The legally binding text is the original French version

**TRANSPARENCY COMMITTEE**

Opinion

17 October 2012

**BETESIL 2.25 mg, medicated plaster**

B/8 medicated plasters in sachets (CIP code: 34009 377 977 4 0)

Applicant: GENEVRIER

<table>
<thead>
<tr>
<th>INN</th>
<th>Betamethasone valerate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATC Code (2012)</td>
<td>D07AC01 (DERMATOLOGICAL PREPARATIONS / CORTICOSTEROIDS, POTENT)</td>
</tr>
<tr>
<td>Reason for review</td>
<td>Inclusion</td>
</tr>
<tr>
<td>Lists concerned</td>
<td>Medicines reimbursed by National Health Insurance (CSS L.162-17) Medicines approved for hospital use (CSP L.5123-2)</td>
</tr>
</tbody>
</table>

Indications concerned

“Treatment of inflammatory skin disorders which do not respond to treatment with less potent corticosteroids, such as eczema, lichenification, lichen planus, granuloma annulare, palmoplantar pustulosis and mycosis fungoides. Due to its particular bioadhesive pharmaceutical form, BETESIL is suitable for chronic plaque psoriasis localized in difficult to treat areas (e.g. knees, elbows and anterior face of the tibia on an area not greater than 5% of the body surface).”

**Actual benefit**

The actual benefit of BETESIL 2.25 mg medicated plaster in the Marketing Authorisation indication is substantial.

**IAB**

BETESIL 2.25 mg medicated plaster does not offer any improvement in actual benefit (non-existent IAB V) in the treatment strategy for psoriasis and other inflammatory skin disorders that do not respond to less potent corticosteroids.

**Therapeutic use**

BETESIL is a first-line treatment in plaque psoriasis and a second-line treatment in other inflammatory skin disorders that do not respond to less potent topical corticosteroids.

**Recommendations**
**Administrative and Regulatory Information**

<table>
<thead>
<tr>
<th>Marketing Authorisation (procedure)</th>
<th>9 January 2007 (mutual recognition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription and dispensing conditions / special status</td>
<td>List I</td>
</tr>
</tbody>
</table>

**ATC classification**

| 2012 |
| D: Dermatologicals |
| D07: Corticosteroids, dermatological preparations |
| D07A: Corticosteroids, plain |
| D07AC: Corticosteroids, potent (group III) |
| D07AC01: Betamethasone |

**Context**

BETESIL is a potent corticosteroid available as a betamethasone plaster containing 2.25 mg per plaster, measuring 7.5 cm x 10 cm and made up of an unwoven backing and an adhesive layer. It is transparent and semipermeable and adheres to the skin through pressure. It can be cut to the shape and size of the plaque to be treated. BETESIL use enables corticosteroid administration to be standardised at a maximum dose of 2.25 mg x 6.

Betamethasone is already available in other dosage forms (cream, ointment, lotion, emulsion, etc.).

**Therapeutic Indications**

“Treatment of inflammatory skin disorders which do not respond to treatment with less potent corticosteroids, such as eczema, lichenification, lichen planus, granuloma annulare, palmpoplantar pustulosis and mycosis fungoides.

Due to its particular bioadhesive pharmaceutical form, BETESIL is suitable for chronic plaque psoriasis localized in difficult to treat areas (e.g. knees, elbows and anterior face of the tibia on an area not greater than 5% of the body surface).”

**Dosage**

“Adults: Apply the medicated plaster to the skin area to be treated once a day. Do not exceed the maximum daily dose of six medicated plasters and the maximum treatment period of 30 days. A new medicated plaster must be applied every 24 hours. It is also advisable to wait at least 30 minutes between one application and the next. Once an appreciable improvement has been obtained, you can discontinue the application and possibly continue the treatment with a less potent corticosteroid.”
Many inflammatory skin disorders are treated with topical corticosteroids. Some of these present with well-localised lesions that are difficult to treat with standard topical products (such as creams and ointments) because they are often rubbed, rapidly removing the product, and because the thickness of the lesion limits the local action of the topical corticosteroid. These conditions are primarily psoriasis, eczema, neurodermatitis, lichen planus and chronic lupus erythematosus.

