HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

1 April 2009

ENBREL 25 mg, solution for injection in pre-filled syringe
Box of four pre-filled 0.5 ml syringes with needles and alcohol swabs (CIP: 377 191-0)

ENBREL 50 mg, solution for injection in pre-filled syringe
Box of four pre-filled 1 ml syringes with needles and alcohol swabs (CIP: 377 195-6)

ENBREL 25 mg/ml, powder and solvent for solution for injection for paediatric use
Box of four 4 ml vials and four pre-filled syringes, with 8 syringes, 20 needles and 24 alcohol swabs (CIP: 376 841-1)

ENBREL 25 mg, powder and solvent for solution for injection
Box of four vials and four pre-filled 1 ml syringes with four needles, four vial adapters and eight alcohol swabs (CIP: 360 649-9)

ENBREL 50 mg, powder and solvent for solution for injection
Box of four vials and four pre-filled 1 ml syringes with four needles, four vial adapters and eight alcohol swabs (CIP: 365 862-2)

Applicant: WYETH PHARMACEUTICALS FRANCE

etanercept
ATC code: L04AB01

List I
Medicine requiring initial annual hospital prescription. Initial prescription and renewal restricted to specialists in rheumatology, internal medicine, paediatrics or dermatology.
Exception drug status.

Date of Marketing Authorisation:
EBNREL 25 mg and 50 mg, solutions for injection in pre-filled syringe: 26 September 2006
ENBREL 25 mg/ml, powder and solvent for solution for injection for paediatric use: 4 August 2006
ENBREL 25 mg, powder and solvent for solution for injection: 16 September 2002
ENBREL 50 mg, powder and solvent for solution for injection: 28 April 2005
Most recently corrected on: 22 December 2008 (extension of indication to include children with psoriasis)

Reason for request: Inclusion on the list of medicines reimbursed by National Health Insurance and approved for hospital use in the extension of indication “Treatment of severe chronic plaque psoriasis in children aged eight and over and adolescents where other systemic treatments or phototherapy are insufficiently effective or are not tolerated.”

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Etanercept

1.2. Novel aspects

ENBREL is the first anti-TNFα to be indicated for treatment of plaque psoriasis in children.

1.3. Indication

Rheumatoid arthritis

- "ENBREL in combination with methotrexate is indicated for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated) has been inadequate.
- ENBREL may be given as monotherapy in cases of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.
- ENBREL is also indicated in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.
- ENBREL, alone or in combination with methotrexate, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function."

Polyarticular juvenile idiopathic arthritis

- "Treatment of active polyarticular juvenile idiopathic arthritis in children and adolescents from the ages of 4 to 17 who have had an inadequate response to, or who have proved intolerant of, methotrexate. ENBREL has not been studied in children aged less than 4 years."

Psoriatic arthritis

- "Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic drug therapy has been inadequate. ENBREL has been shown to improve physical function in patients with psoriatic arthritis, and to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease."

Ankylosing spondylitis

- "Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

Plaque psoriasis

- Treatment of adults with moderate to severe plaque psoriasis who failed to respond to, or who have a contraindication to, or are intolerant to other systemic treatments, including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA)."

Paediatric plaque psoriasis

- **"Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 8 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies."**

1.4. Dosage

ENBREL treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis or paediatric plaque psoriasis. Patients treated with ENBREL should be given the Patient Alert Card.
ENBREL is available in strengths of 25 mg and 50 mg.

• Adults (aged 18-64)

Rheumatoid arthritis

25 mg ENBREL administered twice weekly is the recommended dose. Alternatively, 50 mg administered once weekly has been shown to be safe and effective.

Psoriatic arthritis and ankylosing spondylitis

The recommended dose is 25 mg ENBREL administered twice weekly, or 50 mg administered once weekly.

