HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

22 June 2011

STELARA 45 mg, solution for injection, 0.5 mL in vial
B/1 (CIP code: 392 586-2)

STELARA 45 mg, solution for injection, 0.5 mL in pre-filled syringe
B/1 (CIP code: 374 848-9)

STELARA 90 mg, solution for injection, 1 mL in pre-filled syringe
B/1 (CIP code: 374 849-5)

Applicant: JANSSEN-CILAG

Ustekinumab
ATC Code: L04AC05

List I
Initial six-month hospital prescription.
Initial prescription and renewal restricted to specialists in dermatology or internal medicine.

Date of Marketing Authorisation: 16 January 2009

Reason for request: Re-assessment of actual benefit in accordance with article R163-12 of the Social Security code following submission of new clinical data (long-term patient follow-up).

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Ustekinumab

1.2. 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 or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA."

1.3. Dosage

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

Posology

The recommended posology of STELARA is an initial dose of 45 mg administered subcutaneously at week 0, followed by a 45 mg dose four weeks later, and then every 12 weeks thereafter.

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

- *Patients with body weight > 100 kg*

For patients with a body weight > 100 kg` the dose is 90 mg administered subcutaneously at week 0, followed by a 90 mg dose four 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.

- *Elderly patients (≥ 65 years)*

No dose adjustment is needed for elderly patients.

- *Children and adolescents (< 18 years)*

  STELARA is not recommended for use in children and adolescents below age 18 due to a lack of data on tolerance and efficacy.

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- *Renal and hepatic impairment*

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

Method of administration

STELARA is for subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

After proper training in subcutaneous injection technique, patients may self-inject STELARA if a physician determines that it is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients should be instructed to inject the full amount of STELARA according to the directions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet."

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2011)

L	Antineoplastics and immunomodulating agents
L04	Immunosuppressants
L04A	Immunosuppressants
L04AC	Interleukin inhibitors
L04AC05	Ustekinumab

2.2. Medicines in the same therapeutic category

2.2.1. Strictly comparable medicines in the same therapeutic category

Not applicable

2.2.1. Not strictly comparable medicines in the same therapeutic category

These are other biological immunosuppressant therapies with an indication for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to or who have a contraindication or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA:

- ENBREL (etanercept), soluble TNF-alpha inhibitor,
- REMICADE (infliximab), chimeric anti-TNF alpha monoclonal antibody
- HUMIRA (adalimumab), human anti-TNF alpha monoclonal antibody

For these proprietary medicinal products, the actual benefit is substantial in patients with serious chronic refractory plaque psoriasis (patients who have failed to respond, or who have a contraindication or are intolerant) to at least two systemic therapies from phototherapy, methotrexate and ciclosporin.

2.3. Medicinal products with the same therapeutic aim

Local treatments:: keratolytics (including salicylic acid), high-potency dermatological corticosteroids, vitamin D analogues and vitamin A derivatives.

Systemic therapies: SORIATANE (acitretin), NEORAL and SANDIMMUN (ciclosporin), NOVATREX 2.5 mg tablets, METHOTREXATE BELLON, METOJECT (methotrexate)

Other therapies: UVA photochemotherapy (combined with photosensitizing agents), UVB phototherapy.

3 SUMMARY OF PREVIOUS TRANSPARENCY COMMITTEE OPINIONS

Transparency Committee opinion of 13 May 2009:
"Psoriasis is a chronic inflammatory dermatosis, usually benign, which can in moderate to severe forms have a major impact on quality of life.

This proprietary product suspends the symptoms.

Public health benefit:

Psoriasis constitutes a significant public health burden. It is moderate in the small population likely to benefit from treatment.
In view of the rare but serious situations of psoriasis for which no other systemic treatment is possible, and the cumulative toxicity of these systemic treatments which restricts their use, it can be concluded that an unmet therapeutic need exists which can be regarded as significant from the point of view of public health as a consequence of the severe condition of the patients who could benefit.