In order to prevent adverse effects from topical corticosteroids, the smallest effective dose of corticosteroid is always used for as short a period as possible. The topical corticosteroid chosen should have an appropriate potency for the skin disorder and the nature of the lesion.

The most common inflammatory skin disorder in these circumstances is psoriasis. Plaque psoriasis is a chronic, non-infectious, non-contagious and usually benign inflammatory skin disorder, which can have a significant psychosocial impact in some forms.

Treatments for psoriasis are not only determined by the severity and extent of the lesions, but also their detrimental effect on the patient’s functioning, aesthetic appearance, career or relationships, the psychological impact of the disease, and how strongly the patient desires remission. As a general rule, patients with very limited and/or psychologically well-accepted psoriasis are not routinely treated.

In all cases, hydration of the skin with an emollient is advised.

Topical corticosteroids and vitamin D3 analogues are the first-line treatments for plaque psoriasis (excluding sensitive areas such as skin folds or the face). Topical corticosteroids may be used alone or in combination with calcipotriol, or more rarely with a keratolytic agent where there is very significant keratosis.

The potency of the topical corticosteroid is determined by the location of the psoriasis. Outside sensitive areas such as skin folds or the face, treatment begins with a potent or very potent topical corticosteroid\(^1\) and the doses are then gradually reduced, with maintenance treatment sometimes offered.

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06 CLINICALLY RELEVANT SIMILAR MEDICINES

06.1 Medicinal products

BETESIL is the only topical corticosteroid available in plaster form.

Medicinal products that are similar are other potent topical corticosteroids alone or in combination with calcipotriol, as these are used in inflammatory skin disorders that do not respond to topical corticosteroids with moderate potency.

<table>
<thead>
<tr>
<th>INN</th>
<th>Identical pharmacotherapeutic class</th>
<th>Name</th>
<th>Max. corticosteroid dose in mg</th>
<th>Pharma. company</th>
<th>Date of opinion</th>
<th>Actual benefit</th>
<th>Reimbursed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone</td>
<td></td>
<td>BETNEVAL 0.1% (ointment and cream)</td>
<td>10 or 30</td>
<td>GSK</td>
<td>12/08</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Desonide</td>
<td></td>
<td>DIPROSONE 0.05% (ointment, cream and lotion)</td>
<td>15</td>
<td>Schering-Plough</td>
<td>09/11</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Diflucortolone</td>
<td>Yes Potent topical corticosteroid</td>
<td>LOCATOP 0.1% (cream)</td>
<td>30</td>
<td>Pierre Fabre</td>
<td>12/08</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Difluprednate</td>
<td></td>
<td>NERISONE (ointment and cream)</td>
<td>30</td>
<td>Intendis</td>
<td>12/08</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Difluprednate</td>
<td></td>
<td>NERISONE GRAS (cream)</td>
<td>30</td>
<td>Intendis</td>
<td>12/08</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluticasone</td>
<td></td>
<td>FLIXOVATE 0.05% (ointment and cream)</td>
<td>7.5</td>
<td>Gerda</td>
<td>12/08</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td></td>
<td>EFFICORT HYDROPHILE 0.127% (cream)</td>
<td>38</td>
<td>Galderma</td>
<td>06/11</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EFFICORT LIPOPHILE 0.127% (cream)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LOCOID 0.1% (ointment, liquid emulsion, cream and thick cream)</td>
<td>30</td>
<td>Astellas</td>
<td>06/11</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>No Combination of potent topical corticosteroid + calcipotriol</td>
<td>DAIVOBET, ointment, gel</td>
<td>30</td>
<td>Leo</td>
<td>04/09</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Conclusion**

Potent topical corticosteroids and potent topical corticosteroid/topical vitamin D3 combinations are the clinically relevant similar products.
INTERNATIONAL INFORMATION ABOUT THE MEDICINE

<table>
<thead>
<tr>
<th>Country</th>
<th>REIMBURSED</th>
<th>Population(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greece, Slovakia and UK</td>
<td>Yes*</td>
<td>MA or restricted population</td>
</tr>
<tr>
<td>Italy, Czech Republic, Hungary</td>
<td></td>
<td>Marketed but not reimbursable</td>
</tr>
</tbody>
</table>

* Community + hospital

ANALYSIS OF AVAILABLE DATA

08.1 Efficacy

Two trials have been conducted using BETESIL in psoriasis. No specific data has been provided for other skin disorders where management includes topical corticosteroids; for these skin disorders, the applicant’s analysis is based on general data concerning topical corticosteroids.