Plaque psoriasis

The recommended dose of ENBREL is 25 mg administered twice weekly or 50 mg administered once weekly. Alternatively, 50 mg given twice weekly may be used for up to 12 weeks followed, if necessary, by a dose of 25 mg twice weekly or 50 mg once weekly. Treatment with ENBREL should continue until remission is achieved, for up to 24 weeks. Treatment with ENBREL should be discontinued in patients who show no response after 12 weeks of treatment.
If re-treatment with ENBREL is indicated, the same guidance on treatment duration should be followed. The dose should be 25 mg administered twice weekly or 50 mg once weekly.

• Children and adolescents

Juvenile idiopathic arthritis (age 4 years and above)

0.4 mg/kg (up to a maximum of 25 mg per injection given twice weekly as a subcutaneous injection with an interval of 3 to 4 days between injections

Paediatric plaque psoriasis (age 8 years and above)

0.8 mg/kg (up to a maximum of 50 mg per dose) once weekly for up to 24 weeks. Treatment with ENBREL should be discontinued in patients who show no response after 12 weeks of treatment.
If re-treatment with ENBREL is indicated, the same guidance on treatment duration should be followed. The dose should be 0.8 mg/kg (up to a maximum of 50 mg per injection **once weekly.**

• Elderly (≥ 65 years)

No dose adjustment is required. Posology and administration are the same as for adults 18 to 64 years of age.

• Renal and hepatic impairment

No dose adjustment is required.

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2008)

L: Antineoplastic and immunomodulating agents
L04: Immunosuppressants
L04 A: Immunosuppressants
L04 AB: Tumor Necrosis Factor alpha (TNF-α) inhibitors
L04 AB01: etanercept

2.2. Medicines in the same therapeutic category

ENBREL is the only anti-TNFα indicated in children and adolescents for the treatment of psoriasis where other systemic treatments or phototherapy are insufficiently effective or are not tolerated.

2.3. Medicines with a similar therapeutic aim

Local treatments: keratolytics (including salicylic acid), powerful dermocorticoids, vitamin D analogues and vitamin A derivatives.

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

Other treatments: UVA photochemotherapy (in combination with photosensitising agents), UVB phototherapy.

3 ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

The company submitted one efficacy study (study 20030211) versus placebo, the aim of which was to assess the efficacy and safety of etanercept in 211 children and adolescents aged 4 to 17 suffering from moderate to severe plaque psoriasis.

Inclusion criteria:

- Patients aged 4 to 17 suffering from moderate to severe plaque psoriasis, defined as having:
  - a PASI[1] ≥ 12,
  - a psoriasis global assessment score assessed by the dermatologist (PGA[2]) ≥ 3
  - proportion of body area affected ≥ 10%,

[1] PASI ("Psoriasis Area Severity Index"): composite index taking account of values relating to erythema, induration, desquamation and the amount of body surface area affected. It ranges from 0 (no psoriasis) to 72 (maximum severity). However, this score, which is a combination measurement of erythema, induration and area, is valid only if at least 3% of the body surface area is affected. A PASI response of 75 indicates a reduction of at least 75% compared to the baseline PASI score. A PASI response of 100 indicates complete remission.

[2] PGA ("Physician Global Assessment"): overall assessment by the doctor measured on a scale of 0 (no lesions) to 5 (severe erythema, infiltration and flaking).

- Patients whose psoriasis has been progressing for at least 6 months, and who have already undergone or are undergoing treatment involving phototherapy or systemic treatment of psoriasis (methotrexate, ciclosporin or retinoid), or whose psoriasis is in the opinion of their dermatologist not adequately controlled by topical treatment (relatively strong dermocorticoid or vitamin D3 analogue) which has been administered for at least 6 weeks.

Non-inclusion criteria:
- Guttate, erythrodermic or pustular psoriasis
- Another skin condition that might interfere with the assessment
- Patients who have already been treated with anti-TNFα
- Another severe concomitant disease

Prior treatments:
A therapy window of 14 days was required after treatment with PUVA, UVB phototherapy, systemic treatment of psoriasis, oral or topical corticotherapy, topical treatment with vitamin A or vitamin D analogues, anthranol or calcineurin inhibitors.
A therapy window of 30 days was required after biotherapy.

