Psoriasis Management with Stelara®

Stelara®
(ustekinumab)

Please read this booklet carefully as it contains important information about Stelara®

Contents

Stelara® for the treatment of psoriasis

Indication

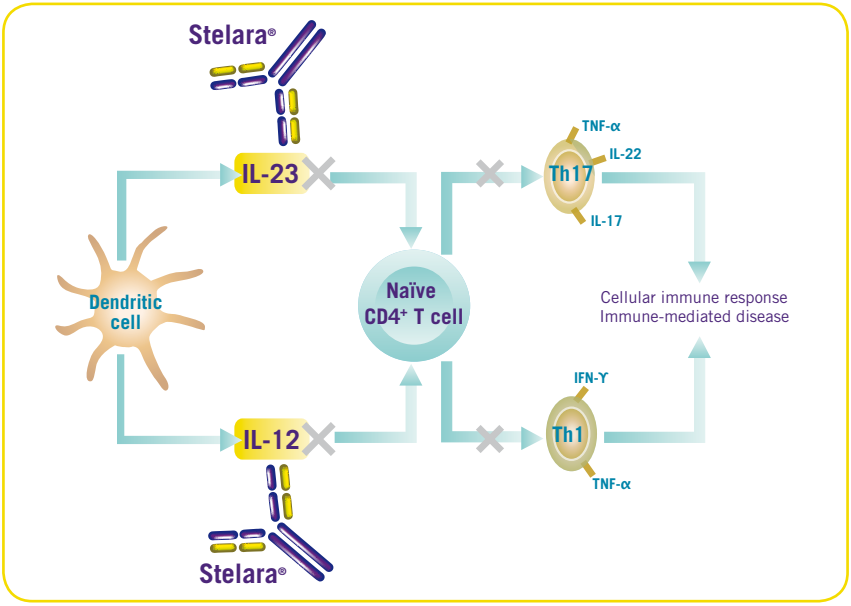
Stelara® is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA.[1]

Mechanism of action

The active substance of Stelara® is ustekinumab, a fully human IgG1κ monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit of the human cytokines IL-12 and IL-23.[1]

IL-12 and IL-23 are heterodimeric cytokines secreted by activated antigen-presenting cells, such as macrophages and dendritic cells. IL-12 and IL-23 participate in immune function by contributing to natural killer (NK) cell activation and $CD4^+$ T-cell differentiation and activation. However, abnormal regulation of IL-12 and IL-23 has been associated with immune-mediated diseases, such as psoriasis.[1]

Ustekinumab prevents IL-12 and IL-23 from binding to receptor proteins expressed on the surface of immune cells and thereby reduces immune cell activation. Thus, ustekinumab is believed to interrupt signalling and cytokine cascades that are relevant to psoriasis pathology.[1]

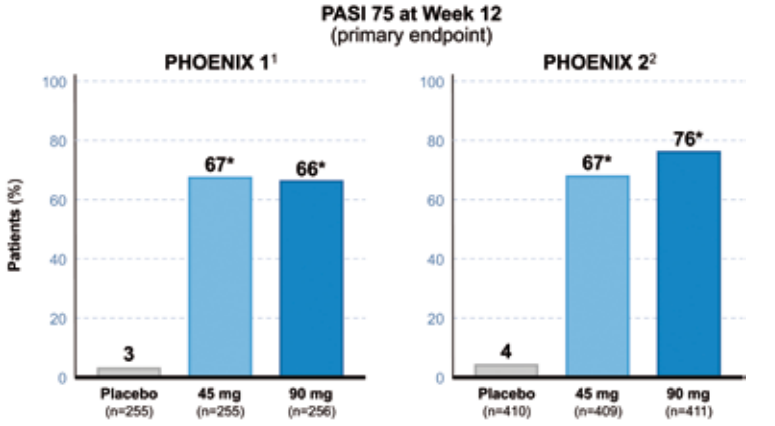


Schematic representation of the mode of action of Stelara®

Stelara® efficacy

Stelara® has been assessed in two randomised, double-blind, placebo controlled studies (PHOENIX 1 and PHOENIX 2) in 1996 patients with moderate-to-severe plaque psoriasis. Follow-up data up to 244 weeks are available. The primary endpoint in both studies was the proportion of patients who achieved PASI 75 response from baseline at Week 12 (after 2 injections).[2-4]