8.1.1 Ortonne trial in plaque psoriasis

The Ortonne trial is an unpublished, randomised, single-blind (investigator), non-inferiority trial that compared one 2.25 mg betamethasone valerate plaster (BETESIL) per day to one daily application of combined calcipotriol 50 µg / betamethasone dipropionate 0.5 mg/g in the form of an ointment (DAIVOBET).

Patients had to have mild-to-moderate plaque psoriasis. On inclusion, the severity of psoriasis was assessed by the Total Severity Score³ (TSS), which had to be ≥ 4. Patients must be at least 18 years old, have stable psoriasis not exceeding 10% of body surface area, have at least 2 bilateral plaques on the limbs measuring between 10 cm² and 75 cm², and not be receiving systemic treatment of psoriasis.

The investigator evaluated the condition of patients’ skin every week without knowing their treatment.

Treatment was continued until a TSS ≤ 1 was obtained and for a maximum period of 4 weeks.

The primary endpoint was TSS at 4 weeks.

The PGA⁴ score at 4 weeks was used as one of the many secondary endpoints.

The statistical test used was ANCOVA and the per-protocol (PP) population was analysed. The non-inferiority hypothesis was based on the TSS score: for BETESIL to be considered not inferior to DAIVOBET, the lower limit of the 95% confidence interval for the difference between the two treatments (BETESIL - DAIVOBET) must be greater than -1.

This limit was determined by analogy to the results of clinical trials performed when developing a drug for psoriasis of the scalp (c.f. XAMIOL file, opinion of 1 April 2009). On a 6-point overall score, a difference of 1.40 between 2 treatments had been assessed as a small effect size.

³ The Total Severity Score for psoriasis (TSS) is reached by adding together scores for erythema, desquamation and plaque thickness, with each of those scores graded on a scale of 0 to 3. The TSS therefore ranges from 0 to 9.
⁴ PGA: physician’s global assessment. An evaluation of the severity of the disease at a particular moment in time, with 6 grades ranging from 0 to 5 (0: completely clear, 1: almost clear, 2: mild, 3: moderate, 4: severe, 5: very severe).
Results
The total number of patients included was 165 in the BETESIL group and 159 in the DAIVOBET arm. The two groups were comparable in terms of gender, age, weight and height. Thirty-two patients were excluded from the BETESIL group and 28 from the DAIVOBET group. Among these, 1 patient in the BETESIL group and 0 in the DAIVOBET group withdrew from the trial because of an adverse effect.

Table 1: TSS at 4 weeks (primary endpoint) in the PP population

<table>
<thead>
<tr>
<th></th>
<th>BETESIL</th>
<th>DAIVOBET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>133</td>
<td>131</td>
</tr>
<tr>
<td>Initial TSS</td>
<td>6.63</td>
<td>6.47</td>
</tr>
<tr>
<td>Change from initial TSS at 4 weeks</td>
<td>-4.69</td>
<td>-4.75</td>
</tr>
<tr>
<td>Difference between groups at 4 weeks</td>
<td>-0.288</td>
<td>95% CI: -0.610; 0.034</td>
</tr>
</tbody>
</table>

After 4 weeks of treatment, the difference between mean BETESIL versus DAIVOBET TSS scores (primary endpoint) was -0.288 (95% CI: [-0.610; 0.034]). The 95% confidence interval was substantially greater than the non-inferiority limit of -1 point.

For the secondary endpoint of PGA after 4 weeks, the difference between the scores of the 2 groups was 0.057 (95% CI [-0.270; 0.241]).