Concomitant treatments:
Patients were permitted to apply weak or moderately strong (level II or III) dermocorticoids to the scalp, armpits or the folds of the groin.

Study design:
This study was divided into three stages:

Stage 1: randomised, double-blind, etanercept versus placebo for 12 weeks (weeks 0 to 12)
Patients treated with etanercept were given a dose of 0.8 mg/kg once a week up to a maximum dose of 50 mg per week.
From week four, patients in both groups whose PASI scores rose:
- by more than 50% compared to the baseline figure and by at least 4 points at one visit, or
- by more than 25% and by at least 4 points at each of two consecutive visits,

were eligible for transfer to an **escape group**, in which they received etanercept plus topical treatments on an open-label basis up to week 12.
The other patients continued the study on a double-blind basis.

Stage II: non-comparative, etanercept for 24 weeks (weeks 13 to 36)
All patients who completed stage I, including those in the escape group, were given etanercept at a dose of 0.8 mg/kg once a week.
Patients who had not achieved a PASI response 50 by week 24 or PASI response 75 by week 36 could stop taking etanercept or add a class II or III dermocorticoid to their etanercept treatment until week 48.

Stage III: randomised, double-blind, etanercept versus placebo for 12 weeks (weeks 37 to 48)
Patients who had obtained a PASI response 50 by week 24 or PASI response 75 by week 36 were randomised to receive placebo or to continue on etanercept at a dose of 0.8 mg/kg once weekly until week 48.
The patients in this group who had not achieved a PASI response 75 were retreated with etanercept on an open-label basis until week 48.

Primary efficacy endpoint: percentage of patients with a reduction of at least 75% in the PASI score (PASI 75) after the 12 weeks of treatment in stage I.

The secondary endpoints included: percentage of PASI 50 and PASI 90 responses, percentage of patients with a PGA score of 0 or 1 and a quality of life score (CDLQI score[3]) after 12 weeks.

Statistical analysis: the analysis was carried out on the intention to treat population. Patients in the escape group and patients with missing values, including those in the escape group, were counted as treatment failures. The protocol specified that patients would be divided into different age groups (4 to 11 and 12 to 17).

Results:

STAGE I (weeks 0 to 12): etanercept versus placebo

A total of 211 children were included in stage I: 106 in the etanercept group and 105 in the placebo group. In both groups, 36% of patients were in the 4 to 11 age group and 64% in the 12 to 17 age group.
The median skin area affected was 20% (min 10.0 - max 95.0).
The median duration of progression of psoriasis was 5.9 years (min 0.3 - max 17.9).
57% of patients had undergone phototherapy or systemic treatment.
The median PASI score was 16.4 (min 12 - max 56.7) and 99% of patients had a PGA score ≥ 3.
The CDLQI score was 9.43 ± 6.20 for the entire cohort.

During stage I (double-blind stage):
- 27 out of 105 patients in the placebo group transferred to the escape group, 78 completed the stage and one withdrew from the study (withdrawal of consent);
- 5 out of 106 patients in the etanercept group transferred to the escape group, 100 completed the stage and one withdrew from the study because of adverse effects.

- **Primary efficacy endpoint (ITT analysis[4]) :**

After 12 weeks of double-blind treatment, the percentage of patients achieving a PASI 75 score was observed to be higher in the etanercept group than in the placebo group: 57% (60/106) versus 11% (12/105), p<0.0001.
The response was similar irrespective of age group (4 to 11 or 12 to 17, see table 1).

Table 1: Percentage of patients with a PASI 75 response according to age group after 12 weeks of treatment (stage I)

% PASI 75 response:	**Etanercept**	**Placebo**
Age 4-11	**58% (22/38)**	**11% (4/38)**
Age 12-17	**56% (38/68)**	**12% (8/67)**

N.B.: As only 19 children aged under 8 were included in the study, the indication has been limited to children aged 8 and over.