Patients receiving Stelara® showed significant improvement in skin symptoms (PASI 75 response) 12 weeks after initiating therapy.[2,3] The highest improvement in PASI scores was reached at Week 20 to Week 24.[2,3] Maintenance of PASI 75 response has been demonstrated in long-term follow-up of up to 5 years in patients following the every-12-week dosing schedule.[4]



*p<0.001 vs placebo for each dose comparison

Patients receiving Stelara® experience improved quality of life. In PHOENIX 1, at Week 2 and Week 12, significantly greater improvements from baseline were demonstrated in the Dermatology Life Quality Index (DLQI) in each Stelara® treatment group compared with placebo. The improvement was sustained through Week 28. Similarly, significant improvements were seen in PHOENIX 2 at Week 4 and 12, which were sustained through Week 24.[2,3]

In PHOENIX 1, improvements in nail psoriasis (Nail Psoriasis Severity Index), in the physical and mental component summary scores of the SF-36 and in the Itch Visual Analogue Scale (VAS) were also significant in each Stelara® treatment group compared with placebo. In PHOENIX 2, the Hospital Anxiety and Depression Scale (HADS) and Work Limitations Questionnaire (WLQ) were also significantly improved in each Stelara® treatment group compared with placebo.[1]

Stelara® has also been assessed in comparison with high-dose etanercept in a randomised clinical trial in 903 patients with moderate-to-severe plaque psoriasis (the ACCEPT study). The primary endpoint was the proportion of patients who achieved a PASI 75 response at Week 12 (after 2 injections of Stelara® 45 mg or 90 mg or twice weekly treatment with etanercept 50 mg).[5]

In ACCEPT, a PASI 75 response was reported at Week 12 in 67% of patients who received Stelara® 45 mg and 74% of those who received Stelara® 90 mg. In comparison, 57% of patients who received etanercept 50 mg reported a PASI 75 response ($p=0.01$ for Stelara® 45 mg and $p<0.001$ for Stelara® 90 mg vs etanercept).[5]

At Week 12, patients who did not respond to etanercept were crossed over to Stelara® treatment. Of these patients, 49% achieved a PASI 75 response after 12 weeks' treatment with Stelara® (2 injections).[5]

Patient eligibility

Special populations

Children and adolescents (<18 years)

Stelara® is not recommended for use in children and adolescents below the age of 18 due to a lack of data on safety and efficacy. [1]

Elderly patients (≥65 years)

No overall differences in efficacy or safety in patients aged 65 and older who received Stelara® were observed compared to younger patients. No dose adjustment is needed for elderly patients. Because there is a higher incidence of infections in the elderly population in general, caution should be used in treating the elderly. [1]

Renal and hepatic impairment

Stelara® has not been studied in these patient populations. No dose recommendations can be made. [1]

Contraindications

Stelara® should not be given to patients with a clinically important, active infection (e.g. active tuberculosis) or to patients with known hypersensitivity to the active substance (ustekinumab) or to any of the excipients.[1]

Special warnings and precautions for use

Infections

Stelara® may have the potential to increase the risk of infections and reactivate latent infections. In clinical studies, serious bacterial, fungal and viral infections have been observed in patients receiving Stelara®.[1]

Caution should be exercised when considering the use of Stelara® in patients with a chronic infection or a history of recurrent infection.[1]

Malignancy

Immunosuppressants like Stelara® have the potential to increase the risk of malignancy. Some patients who received Stelara® in clinical studies developed cutaneous and non-cutaneous malignancies. No studies have been conducted that include patients with a history of malignancy or that continue treatment in patients who develop malignancy while receiving Stelara®. Thus, caution should be exercised when considering the use of Stelara® in these patients.