In the light of the trial data available (especially the increased short-term efficacy compared to ENBREL), STELARA can be expected to have a small impact on morbidity and quality of life. However, neither this proprietary product nor other biotherapies/anti-TNF therapies are likely to have any long-term impact because of:

- tolerance concerns, especially the risk of patients developing cancer,
- uncertainty as to the transposability of the results of studies carried out over relatively short periods with very little data in the small population of patients who have actually failed therapy.

Accordingly, in the current state of knowledge, STELARA is not expected to have an impact on public health, as it is also the case for the other biotherapies which are available.

The efficacy/adverse effects ratio is high.

This proprietary product is a fallback treatment in the case of patients suffering from severe plaque psoriasis in whom at least two other systemic treatments from among phototherapy, methotrexate and ciclosporin have failed, are contraindicated or are not tolerated.

There are alternative treatments (anti-TNFα).

The opinion's Committee is of the actual benefit provided by STELARA 45 mg solution for injection is **substantial** in adult patients suffering from serious chronic plaque psoriasis who have failed at least two systemic treatments, including phototherapy, methotrexate and ciclosporin (i.e. have not responded or cannot receive these treatments because of contraindication or intolerance).

The actual benefit for other patients who do not meet these criteria for receiving this treatment is **insufficient**."

4 ANALYSIS OF AVAILABLE DATA

4.1. Efficacy

The company submitted long-term data from the PHOENIX 1 and 2 and ACCEPT studies previously assessed by the Transparency Committee.

PHOENIX 1 study

Randomised double-blind study to assess the efficacy and tolerance of ustekinumab compared with placebo in patients with moderate to severe plaque psoriasis (see protocol details in the Opinion (in French) of 13 May 2009).

The study was divided into four phases:

- PHASE 1 (weeks 0-11): comparative, randomised, ustekinumab 45 mg (group 1) or ustekinumab 90 mg (group 2) compared with placebo (group 3). Injections at weeks 0 and 4.
- PHASE 2 (weeks 12-27): non-comparative, all patients received ustekinumab.
  Patients in the ustekinumab 45 mg or 90 mg groups (groups 1 and 2) continued treatment (injections at weeks 16 and 28).
  Patients in the placebo group (group 3) received injections of ustekinumab 45 mg or 90 mg at weeks 12, 16 and 28.
- PHASE 3 (weeks 28-39): continuation of treatment and adjustment of period between injections for patients with partial response (dosage regimen of injection every eight weeks not included in the Marketing Authorisation).
- PHASE 4 (weeks 40-264): long-term open phase. Patients in groups 1 and 2 were randomised to continue treatment or receive placebo. Patients in group 3 continued to receive placebo. Patients on placebo who relapsed during this phase were treated with ustekinumab again.

A total of 766 patients were randomised, 255 to the ustekinumab 45 mg group, 256 to the ustekinumab 90 mg group and 255 to the placebo group.

After the first 12 weeks of treatment, the proportion of patients with a PASI 75[1] response was higher in the ustekinumab 45 mg (67.1%) and ustekinumab 90 mg (66.4%) groups than in the placebo group (3.1%) ($p<0.001$).

At week 76, in patients who had stopped treatment with ustekinumab and who had been randomised to receive placebo (phase 4), median time to loss of PASI 75 response was 15 weeks. No rebound phenomena were observed.
In patients who had received ustekinumab continuously up to week 76 ($n = 77$ for ustekinumab 45 mg and $n = 82$ for ustekinumab 90 mg), the percentage of PASI 75 responses remained stable up to 76 weeks (see Table 1), as did the percentage of subjects with a PGA response (score 0 or 1).
About 15-20% of patients who had stopped ustekinumab at week 40 had a PASI 75 response at week 76.

[1] PASI (Psoriasis Area Severity Index): composite index assessing values for erythema, induration, scaling and body surface area involved. The index ranges from 0 (no psoriasis) to 72 (maximum severity). However, the score is only valid if the skin involvement covers at least 3% of body surface area with a combined assessment of erythema, induration and body surface area. A PASI 75 response shows a reduction of at least 75% from the initial PASI score. A PASI 100 response corresponds to complete remission.