[3] "Children Dermatology Life Quality Index": quality of life questionnaire completed by patients and designed for children of school age suffering from dermatological conditions. The CDLQI is made up of 10 questions relating to the preceding week. The scale is from 0 to 30. A higher score indicates a worse quality of life.
[4] Patients in the escape group were regarded as failures.

- **Secondary endpoints:**

A statistically significant difference in favour of etanercept compared to placebo was observed after 12 weeks in terms of the PASI 50 and PASI 90 response rates, the percentage of patients with a PGA score of 0 or 1 and for improvement to quality of life (CDLQI score[5]) (see table 2).

Table 2: Results after 12 weeks for the secondary endpoints

Endpoints	Etanercept	Placebo	p
% PASI 50 response	**79/106 (75%)**	**24/105 (23%)**	**<0.001**
% PASI 90 response	**29/106 (27%)**	**7/105 (7%)**	**<0.001**
PGA (% of patients scoring 0 or 1)	**56/106 (53%)**	**14/105 (13%)**	**<0.001**
Baseline CDLQI	**8.86 ± 5.99**	**9.99 ± 6.37**	**-**
CDLQI after 12 weeks	**3.2 ± 4.1**	**5.7 ± 5.2**	**<0.001**

STAGE II (weeks 13 to 36): all patients on etanercept for 24 weeks

208 of the 211 patients who took part in stage I progressed to stage II. 105 of them had been in the etanercept group (five of whom had been transferred to the escape group) and 103 had been in the placebo group (77 had only received placebo and 26 had been transferred to the escape group in which etanercept was administered).

Among patients treated with etanercept in stages I and II:
- the percentage of PASI 75 responses was 69% in week 24 and 68% in week 36;
- the percentage of patients with a PGA score of 0 or 1 was 57% in week 24 and 53% in week 36;
- the CDLQI score improved by 63% (baseline score of 9.99 ± 6.37) at week 36.

Among the patients treated with placebo (stage I) and then by etanercept (stage II), the PASI 75 responses, PGA and CDLQI scores (weeks 24 and 36) were similar to those achieved in patients treated with etanercept in stages I and II.

STAGE III (weeks 37 to 48): 12-week extension of treatment with etanercept versus placebo

138 responders among the patients in stage II (all of whom received etanercept) were included in stage III (94% of them had had a PASI 75 response by week 36) and were randomised into two groups:
- etanercept: 69 patients, 64 of whom had had a PASI 75 response
- placebo: 69 patients, 65 of whom had had a PASI 75 response

After the 12 weeks of treatment in stage III:
- 49% of patients in the placebo group had a PASI 75 response;
- 80% of patients in the etanercept group had a PASI 75 response.

N.B.: the results of stages II and III should be interpreted with caution as the data is exploratory.

[5] CDLQI ("Children Dermatology Life Quality Index"): quality of life questionnaire completed by patients and designed for children of school age suffering from dermatological conditions. The CDLQI is made up of 10 questions relating to the preceding week. The scale is from 0 to 30. A higher score indicates a worse quality of life.

3.2. Adverse effects

The tolerance data for study 20030211 described above relate to the 210 patients who received at least one dose of etanercept. The data was collected from the start of the study until 30 days after the end of the study.

The most frequent adverse events were upper respiratory tract infections (229.3 per 100 patient-years) and reactions at the injection site (37.6 per 100 patient-years). These were slight to moderate in intensity and generally transient.
Four serious adverse events affected three patients during the second stage of the study (open-label stage). Only one of these (lobar pneumonia in a seven-year-old girl with a history of asthma) was regarded as related to etanercept.
Six patients withdrew from the study because of adverse events: one in the first (double-blind) stage of the study because of a bronchial spasm (not serious) and five in the second (open-label) stage because of lobar pneumonia (serious), aggravation of psoriasis, atopic dermatitis, muscular spasms and skin infection (not serious).
No cases of cancer, opportunistic infection, tuberculosis, demyelinisation, pancytopenia, medullary aplasia or lupus-type reactions were reported during the study.