Hypersensitivity reactions

Serious hypersensitivity reactions have been reported in the postmarketing setting, in some cases several days after treatment. Anaphylaxis and angioedema have occurred. If an anaphylactic or other serious hypersensitivity reaction occurs, administration of Stelara® should be discontinued immediately and appropriate therapy instituted.

Concomitant medications

No interaction studies have been performed with Stelara®. However, population pharmacokinetic analyses have shown no interaction with frequently used medicinal products in patients with psoriasis (including paracetamol, ibuprofen, acetylsalicylic acid, metformin, atorvastatin, levothyroxine).

The safety and efficacy of Stelara® in combination with other immunosuppressants, including biologics, or phototherapy have not been evaluated. Caution should be exercised when considering concomitant use of other immunosuppressants and Stelara® or when transitioning from other immunosuppressive biologics.[1]

Stelara® has not been evaluated in patients who have undergone allergy immunotherapy. It is not known whether Stelara® may affect allergy immunotherapy.[1]

Pregnancy and breastfeeding

There are no adequate data from the use of Stelara® in pregnant women. As a precautionary measure, it is preferable to avoid the use of Stelara® in pregnancy. Women of childbearing potential should use effective methods of contraception during treatment and up to 15 weeks after treatment.[1]

It is unknown whether Stelara® is excreted in human breast milk or if it is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from Stelara®, a decision on whether to discontinue breastfeeding during treatment and up to 15 weeks after treatment, or to discontinue therapy with Stelara®, must be made taking into account the benefit of breastfeeding to the child and the benefit of Stelara® therapy to the woman. [1]

Latex sensitivity

The needle cover on the syringe in the pre-filled syringe is manufactured from dry natural rubber (a derivative of latex), which may cause allergic reactions in individuals sensitive to latex.[1]

Before starting treatment with Stelara®

Guidelines for the use of biologics in the treatment of psoriasis suggest that patients should first undergo a full clinical history and physical examination.[6] Investigations should include screening for tuberculosis (see p.11),[7] salmonella, non-tuberculous mycobacteria and malignancies.

