופל בקוסנטיקס.

הפסק הטיפול בקוסנטיקס וספר לרופא, או פנה לעזרה רפואית באופן מיידי אם אתה חווה אחד מן הסימנים שמצביעים על אפשרות לזיהום חמור או תגובה אלרגית. רשימת הסימנים מפורטת בסעיף "תופעות לוואי חמורות" בפרק 4.

**⚠ ילדים ומתבגרים**

קוסנטיקס אינה מיועדת עבור ילדים ומתבגרים (מתחת לגיל 18 שנים) מאחר שהתכשיר לא נחקר בקבוצת גיל זו.

**⚠ אינטראקציות/תגובות בין תרופתיות**

**⚠ אם אתה לוקח או אם לקחת לאחרונה, תרופות אחרות כולל תרופות ללא מרשם ותוספי תזונה, ספר על כך לרופא או לרוקח.**

- אם קיבלת חיסון לאחרונה או אם אתה מתכנן לקבל חיסון. עליך להימנע מקבלת תרכיבי חיסון מסוגים מסוימים (תרכיבי חיסון חיים) בעת שימוש בקוסנטיקס.

**⚠ היריון, הנקה ופוריות**

- עדיף להימנע משימוש בקוסנטיקס במהלך היריון. אין מידע לגבי השפעת התרופה בנשים בהיריון. אם הינך אשה בגיל הפוריות, מומלץ למנוע היריון על ידי שימוש באמצעים מתאימים למניעת היריון, זאת במהלך השימוש בקוסנטיקס, ולפחות במשך 20 שבועות אחרי המנה האחרונה של קוסנטיקס.
- ספרי לרופא שלך אם הינך בהיריון, אם הינך חושבת שאת בהיריון או שאת מתכננת להיות בהיריון.
- ספרי לרופא שלך אם הינך מיניקה או מתכננת להניק. את והרופא שלך תחליטו אם להניק או להשתמש בקוסנטיקס. אינך אמורה לעשות את שניהם. אחרי השימוש בקוסנטיקס אין להניק לפחות 20 שבועות אחרי המנה האחרונה של קוסנטיקס.

**⚠ הנגיה ושימוש במכונות**

קוסנטיקס אינה צפויה להשפיע על היכולת לנהוג או להשתמש במכונות.

### 3.כיצד תשתמש בתרופה?

יש להשתמש בקוסנטיקס תמיד בהתאם להוראות הרופא. עליך לבדוק עם הרופא, האחות או הרוקח אם אינך בטוח בנוגע למינון ואופן הטיפול בתכשיר. המינון ואופן הטיפול יקבעו על ידי הרופא בלבד. את קוסנטיקס יש להזריק מתחת לעור (הזרקה הקרויה תת-עורית). אתה והרופא שלך צריכים להחליט האם אתה אמור להזריק קוסנטיקס בעצמך.

חשוב שלא תנסה להזריק לעצמך עד שתזדרך על ידי הרופא שלך, האחות, או הרוקח. גם מטפל יכול להזריק לך קוסנטיקס אחרי הדרכה מתאימה.

להוראות מפורטות לגבי הזרקת קוסנטיקס, ראה "הוראות לשימוש בקוסנטיקס 150 מ"ג תמיסה להזרקה, בעט מוכן לשימוש, קוסנטיקס עט-סנסורדי" בסוף עלון זה.

**משך הטיפול**

הרופא יחליט לאיזו כמות של קוסנטיקס אתה זקוק ומהו משך הטיפול.

**ספחת רובידית**

- המנה המומלצת היא 300 מ"ג בהזרקה תת-עורית
- כל מנה של 300 מ"ג ניתנת כשתי זריקות תת-עוריות של 150 מ"ג**

לאחר המנה הראשונה אתה תקבל זריקות שבועיות נוספות בשבועות 1, 2, 3 ו-4 ובהמשך הזרקות אחת לחודש. בכל פעם תקבל מנה של 300 מ"ג שיתנתן בשתי הזרקות של 150 מ"ג כל אחת.

**דלקת מפרקים ספחתית**

לחולי דלקת מפרקים ספחתית אשר יש להם גם ספחת רובידית ברמה בינונית עד חמורה או חולים שלא הגיבו כראוי לתרופות הנקראות TNF blockers (tumour necrosis factor blockers):

- המנה המומלצת הינה 300 מ"ג בהזרקה תת-עורית
- כל מנה של 300 מ"ג ניתנת כשתי זריקות תת-עוריות של 150 מ"ג**

לאחר המנה הראשונה אתה תקבל זריקות שבועיות נוספות בשבועות 1, 2, 3 ו-4 ובהמשך הזרקות אחת לחודש. בכל פעם תקבל מנה של 300 מ"ג שיתנתן בשתי הזרקות של 150 מ"ג כל אחת.