Published case studies did not reveal any unexpected adverse effects among 28 children and adolescents suffering from moderate to severe psoriasis who were exposed to etanercept for periods of up to 31 months.

Study 20030211 needs to be continued on an open-label basis in order to obtain long-term tolerance information. However, data for patients aged under eight (17 patients in the extension phase) will remain inadequate.
A long-term (5-year), prospective, open-label observational study is planned to obtain more information about long-term tolerance (risk of serious infection, carcinogenic effect, effects on growth, other unexpected effects) among 200 paediatric patients (including 100 in Europe).

The tolerance profile of etanercept in children and teenagers suffering from psoriasis appears to be similar to that observed in adults with psoriasis.

Furthermore, the FDA is assessing the possibility of a link between the class of anti-TNFα drugs to which etanercept belongs and the occurrence of lymphomas or other cancers in children and adolescents (statement issued on 4 June 2008). This assessment follows around thirty cases of cancer reported over a 10-year period among children and young adults being treated with anti-TNFα agents for various indications including juvenile arthritis and Crohn's disease. The results of this assessment are not yet available.

3.3. Conclusion

A randomised, double-blind, three-month study carried out on 211 patients aged between 4 and 17 found that the percentage of patients with a reduction in their PASI score of at least 75% was higher in the etanercept group than in the placebo group (57% vs. 11%, $p<0.0001$). The patients had moderate to severe psoriasis which had been progressing for at least 6 months and had already undergone or were undergoing treatment involving phototherapy or systemic treatment of psoriasis (methotrexate, ciclosporin or retinoid), or their psoriasis was in the opinion of their dermatologist not adequately controlled by topical treatment (relatively strong dermocorticoid or vitamin D3 analogue) which had been being administered for at least 6 weeks.
The results of the extension stages of this study suggest that the effect observed after three months treatment with etanercept continued until a year after the start of treatment. This persistent effect of etanercept seems to be weak in patients who stopped taking etanercept and were put on placebo (half of patients relapsed after three months).

The adverse effects profile of etanercept in this population was similar to that observed in adults, comprising mainly upper respiratory tract infections and reactions at the injection site. The adverse effects were slight to moderate in intensity and generally transient. However, since around thirty cases of cancer have been reported over ten years among children or young adults in various indications, including juvenile arthritis and Crohn's disease, the FDA has launched an assessment of the risk of cancer, which cannot be ruled out. Long-term (5-year) tolerance data from an observational study on the paediatric population is expected.

4 TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit in the extension of the indication

Psoriasis is a chronic inflammatory dermatosis, usually benign, which can in some of its forms have a major impact on quality of life.
These proprietary products suspend the symptoms.

Public health benefit:

Psoriasis constitutes a significant public health burden. The public health burden represented by children aged eight or over suffering from severe psoriasis which is resistant to other treatments, or where other treatments are not tolerated, is minor.

Improving the management of these children can be regarded as a public health need since the development of paediatric medication is an established priority and in view of the situations in which other systemic treatments cannot be used, as well as the cumulative toxicity of these treatments.

In view of the data available (particularly short-term efficacy versus placebo in respect of PASI 75), ENBREL is expected to have a minor short-term impact on morbidity and quality of life for children.

As the data available was obtained over a relatively short period, it is not certain that these results can be transposed into clinical practice because of uncertainties as to whether efficacy would be maintained after discontinuation of treatment with ENBREL, how often relapses might occur, and long-term tolerance, in particular the risk of cancer and infections.

In children, ENBREL is therefore unlikely to be able to provide a response to the identified public health need.
Consequently, in the present state of knowledge, ENBREL is not expected to have an impact on public health for this indication in children.

The efficacy/adverse effects ratio in the population covered by the extension of indication (ages 8 to 17) is medium, since efficacy is moderate and there is uncertainty as to long-term tolerance (opportunistic infections, carcinogenity risk).