New results:

In patients receiving ustekinumab at week 152 (n = 320 for ustekinumab 45 mg and n = 295 for ustekinumab 90 mg), the percentage of PASI 75 responses remained stable (see Table 1).
After three years, in the population of patients who had stopped ustekinumab at week 40, one patient in the ustekinumab 45 mg group and two patients in the ustekinumab 90 mg group had a PASI 75 response, while 3.1% had a PASI 50 response.

Table 1: Percentage of subjects with a PASI 75 response at weeks 76 and 152 (PHOENIX 1)

Number of patients:	**Ustekinumab 45 mg**	**Ustekinumab 90 mg**
randomised at week 0	382	384
assessed at week 76	286	251
subjects with a PASI 75 response at week 76, n (%)	**178 (62.2)**	**189 (75.3)**
assessed at week 152	320	295
subjects with a PASI 75 response at week 152, n (%)	**205 (64.1)**	**223 (75.6)**

PHOENIX 2 study

Randomised double-blind study to assess the efficacy and tolerance of ustekinumab compared with placebo in patients with moderate to severe plaque psoriasis (see protocol details in the Opinion (in French) of 13 May 2009).

The study was divided into four phases:

- PHASE 1 (weeks 0-11): comparative, randomised, ustekinumab 45 mg (group 1) or ustekinumab 90 mg (group 2) versus placebo (group 3). Injections at weeks 0 and 4.
- PHASE 2 (weeks 12-27): non-comparative, all patients received ustekinumab.
  Patients in the ustekinumab 45 mg or 90 mg groups (groups 1 and 2) continued treatment (injections at weeks 16 and 28).
  Patients in the placebo group (group 3) received injections of ustekinumab 45 mg or 90 mg at weeks 12, 16 and 28.
- PHASE 3 (weeks 28-51): continuation of treatment and adjustment of period between injections for patients with partial response (dosage regimen not included in the Marketing Authorisation).
- PHASE 4 (weeks 52-239): continuation of the different long-term treatments as an open study

A total of 1230 patients were randomised, 409 to the ustekinumab 45 mg group, 411 to the ustekinumab 90 mg group and 410 to the placebo group.

After the first 12 weeks of treatment (phase 1), the proportion of patients with a PASI 75 response was higher in the ustekinumab 45 mg (66.7%) and ustekinumab 90 mg (75.7%) groups than in the placebo group (3.7%) ($p<0.001$).

At week 52, the percentage of patients randomised at week 0 who had a PASI 75 response remained stable: 72.3% of patients had a PASI 75 response with ustekinumab 45 mg and 80.0% with ustekinumab 90 mg.

New results:

The percentage of patients randomised at week 0 who had a PASI 75 response remained stable up to week 100 with 75.9% of patients having a PASI 75 response with ustekinumab 45 mg and 79.9% with ustekinumab 90 mg.

ACCEPT study
Randomised, single-blind (investigator) study, with the primary objective of comparing the efficacy and tolerance of ustekinumab to those of etanercept in patients with moderate to severe plaque psoriasis.

The study was divided into three phases:

PHASE I (weeks 0-11): comparative, single-blind (investigator), randomised, ustekinumab 45 mg (group 1) or ustekinumab 90 mg (group 2) versus etanercept (group 3).

PHASE 2 (weeks 12-39): non-comparative, discontinuation of treatment at week 12 in responder patients and extension or change of treatment in patients who failed to respond.

- Patients who had failed to respond (PGA[2] ≥ 3) at week 12 continued their treatment (group 1 and 2) or changed treatment (group 3) to receive ustekinumab 90 mg at weeks 16, 20 and 32.
- Patients who had responded (PGA ≤ 2) stopped treatment until recurrence (PGA ≥ 3). In this case, patients restarted treatment with ustekinumab (two subcutaneous injections four weeks apart, then every 12 weeks thereafter):
  - group 1: ustekinumab 45 mg
  - group 2: ustekinumab 90 mg
  - group 3: ustekinumab 90 mg

PHASE 3 (weeks 40-63): continuation of long-term treatment.