**לחולי דלקת מפרקים ספחתית אחרים**

- המנה המומלצת הינה 150 מ"ג בהזרקה תת-עורית

לאחר המנה הראשונה אתה תקבל זריקות שבועיות נוספות בשבועות 1, 2, 3 ו-4 ובהמשך הזרקה אחת לחודש.

בהתבסס על התגובה שלך, הרופא שלך עשוי להגדיל את המנה ל- 300 מ"ג.

**דלקת חוליות מקשחת**

- המנה המומלצת הינה 150 מ"ג בהזרקה תת-עורית
- לאחר המנה הראשונה אתה תקבל זריקות שבועיות נוספות בשבועות 1, 2, 3 ו-4 ובהמשך הזרקה אחת לחודש.

זהו טיפול ארוך טווח. הרופא יעקוב אחר מצבך באופן סדיר על מנת להתבסס על התגובה שלך, הרופא שלך עשוי להגדיל את המנה.

**אין לעבור על המנה המומלצת.**

**אם השתמשת במינון גבוה מהנדרש של קוסנטיקס**

אם נטלת מנת יתר, או אם המנה ניתנה במועד מוקדם יותר מזה אשר נקבע על פי מרשם הרופא, או אם בטעות בלע ילד מן התרופה או הזריק לעצמו, יש לפנות מיד לרופא או לחדר מיון של בית חולים ולהביא את אריזת התרופה איתך.

**אם שכחת להזריק קוסנטיקס**

אם שכחת להזריק מנת קוסנטיקס בזמן המיועד, עליך להזריק את המנה הבאה מיד לאחר שתיזכר בכך. לאחר מכן עליך לשוחח עם הרופא על מנת לדון במועד ההזרקה של המנה הבאה.

יש להתמיד בטיפול כפי שהומלץ על ידי הרופא.

**אם תפסיק את השימוש בקוסנטיקס**

אין סכנה בהפסקת השימוש בקוסנטיקס. עם זאת, אם תפסיק, תסמיני ספחת, דלקת מפרקים ספחתית או דלקת חוליות מקשחת מהם סבלת עלולים לחזור.

**אין ליטול תרופות בחושך! בדוק התווית והמנה בכל פעם שהינך לוקח תרופה. הרכב משקפיים אם הינך זקוק להם.**

**אם יש לך שאלות נוספות בנוגע לשימוש בתרופה, היוועץ ברופא או ברוקח.**

### 4.תופעות לוואי

כמו בכל תרופה, השימוש בתרופה זו עלול לגרום לתופעות לוואי בחלק מהמשתמשים. אל תיבהל למקרא רשימת תופעות הלוואי. ייתכן שלא תסבול מאף אחת מהן.

**תופעות לוואי חמורות**

- עליך להפסיק את השימוש בקוסנטיקס ולדווח לרופא או לפנות לעזרה רפואית באופן מיידי** אם תסבול מאחת מבין תופעות הלוואי שלהלן:

- סימנים **לאפשרות של זיהום חמור** עשויים לכלול: חום, תסמינים דמויי שפעת, הזעות לילה.
- תחושת עייפות או קוצר נשימה, שיעול שאינו חולף.
- עור חם, אדום וכואב או פריחה כואבת בעור עם שלפוחיות.
- תחושת צריבה בעת מתן שתן.
- סימנים **לתגובה אלרגית חמורה** עשויים לכלול: קשיי נשימה או בליעה.
- לחץ דם נמוך, העלול לגרום לסחרחורת או לערפול חושים.
- נפיחות של הפנים, השפתיים, הלשון או הגרון.
- גרד חמור של העור, המלווה בפריחה אדומה או בנגעי עור מורמים.

הרופא שלך יחליט האם ומתי אתה יכול להתחיל מחדש את הטיפול.

**תופעות לוואי אחרות**

מרבית תופעות הלוואי המפורטות להלן הן קלות עד מתונות. אם תופעות לוואי אלו הופכות לחמורות, אנא פנה לרופא, לרוקח או לאחות.