Tuberculosis

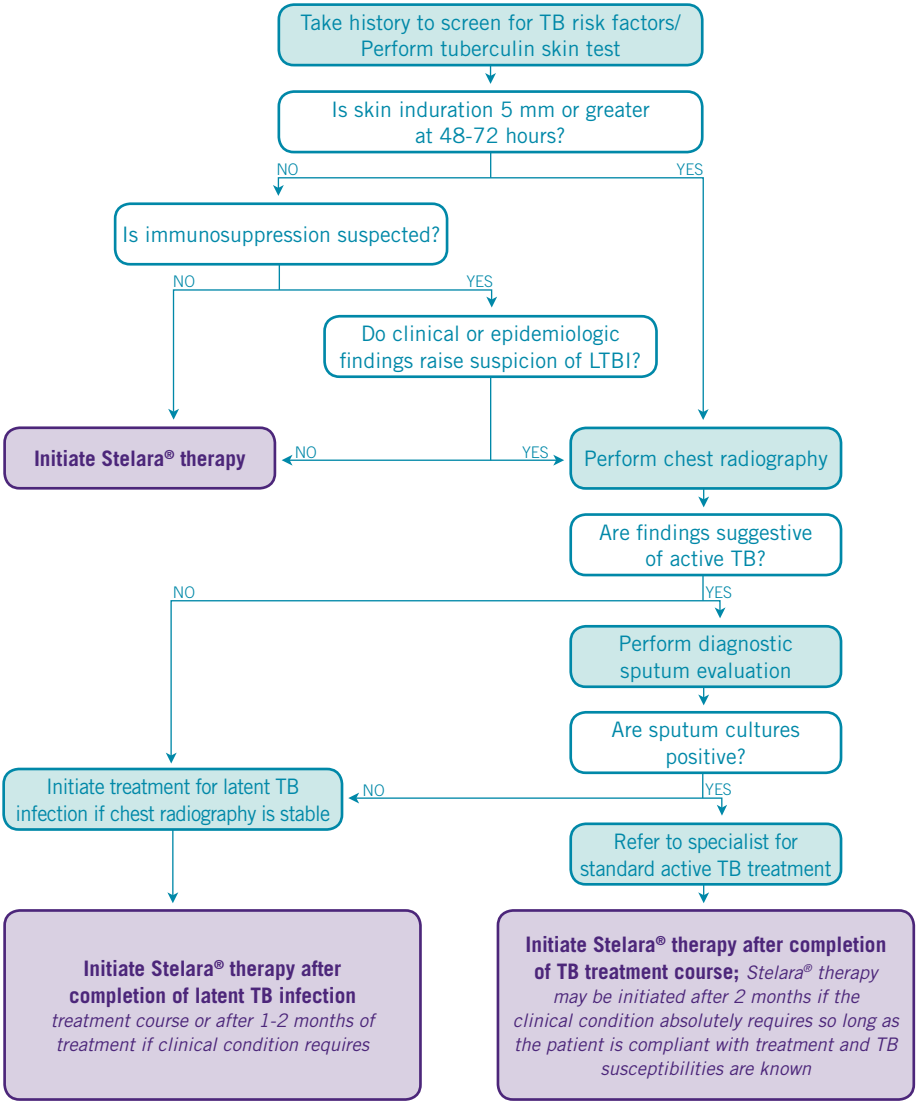
Stelara® may have the potential to increase the risk of infections and reactivate latent tuberculosis. Prior to initiating treatment with Stelara®, patients should be evaluated for tuberculosis (TB) infection.[1]

The TB screening procedure may be defined in local guidelines, or may follow other published advice, e.g. the National Psoriasis Foundation consensus statement on screening for latent tuberculosis infection in patients with psoriasis treated with systemic and biologic agents.[8]

Treatment of latent tuberculosis infection should be initiated prior to administering Stelara®. Anti-tuberculosis therapy should also be considered prior to initiation of Stelara® in patients with a history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed.[1]

Patients receiving Stelara® should be monitored closely for signs and symptoms of active tuberculosis during and after treatment. Stelara® must not be given to patients with active tuberculosis.[1]

A suggested screening protocol is shown. Local guidelines and practices should be followed where available.



Sample screening protocol for tuberculosis infection prior to initiation of Stelara® therapy (Adapted from Doherty SD, et al.[7]). Local guidelines and practices should be followed where available.

Treating your patient with Stelara®

Dosing and administration

The recommended posology of Stelara® is an initial dose of 45 mg administered subcutaneously, followed by a 45 mg dose 4 weeks later, then every 12 weeks thereafter.[1]

For patients with a body weight >100 kg the initial dose is 90 mg administered subcutaneously, followed by a 90 mg dose 4 weeks later, and then every 12 weeks thereafter. In these patients, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy.[1]

Consideration should be given to discontinuing treatment in patients who have shown no response up to 28 weeks of treatment.[1]

Stelara® is intended to be used under the guidance of a physician with experience in diagnosing and treating psoriasis. Patients may self-inject following adequate training in subcutaneous injection techniques if a physician determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients (see p. 16). Instructions for self-administration and correct handling of Stelara® can be found in the Patient Information leaflet.[1]

For patients who self-administer, and require the 90 mg dose of Stelara®, it is recommended that a single 90 mg syringe is prescribed for their convenience. However, if only 45 mg syringes are available, the patient should be advised to inject two of them, one immediately after the other.[1]

Training for self-administration is also available through the JCare programme (see p. 17).