A total of 903 patients were randomised, 209 to the ustekinumab 45 mg group, 347 to the ustekinumab 90 mg group and 347 to the etanercept group.

After 12 weeks of treatment (phase 1), the proportion of patients with a PASI 75 response was higher in the ustekinumab 45 mg and ustekinumab 90 mg groups than in the etanercept group (see Table 3).

In patients with a response who discontinued treatment at the end of the initial 12-week treatment period (i.e. two injections of ustekinumab at weeks 0 and 4), the percentage of patients who maintained a PGA score of 0 or 1 up to week 24 was higher in the ustekinumab 45 and 90 mg groups than in the etanercept group (see Table 4).

[2] The PGA (physician's global assessment) score represents a global evaluation by the physician of disease severity, with six levels of severity. It provides information on the global evaluation of psoriasis at a given point in time; lesions are classified according to induration, extent and erythema. The higher the score is, the more severe the psoriasis is considered to be.
The PGA severity levels are:

0 = clear	3 = moderate
1 = minimal	4 = marked
2 = mild	5 = severe.

Table 3: Results: percentage of patients with a PASI 75 response after 12 weeks of treatment (ACCEPT)

Patients with a PASI 75 response at week 12	**Ustekinumab 45 mg N = 209**	**Ustekinumab 90 mg N = 347**	**Etanercept 50 mg N = 347**
Mean (%)	67.5	73.8	56.8
95% CI for difference between ustekinumab and etanercept	[2.4; 19.0]	[10.0; 24.0]	-
p	0.012	<0.001	-

Table 4: Percentage of patients with a PGA response at weeks 16, 20 and 24

	Ustekinumab 45 mg	**Ustekinumab 90 mg**	**Etanercept 50 mg**
Number of randomised patients with a PGA response at week 12	179	315	281
% of patients with a PGA response at week 16 (95% CI)	89.3 [84.8; 93.9]	92.6 [89.7; 95.5]	71.9 [66.7; 77.2]
% of patients with a PGA response at week 20 (95% CI)	79.2 [73.2; 85.2]	82.6 [78.4; 86.8]	45.5 [39.6; 51.4]
% of patients with a PGA response at week 24 (95% CI)	59.9 [52.7; 67.1]	71.6 [66.6; 76.6]	36.7 [31.0; 42.4]

New results:

In patients with a response at week 12 who discontinued treatment, the median duration of PGA response (PGA ≤ 2 at discontinuation up to recurrence with PGA ≥ 3) evaluated at week 63 was 14.4 weeks in the ustekinumab 45 mg group, 18.1 weeks in the ustekinumab 90 mg group and 7.3 weeks in the etanercept group.

The number of randomised patients with a PGA score of 0 or 1 after week 12 was 136 in the ustekinumab 45 mg group, 245 in the 90 mg group and 170 in the etanercept group.
Fifty percent (50%) of patients maintained a PGA score of 0 or 1 for 16.5 weeks in the ustekinumab 45 mg group, for 20.4 weeks in the ustekinumab 90 mg group and for 12.5 weeks in the etanercept group.

4.2. Adverse effects

Data from clinical studies

- PHOENIX 1 and PHOENIX 2 studies: long-term results

In the PHOENIX 1 study, the most common adverse events for all ustekinumab 45 and 90 mg groups over the three years of the study (noncomparative phases), were nasopharyngitis (29.9%), upper respiratory tract infection (27.4%) and to a lesser extent, joint pain (12.0%), sinusitis (11.3%), back pain (10.8%) and headache (10.1%).
2.3% of patients had at least one serious adverse event potentially related to treatment, mainly infection (seven cases), prostate cancer (three cases) and other benign, malignant or unspecified tumour (four cases).