These proprietary medicinal products are second-line treatments following the failure of systemic treatments or phototherapy (patients who are non-responders, intolerant, or who have a contraindication).

There is no alternative treatment in this indication for this population.

The actual benefit of the ENBREL proprietary medicinal products is moderate in children aged eight and over and adolescents in the extension of indication.

4.2. Improvement in actual benefit (IAB)

The ENBREL proprietary medicinal products provide a minor improvement in actual benefit (IAB IV) in the management of patients aged eight to 17 suffering from chronic severe plaque psoriasis where other systemic treatments or phototherapy are not sufficiently effective or are not tolerated.

4.3. Therapeutic use

4.3.1. Therapeutic strategy[6, 7, 8, 9, 10, 11, 12, 13]

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. In children, treatment depends on age, type of lesions, their severity, how long the child has had the disease, his or her attitude to the disease and the effect it has on his or her quality of life.

Benign forms are given local treatments: emollient and keratolytic agents, vitamin D3 analogues (although there is no marketing authorisation for paediatric use) and dermocorticoids. Local treatments are used alone or in combination with other local treatments or systemic treatments.

PUVA therapy and narrow-band TL-01 UVB phototherapy are offered in cases of extensive psoriasis which is resistant to topical treatments (second-line treatments). These treatments can only be administered to children from the age of six or seven when they can be left alone in a treatment booth. PUVA therapy is hardly ever used nowadays as it appears to be associated with a greater long-term risk of cancer than narrow-band UVB phototherapy. A lower dose of UVB can be applied when phototherapy is combined with a local treatment, such as a vitamin D3 analogue.

Systemic treatments are reserved for severe forms of psoriasis in children which are resistant to local treatments and phototherapy. However, fewer systemic treatments are available for children and they are less well validated than those available for adults.

Acitretin is usually prescribed as a first-line systemic treatment in severe forms which do not respond to local treatments or phototherapy (where this is an option). It is particularly effective in the treatment of extensive plaque psoriasis and cases of pustular, erythrodermic and palmoplantar psoriasis which have a major impact on quality of life. Acitretin is used at a dose of 0.5 mg/kg/day. Practitioners must strive to find the minimum effective dose in order to reduce long-term adverse effects as much as possible, and must monitor bone development and growth very closely. Girls who have started to menstruate must be given contraception.

[6] Leaute-Labreze C. Traitement du psoriasis de l'enfant. Ann Dermatol Venereol 2001 ; 128 : 286-90.

[7] Wilson JK et al Treatment of psoriasis in children: Is there a role for antibiotic therapy and tonsillectomy? Pediatr Dermatol 2003; 20:11-5.

[8] Brecher AR et al Oral retinoid therapy for dermatologic conditions in children and adolescents. J Am Acad Dermatol 2003; 49:171-82.

[9] Perrett CM et al Cyclosporin in childhood psoriasis. J Dermatol Treat 2003; 14: 113-118.

[10] Mahé E et al Cyclosporine in childhood psoriasis. Arch Dermatol 2001; 137 : 1532-3.

[11] Pereira TM et al A. Cyclosporin A treatment in severe childhood psoriasis. J Eur Acad Dermatol Venereol 2006; 20:651-6.

[12] Jain VK et al Narrow-band UV-B phototherapy in childhood psoriasis. Int J Dermatol 2007; 46:320-2.

[13] Kopp T et al Successful use of acitretin in conjunction with narrowband ultraviolet B phototherapy in a child with severe pustular psoriasis, von Zumbusch type. Br J Dermatol 2004; 151: 912-6.

Ciclosporin can be considered if acitretin fails, is not tolerated or is contraindicated, especially in severe forms of pustular or erythrodermic psoriasis. Treatment must be given for a short period (1 to 2 years) in view of the long-term risks of nephrotoxicity, arterial hypertension and immunosuppression. The initial dose is 2.5 mg/kg/day, which may be increased to 5 mg/kg/day if clinically (arterial hypertension) and biologically (creatinaemia) well tolerated.