Altogether, this trial demonstrates that one BETESIL plaster per day is not inferior to 2 applications of DAIVOBET per day. It cannot indicate the saving made in terms of dose of corticosteroid administered.

8.1.2 Naldi trial in plaque psoriasis

The Naldi trial is a randomised (1:1), single-blind (investigator), superiority trial that compared efficacy and safety in a group treated with betamethasone plasters (BETESIL) applied once a day versus a group treated with betamethasone cream (BETNEVAL) applied twice a day.

On inclusion, patients had stable psoriasis not exceeding 10% of body surface area, must have 2 to 4 plaques on the limbs measuring between 10 cm² and 150 cm², and must not be receiving systemic treatment of psoriasis. They must also be at least 18 years in age.

The treatment was applied only to those plaques targeted by a doctor, who knew which product was prescribed. The patient applied either the cream or the plaster and was therefore not blinded. However, the primary endpoint was evaluated remotely by an investigator blind to the treatment administered, using standardised photos.

The duration of treatment was 3 to 5 weeks depending on the course of the disease, with a follow-up period of 3 months. At 3 weeks, treatment was stopped if the TSS score was ≤ 1, and otherwise treatment was continued for a further 2 weeks.

The primary endpoint was the number of patients with a PGA score of 0 at 3 weeks of treatment.

Among the secondary endpoints, PGA was also evaluated at 5 weeks. No other overall evaluation of psoriasis was performed in order to confirm this efficacy. Pruritus and irritation were evaluated by the patient.

Intention-to-treat (ITT) analysis was performed using the Cochran-Mantel-Haenszel statistical test.

Results
A total of 231 patients were included. On inclusion, the number of plaques and severity of psoriasis according to the PGA were distributed as follows between the groups. The patients in the BETESIL group had more plaques.

Table 2: description of patients on inclusion in the Naldi trial

<table>
<thead>
<tr>
<th>Number of patients (%)</th>
<th>BETESIL (plaster)</th>
<th>BETNEVAL (cream)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On inclusion</td>
<td>116 (100)</td>
<td>114 (100)</td>
</tr>
<tr>
<td>With: 2 plaques</td>
<td>58 (50)</td>
<td>75 (66)</td>
</tr>
<tr>
<td>3 plaques</td>
<td>20 (17)</td>
<td>21 (18)</td>
</tr>
<tr>
<td>4 plaques</td>
<td>38 (33)</td>
<td>18 (16)</td>
</tr>
<tr>
<td>PGA 2</td>
<td>14 (12)</td>
<td>19 (17)</td>
</tr>
<tr>
<td>PGA 3</td>
<td>65 (56)</td>
<td>57 (50)</td>
</tr>
<tr>
<td>PGA 4</td>
<td>29 (25)</td>
<td>26 (23)</td>
</tr>
<tr>
<td>PGA 5</td>
<td>8 (7)</td>
<td>12 (10.5)</td>
</tr>
</tbody>
</table>

After 3 weeks of treatment, 52.68% of patients in the BETESIL group no longer had any plaques (PGA = 0) versus 31.9% in the BETNEVAL group (p < 0.001).

At 5 weeks, better efficacy with BETESIL (58%) than BETNEVAL (40.18%) was also shown by the PGA (p = 0.006).
However, no significant difference could be demonstrated in terms of the pruritus and irritation experienced by patients.

In conclusion, this trial shows that BETESIL has greater efficacy than BETNEVAL. However, it cannot indicate the saving made in terms of dose of corticosteroid administered.

8.1.3 Data for other inflammatory skin disorders treated with a topical corticosteroid

The applicant did a literature search for other inflammatory skin disorders in which treatment may include topical corticosteroids. Publications were found for atopic eczema, granuloma annulare, lichen planus and discoid lupus erythematosus.
These conditions may have characteristics (thick, well-localised lesions in difficult-to-treat places) that correspond to the indications for BETESIL.

No trial has been performed using BETESIL in inflammatory skin disorders other than psoriasis.

For atopic eczema, the role of topical corticosteroids is supported by the French Dermatology Society guideline and confirmed by NICE.