In the PHOENIX 2 study, the most common adverse events for all ustekinumab 45 and 90 mg groups over the three years of the study were nasopharyngitis (29.8%), upper respiratory tract infection (21.9%) and to a lesser extent headache (9.8%), influenza (8.4%), back pain (8.2%) and joint pain (8.0%).

2.6% of patients had at least one serious adverse event potentially related to treatment, mainly infection or infestation (nine cases), heart disorder (six cases), benign, malignant or unspecified tumour (six cases) and gastrointestinal disorder (four cases).

These adverse events are similar to those observed during the first phases of the trials up to week 76.

Specific adverse events:

- Serious infection

In the PHOENIX 1 study, 15 patients had a serious infection, eight during the first 76 weeks of the study and seven between week 76 and the third year.
In the PHOENIX 2 study, twenty patients had at least one serious infection during the first hundred weeks of the study. Six cases were reported between weeks 52 and 100.
Administration of ustekinumab was not associated with any particular profile of infection. No cases of active tuberculosis or opportunistic infection occurred during the extension phases.

- Immunogenicity

The percentage of patients who developed antibodies against ustekinumab was unchanged during the trial extension phases (about 5%, generally at a low concentration).

- Malignant tumours

In the PHOENIX 1 study, during the three-year treatment period malignant tumours were reported in eighteen patients, eleven during the first 76 weeks, including five cases of non-melanoma skin cancer, and seven new cases between week 76 and the third year, four of which were non-melanoma skin cancers (three basal cell carcinomas and one squamous cell carcinoma). The other three cases that occurred between week 76 and the third year were cases of prostate cancer.
In the PHOENIX 2 study, up to week 100, 30 cases of malignant tumours were observed in 25 patients, 11 patients during the first 52 weeks and 14 between week 52 and week 100. During this period, 16 cases of non-melanoma skin cancer were reported in 13 patients treated with ustekinumab and one patient on placebo. Thirteen (13) solid tumours were reported in 12 patients treated with ustekinumab and one patient on placebo. No cases of lymphoma were reported.

- ACCEPT study

In the etanercept group (n = 347) the mean number of injections was 23.2. Of these 347 patients, 295 (85%) were exposed to a mean of two injections of ustekinumab 90 mg. In the ustekinumab 45 and 90 mg groups, the mean number of injections was 3.5.

In the patients treated with ustekinumab:
During the 64 weeks of the study (noncomparative phases), tolerance was assessed in 209 patients in the 45 mg group and 347 patients in the 90 mg group.
There was no difference between the 45 mg and 90 mg groups for onset of adverse events.
The most common adverse events under ustekinumab 45 and 90 mg were nasopharyngitis (24.1%), upper respiratory tract infection (19.4%), headache (16.2%) and back pain (9.5%).

Most of these events were mild to moderate. Serious adverse events possibly related to treatment were infection and infestation.
Malignant tumours were reported at similar rates for both the 45 and 90 mg doses (4/209, 1.9% and 8/347, 2.3%). Four cases of malignant tumour were reported apart from the cases of non-melanoma skin cancer, including one breast cancer, one oral cavity tumour, one case of chronic lymphocytic leukaemia and one of mycosis fungoides (diagnosed in error as psoriasis). There were eight cases of non-melanoma skin cancer: six of basal cell carcinoma, one of squamous cell carcinoma and one of basal cell carcinoma, combined with squamous cell carcinoma.

In the patients treated with etanercept:
The percentage of patients who reported adverse events in the etanercept group before change of treatment was 79.3% versus 64.7% after starting treatment with ustekinumab 90 mg. In both cases, the most common adverse events were infection and infestation (40.6% and 37.6% respectively). The most significant differences before and after change of treatment concerned general disorders and disorders at the injection site (30.8% compared with 4.4%), nervous system disorders (17.0% compared with 8.1%), gastrointestinal disorders (16.7% compared with 6.8%) and skin and subcutaneous tissue disorders.
In the etanercept group 3.2% of patients had at least one serious adverse event before change of treatment, and 4.4% afterwards.
Two patients out of 347 (0.6%) reported malignant tumours (prostate cancer and basal cell carcinoma) after change of treatment.