**תופעות לוואי שכיחות מאוד** (תופעות שמופיעות ביותר ממשתמש 1 מתוך 10 משתמשים)

- זיהומים בדרכי הנשימה העליונות המלווים בתסמינים כגון כאב גרון וגודש באף (נאזופרינגיטיס, נזלת).

**תופעות לוואי שכיחות** (תופעות שמופיעות עד משתמש 1 מתוך 10 משתמשים)

- פצעי קור (פצעי הרפס באזור הפה)
- שלשול
- אף דולף (נזלת)

**תופעות לוואי לא שכיחות** (עשויות להופיע עד משתמש 1 מתוך 100 משתמשים)

- זיהום פטרייתי בפה (זיהום בקנדידה בפה)
- סימנים של רמות נמוכות של תאי הדם הלבנים, כגון חום, כאב גרון או כיבים בפה בשל זיהומים (נויטרופניה)
- פטרת כף הרגל
- זיהום באוזן החיצונית (אוזטיטי חיצוני)
- הפרשה מהעניים בליווי גרד, אודם ונפיחות (דלקת הלחמית)
- פריחה מלווה בגרד (סרפדת)
- זיהומים בדרכי הנשימה התחתונות
- התכווצויות וכאבים בבטן, שלשול, אובדן משקל או דם בצואה (סימנים לבעיות במעי)

**תופעות לוואי נדירות** (עשויות להופיע עד משתמש 1 מתוך 1,000 משתמשים)

- תגובה אלרגית חריפה עם שוק אנפילקטי
- אדמומיות וקילוף עור על פני אזור גדול בגוף, אשר עלולים להיות מגדירים או כואבים (exfoliative dermatitis)

**תופעות לוואי שכיחות לא ידועה** (תופעות שכיחותן טרם נקבעה)

- זיהום פטרייתי של העור והרריות (כולל קנדידה (סוג של פטריה) בוושט]

**אם הופיעה תופעת לוואי, אם אחת מתופעות הלוואי מחמירה או כאשר אתה סובל מתופעת לוואי שלא צוינה בעלון, עליך להתייעץ עם הרופא.**

**דיווח תופעות לוואי**

ניתן לדווח על תופעות לוואי למשרד הבריאות באמצעות לחיצה על הקישור "דיווח על תופעות לוואי עקב טיפול תרופתי" שנמצא בדף הבית של אתר משרד הבריאות (www.health.gov.il) המפנה לטופס המקוון לדיווח על תופעות לוואי, או על ידי כניסה לקישור: https://sideeffects.health.gov.il

### 5.אין לאחסן את התרופה?

- מנע הרעלה! תרופה זו וכל תרופה אחרת יש לשמור במקום סגור מחוץ להישג ידם וטווח ראייתם של ילדים ו\או תינוקות ועל ידי כך למנוע הרעלה. אין לגרום להקאה ללא הוראה מפורשת מרופא. אין להשתמש בתרופה אחרי תאריך התפוגה (exp. date) המופיע על גבי האריזה או על תווית העט המוכן לשימוש. תאריך התפוגה מתייחס ליום האחרון של החודש.
- אין להשתמש אם הנוזל מכיל חלקיקים שנראים בקלות, אם הוא עכור או אם צבעו חום כהור.

**תנאי אחסון:**

יש לאחסן קוסנטיקס בקופסה המקורית כדי להגן מפני אור. יש לאחסן במקרר בין 2°C ל- 8°C. אין להקפיא. אין לנער. אם נחוץ, ניתן לאחסן את קוסנטיקס מחוץ למקרר לתקופה אחת של עד 4 ימים בטמפרטורת החדר, אך לא מעל 30°C. קוסנטיקס מיועדת לשימוש חד פעמי בלבד.

אין להשליך תרופות לשפכים או לפסולת ביתית. התייעץ עם הרוקח כיצד יש להיפטר מתרופות שאינן בשימוש עוד. אמצעים אלו יסייעו לשמירה על הסביבה.

### 6.מידע נוסף

**נוסף על החומר הפעיל, התרופה מכילה גם:**

Water for injection, Trehalose dihydrate, L-histidine/L-histidine hydrochloride monohydrate, L-methionine and Polysorbate 80 low peroxide quality.

**כיצד נראית התרופה ומה תוכן האריזה:**

קוסנטיקס תמיסה להזרקה היא נוזל שקוף. צבעה עשוי להשתנות מחסר צבע עד צהבהב.