Methotrexate is also used to treat severe forms of psoriasis in children, although this indication has not been validated.

4.3.2. Role of ENBREL

ENBREL (etanercept) is an anti-TNFα that is already indicated for adults in the systemic treatment of severe, chronic plaque psoriasis where at least two other systemic treatments, which include methotrexate, ciclosporin and phototherapy, have failed, are not tolerated or are contraindicated.

It is a second-line treatment for children aged 8 and over and adolescents suffering from severe, chronic plaque psoriasis where other systemic treatments or phototherapy have failed, are not tolerated or are contraindicated.

4.4. Target population

The target population for ENBREL in the extension of indication is defined as patients aged 8 to 17 suffering from severe plaque psoriasis where other systemic treatments or phototherapy have failed or are contraindicated.

A British epidemiological study[14] carried out on a population of around 7.5 million people allows the prevalence of psoriasis to be estimated at 0.55% in children aged 0 to 9 and 1.5% among those aged 10 to 19.
A Spanish epidemiological study[15] conducted on a sample of 12,938 people representative of the general population estimated the prevalence of psoriasis at 0.4% in children aged 0 to 10 and 0.8% among those aged 11 to 20.
In the light of this data, the prevalence of psoriasis among individuals aged 8 to 17 can be estimated at around 1%, i.e. 62,000 children and adolescents.

55 to 70% of these cases are likely to involve plaque psoriasis[16, 17, 18, 19], i.e. 34,000 to 43,400 children and adolescents aged 8 to 17 suffer from plaque psoriasis.

The epidemiological data does not allow us to estimate the prevalence of severe plaque psoriasis among children. However, it can be accepted that severe forms are in the minority, accounting for around 5% of cases (according to data in the literature, 20% of cases are moderate or severe[20, 21] and the British epidemiological study found that 2.3% of patients were having systemic treatment), i.e. 1,700 to 2,150 children and adolescents.

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[14] Gelfand JM. Prevalence and treatment of psoriasis in the United Kingdom. Arch Dermatol 2005 ; 41(December) : 1537-41
[15] Ferrandiz C. Prevalence of psoriasis in Spain (Epiderma project: phase I). European Academy of Dermatology and Venerology 2001 ; 15 : 20-3
[16] Seyhan M. Psoriasis in childhood and adolescence : evaluation of demographic and clinical features. Pediatrics International 2006 ; 48 : 526-30
[17] Kumar B. Epidemiology of childhood psoriasis: a study of 419 patients from northern India. International Journal of Dermatology 2004 ; 43 : 654-58
[18] Fan X. Childhood psoriasis: a study of 277 patients from India. JEAVD 2007 ; 21 : 762-65
[19] Boudaya S. Le psoriasis de l'enfant : etude épidémiologique de 196 observations. Nouvel. Dermatol. 2004 ; 23 : 13-6
[20] Choi J et al. Quality of life issues in psoriasis. J Am Acad Dermatol 2003 ; 49(2) : S57-61
[21] Krueger G et al. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Foundation patient-membership survey. Arch Dermatol 2001; 137: 280-4

Similarly, there is no epidemiological data which would allow us to estimate the population of patients suffering from psoriasis in whom other treatments, including systemic treatments and phototherapy, have failed. However, the expert view, taking account of previous estimates for adults, is that this population is unlikely to exceed 500 patients in the 8 to 17 age group.

4.5. Transparency Committee recommendations

The Transparency Committee recommends inclusion on the list of medicines reimbursed by National Health Insurance and on the list of medicines approved for use by hospitals and various public services for the extension of indication.

4.5.1. Exception drug status

The treatment information sheet for ENBREL will be updated accordingly.

4.5.2. Packaging: Appropriate for the prescription conditions.

4.5.3. Reimbursement rate: 65%