4.3. Conclusion

Ustekinumab has been compared with placebo in two randomised double-blind studies (PHOENIX 1 and 2) in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy (either treatment-naive, so not in compliance with the Marketing Authorisation, or with a history of previous treatment not in compliance with the Marketing Authorisation unless they had failed treatment, had a contraindication or were intolerant to other systemic therapies including ciclosporin, methotrexate or PUVA). Ustekinumab was administered by subcutaneous (SC) injection at the 45 mg or 90 mg dose at four week intervals, then every 12 weeks thereafter.
In the PHOENIX 1 study, after 12 weeks, ustekinumab was superior to placebo in terms of percentage of patients who had improved their initial PASI score by at least 75% (PASI 75), i.e. 67.1% on ustekinumab 45 mg, 66.4% on ustekinumab 90 mg versus 3.1% on placebo ($p<0.001$). The efficacy of ustekinumab was maintained up to week 152 with 64.1% of patients achieving a PASI 75 response with the 45 mg dose and 75.6% with the 90 mg dose. The trial was to be continued up to 264 weeks.
In the PHOENIX 2 study, ustekinumab was superior to placebo after 12 weeks in terms of percentage of patients with a PASI 75 response, i.e. 66.7% on ustekinumab 45 mg, 75.7% on ustekinumab 90 mg compared with 3.7% on placebo ($p<0.001$). The efficacy of ustekinumab was maintained in the long term up to week 100 with 75.9% of patients achieving a PASI 75 response on the 45 mg dose and 79.9% on the 90 mg dose. The study was to be continued up to 239 weeks.

In a single-blind randomised study (ACCEPT), ustekinumab 45 or 90 mg in two SC injections, at 0 and then at 4 weeks, repeated at week 16 in patients without a response, was compared with etanercept 50 mg administered as two SC injections a week in a population of patients who were similar to those in the PHOENIX 1 and 2 trials. After 12 weeks, ustekinumab was superior to etanercept in terms of percentage of patients achieving a PASI 75 response, i.e. 67.5% on ustekinumab 45 mg ($p = 0.012$), and 73.8% on ustekinumab 90 mg compared with 56.8% on etanercept ($p < 0.001$). Similarly, ustekinumab was superior to etanercept for percentage of patients with a PGA response (score of 0 or 1), i.e. 65.1% on ustekinumab 45 mg, 70.6% on ustekinumab 90 mg and 49.0% on etanercept ($p < 0.001$). After discontinuation of treatment at week 12, efficacy was maintained up to week 24 (59.9%

on ustekinumab 45 mg, 71.6% on ustekinumab 90 mg and 36.7% on etanercept). At week 64, patients had maintained a PGA score of 0 or 1 in 50% of cases for 16.5 weeks in the ustekinumab 45 mg group, 20.4 weeks in the ustekinumab 90 mg group and 12.5 weeks in the etanercept group.

In all three studies, the long-term tolerance profile of ustekinumab did not differ from that in the initial phases of these studies.
In the PHOENIX studies after three years' follow-up, adverse events were similar to those observed during the first phases of the studies up to week 76, particularly serious infection (n=35) with no cases of active tuberculosis or opportunistic infection. The percentage of patients who developed antibodies against ustekinumab remained at about 5%.

In the PHOENIX 1 study, during the three years of treatment, 18 patients had a malignant tumour (11 during the first 76 weeks and seven between week 76 and the third year). In the PHOENIX 2 study, during the 100-week treatment period, 25 patients had 30 malignant tumours (11 patients during the first 52 weeks and 14 between week 52 and week 100).

In the ACCEPT study, apart from infection, four cases of malignant tumour (same frequency as in the general population) and eight cases of non-melanoma skin cancer were reported.