Safety and tolerability

Long-term follow-up data from clinical studies show that after 5 years, Stelara® was generally well tolerated without evidence of cumulative toxicity with increased duration of exposure.[4]

Possible side-effects

The following side-effects were recorded in clinical studies of Stelara®:[1]

- In more than 1 in 10 patients – upper respiratory tract infection, nasopharyngitis

- In 1 to 10 per 100 patients – cellulitis, viral upper respiratory tract infection, depression, dizziness, headache, pharyngolaryngeal pain, nasal congestion, diarrhoea, pruritus, back pain, myalgia, arthralgia, fatigue, hypersensitivity reactions (including rash, urticaria), injection-site erythema
- In 1 to 10 per 1000 patients – herpes zoster, injection site reactions (including pain, swelling, pruritus, induration, haemorrhage, bruising and irritation)
- In 1 to 10 per 10,000 patients - serious hypersensitivity reactions including anaphylaxis and angioedema - symptoms of serious allergic reaction may include wheezing, dizziness and swelling of the face, lips, mouth or throat which may make it difficult to swallow or breathe. Serious allergic reactions have been reported in the postmarketing setting, in some cases several days after treatment. Facial palsy has also been reported with rare frequency.

Risk of serious infections includes salmonella, tuberculosis and other mycobacterial infections, and herpes zoster.

Infections

In the placebo-controlled period of the psoriasis clinical studies, rates of infection or serious infection were similar between Stelara®-treated patients and those treated with placebo:[1]

- Infection rates were 1.39 / patient year of follow up (PYFU) in Stelara®-treated patients and 1.21 / PYFU in placebo-treated patients
- Serious infection rates were 0.01 / PYFU in Stelara®-treated patients and 0.02 / PYFU in placebo-treated patients.

For Stelara®-treated patients in the controlled and non-controlled portions of the psoriasis clinical studies:[1]

- The rate of infection was 1.24 / PYFU
  - The rate of serious infection was 0.01 / PYFU
  - Serious infections reported included cellulitis, diverticulitis, osteomyelitis, viral infections, gastroenteritis, pneumonia and urinary tract infections.
  - Among 3117 patients treated in four psoriasis clinical trials of Stelara® representing 6791 patient-years of exposure (1129 patients treated for at least 3 years, and 619 patients for at least 4 years), the rates of infection or serious infection were similar to those described above.

In clinical studies, patients with latent tuberculosis who were concurrently treated with isoniazid did not develop tuberculosis.[1]

Patients should be instructed to seek medical advice if they notice signs or symptoms suggestive of an infection or an allergic reaction. If a patient develops a serious infection, the patient should be closely monitored and Stelara® should not be administered until the infection resolves.

Malignancies

In the placebo-controlled period of the psoriasis clinical studies:[1]

- The incidence of malignancies excluding non-melanoma skin cancer was 0.25 / 100 PYFU for Stelara®-treated patients compared with 0.57 / 100 PYFU for placebo-treated patients
- The incidence of non-melanoma skin cancer was 0.74 / 100 PYFU for Stelara®-treated patients compared to 1.13 / 100 PYFU for placebo treated patients.

Among 3117 patients treated in four psoriasis clinical trials of Stelara® (1129 patients treated for at least three years, and 619 patients for at least four years), malignancies excluding non-melanoma skin cancers were reported in 42 patients in 6779 patient-years of follow-up (incidence of 0.62 per 100 patient-years of follow-up for Stelara®-treated patients):[1]

- This rate of malignancies reported in Stelara®-treated patients was comparable to the rate expected in the general population (standardised incidence ratio = 1.1 [95% confidence interval: 0.76, 1.43])
- The most frequently observed malignancies, other than non-melanoma skin cancer, were prostate, colorectal and breast cancers, and melanoma *in situ*
- The incidence of non-melanoma skin cancer was 0.61 per 100 patient-years of follow-up for Stelara®-treated patients (41 patients in 6770 patient-years of follow-up).