כל אריזה מכילה 1 או 2 עט-סנסורדי מוכנים לשימוש (ייתכן שלא כל גודלי האריזה משווקים).

**שם בעל הרישום וכתובתו:**
נוברטיס פארמה שטיין איי ג'י, שטיין, שוויץ

**שם היצרן וכתובתו:**
נוברטיס פארמה איי ג'י, בזל, שוויץ.

עלון זה נבדק ואושר על ידי משרד הבריאות בתאריך יוני 2019 ועודכן בהתאם להוראות משרד הבריאות בתאריך 10 באוקטובר 2019.

מס' רישום התרופה בפנקס התרופות הממלכתי במשרד הבריאות: 154-20-34342

לשם הפשטות ולהקלת הקריאה עלון זה נוסח בלשון זכר. על אף זאת, התרופה מיועדת לבני שני המינים.

**הוראות לשימוש בקוסנטיקס 150 מ"ג תמיסה להזרקה, בעט מוכן לשימוש, קוסנטיקס עט-סנסורדי.**

**קוסנטיקס 150 מ"ג עט-סנסורדי**

תמיסה להזרקה בעט מוכן לשימוש

**סקוקינומאב**

הוראות שימוש למטופל

**קרא את כל ההוראות במלואן לפני ההזרקה.**
הוראות אלו מיועדות לעזור לך בשימוש נכון בקוסנטיקס עט-סנסורדי.
חשוב שלא תנסה להזריק לעצמך עד אשר תקבל הדרכה מאת הרופא, האחות או הרוקח.

**עט קוסנטיקס סנסורדי שלך:**

יש לאחסן את העט שלך בקופסה **במקרר** בין 2°C ל- 8°C **והרחק מהישג ידם של ילדים.**

- אין **להקפיא** את העט.
- אין **לנער** את העט.
- אין להשתמש בעט אם העט **נפל** לאחר שהמכסה הוסר ממנו.

קוסנטיקס עט-סנסורדי' המוצג לאחר הסרת המכסה.
אין להסיר את המכסה עד אשר תהיה מוכן להזרקה.
כיסוי מחט פנימית

להזרקה נוחה יותר, יש להוציא את העט מהמקרר **15-30 דקות לפני ההזרקה** על מנת לאפשר לו להגיע לטמפרטורת החדר.

### למה אתה זקוק לצורך ההזרקה:

כלול בקופסה:
קוסנטיקס עט-סנסורדי חדש
(נדרשים שני עטים לצורך מנה של 300 מ"ג)
לא כלול בקופסה:
• מגבון אלכוהול
• כדור צמר גפן או גזה.
• מכל פסולת חדה.

להוציא את העט מהמקרר
להשתמש בתמיסה
אם היא מכילה חלקיקים הנראים לעין בקלות, עכורה או בעלת צבע חום.
ייתכן כי תראה בועת אוויר קטנה, זוהי תופעה נורמלית.

**אין להשתמש בעט לאחר תאריך התפוגה.**

**אין להשתמש בעט אם סגר הבטיחות פגום.**
פנה לרוקח אם העט אינו עובר את אחת הבדיקות הללו.

#### 1. בדיקת בטיחות חשובה לפני ההזרקה:

הנוזל חייב להיות שקוף. צבעו עשוי להשתנות מחסר צבע עד צהבהב.

**אין להשתמש בתמיסה** אם היא מכילה חלקיקים הנראים לעין בקלות, עכורה או בעלת צבע חום.

ייתכן כי תראה בועת אוויר קטנה, זוהי תופעה נורמלית.

**אין להשתמש בעט לאחר תאריך התפוגה.**

**אין להשתמש בעט אם סגר הבטיחות פגום.**
פנה לרוקח אם העט אינו עובר את אחת הבדיקות הללו.

#### 2. א. בחר את אזור ההזרקה:

- האזור המומלץ הוא קדמת הירכיים. כמו כן, אתה יכול להשתמש בבטן התחתונה, אך לא באזור הממוקם במרחק של 5 ס"מ סביב הטבור.

- יש לבחור במקום שונה בכל פעם שאתה מזריק לעצמך.

- אין להזריק לתוך אזורים בהם העור רגיש, חבול, אדום, מכוסה בקשקשים או קשה. יש להימנע מאזורים המכילים צלקות או סימני מתיחה.

### 2. ב. למטפלים ולאנשי צוות רפואי בלבד:

- אם מטפל או איש צוות רפואי מבצע את ההזרקה, הם יכולים גם להזריק לא