5 TRANSPARENCY COMMITTEE CONCLUSIONS

5.1. Actual benefit

The Committee notes the new data, which are not likely to change the actual benefit of STELARA as assessed by the Committee in its Opinion of 13 May 2009:
“The opinion’s Committee is of the actual benefit provided by STELARA 45 mg solution for injection is substantial in adult patients suffering from serious chronic plaque psoriasis who have failed at least two systemic treatments, including phototherapy, methotrexate and ciclosporin (i.e. have not responded or cannot receive these treatments because of contraindication or intolerance).

The actual benefit for other patients who do not meet these criteria for receiving this treatment is insufficient“.

5.2. Therapeutic use

5.2.1. Treatment strategy

Current treatments of psoriasis do not produce a definitive cure for the disorder, but result in the temporary disappearance of the lesions to a greater or lesser extent. The therapeutic arsenal comprises local and general treatments. Local treatments can be used alone or in combination with other local treatments or general treatments.

Cutaneous hydration by means of emollients is often associated with topical treatments, which are the first-line treatment for limited psoriasis.
Several types of topical treatments exist: dermocorticosteroids, vitamin D3 analogues, retinoids (vitamin A derivatives) and, used to a lesser extent, tars, anthralin and keratolytics.

Systemic treatments are administered for severe forms of psoriasis. These are phototherapy, retinoids (sometimes administered in combination with phototherapy), methotrexate, ciclosporin and biological agents (etanercept, infliximab, adalimumab).

Patients generally respond well to phototherapy (UVA or PUVA and narrow-spectrum UVB), but the conditions under which this treatment is given (frequency of sessions, equipment needed) and the cumulative toxicity of this technique, especially in the case of PUVA, impose restrictions on access to this form of treatment and its long-term use (risk of skin cancer).

Experts believe that methotrexate is still the benchmark treatment for extensive or severe forms of psoriasis despite its severe hepatic adverse effects.
Retinoids alone are less effective, but they have a stronger synergic efficacy when administered in combination with phototherapy. This combination is used particularly in diffuse forms of psoriasis.

Biotherapies (etanercept, infliximab, adalimumab) must be reserved for severe forms of plaque psoriasis when at least two systemic treatments from among ciclosporin, methotrexate and PUVA therapy have failed, are contraindicated or are not tolerated.

The current treatment strategy is to rotate patients between the various alternatives, with the choice of treatment being based on the patient's characteristics and the features of his or her pathology (concomitant pathology, extent of lesions, treatment history) and of the proprietary product (adverse effects, cumulative dose).

5.2.2. Role of the proprietary medicinal product in the treatment strategy

Like other biotherapies indicated for use in psoriasis, STELARA 45 mg is a fallback treatment for adult patients suffering from chronic severe plaque psoriasis who have failed at least two systemic treatments from among phototherapy, methotrexate and ciclosporin (i.e. they have not responded to or tolerated these treatments, or the treatments are contraindicated).

Consideration should be given to discontinue the treatment in patients who have not responded after 28 weeks of treatment.

5.3. Transparency Committee recommendations

Maintenance of previous Opinion:

The transparency Committee recommends maintaining inclusion on the list of medicines refundable by National Insurance and on the list of medicines approved for use by hospitals only in adults with severe chronic plaque psoriasis who have failed to respond to or who have a contraindication or are intolerant to other systemic therapies including phototherapy, methotrexate and ciclosporin.

and:

The transparency Committee recommends not maintaining inclusion on the list of medicines refundable by National Insurance and on the list of medicines approved for use by hospitals for other patients who do not satisfy these criteria for starting treatment.

The Committee remains concerned by the long-term tolerance of STELARA (In particular the risks of cancer and infection) and would like to reassess the actual benefit of STELARA in the light of the results of the post-listing study requested by the Committee in its opinion of 13 May 2009.

Packaging: Appropriate for the prescription conditions.

Reimbursement level: 65%