Hypersensitivity reactions

In clinical studies of ustekinumab, rash and urticaria have each been observed in <2% of patients. If an anaphylactic or other serious allergic reaction occurs, administration of Stelara® should be discontinued immediately and appropriate therapy instituted. Patients who are trained to self-administer the drug should be informed that hypersensitivity reactions may occur. If such a reaction does take place they should immediately contact a physician.[1]

Immunogenicity

Approximately 5% of Stelara®-treated patients in clinical studies developed antibodies (generally low-titer) to ustekinumab, the active ingredient of Stelara®.[1]

- No apparent correlation of antibody development to injection-site reactions was seen.
- Efficacy tended to be lower in patients positive for antibodies to ustekinumab; however, antibody positivity does not preclude a clinical response.

Vaccination

Specific studies have not been conducted in patients who had recently received live viral or live bacterial vaccines. It is recommended that live viral or live bacterial vaccines (such as Bacillus of Calmette and Guérin (BCG)) should not be given concurrently with Stelara®. Before live viral or live bacterial vaccination, treatment with Stelara® should be withheld for at least 15 weeks after the last dose and can be resumed at least 2 weeks after vaccination. Prescribers should consult the SPC for the specific vaccine for additional information and guidance on concomitant use of immunosuppressive agents post-vaccination.[1]

Patients receiving Stelara® may receive concurrent inactivated or non-live vaccinations.[1] A sub-study of a Phase III clinical trial (PHOENIX 2) demonstrated no impact of Stelara® on vaccine response to pneumococcal antigen or tetanus toxoid.[8]

Discontinuation of treatment

If a patient has shown no response to Stelara® following up to 28 weeks of treatment, treatment discontinuation should be considered. No particular precautions are required in the case of discontinuation. Patients should be warned that the symptoms of psoriasis may return following discontinuation.[1]

Monitoring and long-term follow-up

Stelara® is a selective immunosuppressant and may have the potential to increase the risk of infections and malignancies as well as reactivate latent infections.[1]

- Prior to initiating treatment with Stelara®, patients should be evaluated for tuberculosis infection.[1]
- Periodic evaluation is recommended to monitor for potential risks associated with biologic therapies.[9,10]

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. Any patient developing a serious infection should be closely monitored and Stelara® should not be administered until the infection resolves.[1]

Cardiovascular disease and depression are known to be associated with psoriasis and should be included in routine patient monitoring.

Psoriasis360.com

For more information about psoriasis, please visit:

www.psoriasis360.com

Storage and handling

Stelara® is supplied as a sterile solution in a pre-filled syringe.

The syringe should be:

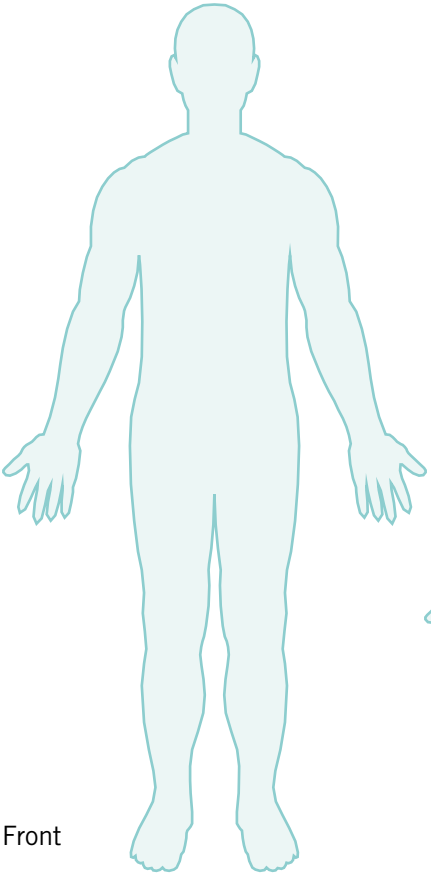
- Stored in a refrigerator at 2-8 °C and not frozen[1]
- Kept in its original outer packaging to protect it from light.[1]

Stelara® solution is clear to slightly opalescent, colourless to light yellow. Prior to use:

- It should not be shaken[1]
- It should not be used if the solution is discoloured or cloudy, or if foreign particulate matter is present.[1]

The syringe should be allowed to reach room temperature (approximately half an hour outside of the refrigerator) before administration.[1]

Anatomical outlines



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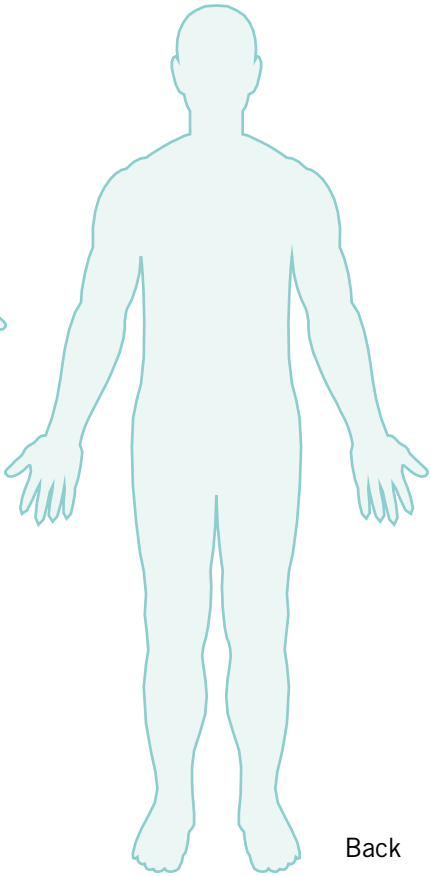

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References

1. Stelara® – European Summary of Product Characteristics. Date: June 2012.

2. Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). Lancet. 2008;371(9625):1665-74.

3. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). Lancet. 2008;371(9625):1675-84.

4. Kimball A, Papp K, Wasfi Y, et al. Long-term Efficacy and Safety of Ustekinumab in Patients With Moderate to Severe Psoriasis Through 5 Years of Follow-up: Results From the PHOENIX 1 Long-term Extension. Poster presented at 9th EADV Spring Symposium, Jun 6-10 2012, Verona. Poster PO582.

5. Griffiths CE, Strober BE, van de Kerkhof P, et al. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. N Engl J Med. 2010;362(2):118-28.

6. Smith CH, Anstey AV, Barker JN, et al. British Association of Dermatologists' guidelines for biologic interventions for psoriasis 2009. Br J Dermatol. 2009;161(5):987-1019.

7. Doherty SD, Van Voorhees A, Lebwohl MG, et al. National Psoriasis Foundation consensus statement on screening for latent tuberculosis infection in patients with psoriasis treated with systemic and biologic agents. J Am Acad Dermatol. 2008;59(2):209-17.

8. Brodmerkel C, Langley R, Papp K, et al. Long-term treatment with ustekinumab does not compromise the immune response to T-cell dependent or T-cell dependent vaccines in patients with moderate to severe psoriasis: a comparison of ustekinumab-treated versus untreated psoriasis patients. Presented at SID, Sep 9-12 2012, Raleigh NC, USA. Poster P545.

9. Lebwohl M, Bagel J, Gelfand JM, et al. From the Medical Board of the National Psoriasis Foundation: monitoring and vaccinations in patients treated with biologics for psoriasis. J Am Acad Dermatol. 2008;58(1):94-105.

10. Papp KA. Monitoring biologics for the treatment of psoriasis. Clin Dermatol. 2008;26(5):515-21.

Any Adverse Drug Reactions and Medication Errors should be reported to:

Medicines Authority Post-licensing Directorate
203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA
Telephone Number: +356 2343 9000

or at:

http://www.medicinesauthority.gov.mt/adrportal

or to:

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