For lupus erythematosus, topical corticosteroids are the standard treatment in localised forms.

The trials submitted by the applicant, which study proprietary medicinal products other than BETESIL, are as follows:
- an open-label randomised trial evaluating the efficacy of betamethasone versus calcipotriol for 12 weeks in 31 patients with cutaneous lichen planus;

- a trial in 10 patients with cutaneous lupus erythematosus\textsuperscript{10}.
These trials have not been taken into account in this opinion because of the very low numbers of patients included.

\textbf{08.2 Adverse effects}

\textbf{8.2.1 Trial data}

The safety data from the clinical trials did not show any adverse effect linked to treatment other than a burning sensation in the BETESIL versus DAIVOBET trial.

An absorption study was performed with BETESIL in patients with psoriasis, showing systemic absorption of the active pharmaceutical ingredient and a slight reduction in plasma cortisol (blood cortisol at 8am fell from 252 µg/l to 216 µg/l between D1 and D12). The duration of the study was 3 days. The doses used were the maximum Marketing Authorisation dose with 6 plasters per day. These results are no different from what is known about other topical corticosteroids with repeated doses applied to damaged skin (c.f. Pharmacokinetics paragraph in the SPCs and Levin study\textsuperscript{11}).

\textbf{8.2.2 SPC data}

The SPC states that skin reactions in the plaster application area are common (15\% of patients): these can include skin atrophy, telangiectasia, pustules, papules, furuncles, erythema, pruritus and skin erosion.

The SPC also reports the known risk of systemic corticosteroid effects from betamethasone, via skin absorption when a product is used on extensive areas of the body and for long periods or when an occlusive plaster is used. These effects have not been observed with BETESIL.

\textbf{8.2.3 PSUR data}

A pharmacovigilance report was provided by the applicant covering the use of 100,844 BETESIL plasters in 3,602 patients between October 2010 and February 2011. Two reactions at the application site, possibly linked to BETESIL, were observed.

\textbf{08.3 Prescribing data}

Since its Marketing Authorisation in 2007, BETESIL has been marketed but is not reimbursable.

According to IMS data (moving annual total February 2012), 2,000 prescriptions were issued for the proprietary medicinal product.

\textbf{08.4 Summary and discussion}

The efficacy of BETESIL in plaque psoriasis has been demonstrated in 2 clinical trials with the same randomised, single-blind methodology, one versus DAIVOBET (betamethasone/calcipotriol) and one versus BETNEVAL (betamethasone cream), which (due to the plaster form of BETESIL) were conducted in patients with psoriasis plaques on the limbs.

- In one trial, the non-inferiority of BETESIL versus DAIVOBET was demonstrated through improvement in total severity score (TSS). In fact, after 4 weeks, the difference in mean TSS score between the 2 groups was -0.288, 95\% CI: [-0.610; 0.034]. The 95\% confidence interval was substantially greater than the non-inferiority limit of -1 point.


- In one trial (Naldi), BETESIL was superior to BETNEVAL after 3 weeks of treatment in terms of the percentage of patients who no longer had plaques, with the presence of plaques evaluated from a photo by an investigator who did not know the treatment received: 52.68% versus 31.9%; p < 0.001. No difference was demonstrated in terms of the pruritus and irritation experienced by patients.

These trials did not show that BETESIL reduced the quantity of topical corticosteroid administered.

The application does not contain any efficacy data for BETESIL in the other skin disorders covered by the Marketing Authorisation indication (eczema, lichenification, lichen planus, granuloma annulare, palmoplantar pustulosis and mycosis fungoides).

BETESIL has been marketed for several years, allowing safety data to be collected. Its local and systemic safety seems comparable to that of equally potent topical corticosteroids in a standard dosage form.

The form of BETESIL enables a maximum, fixed and controlled dose of 2.25 mg per plaster to be delivered. This differs from other forms of topical corticosteroids, i.e. creams, gels, ointments or lotions, where the total corticosteroid dose varies from 1.5 mg to 38 mg per tube and where the quantities applied may differ according to the way it is applied and the number of plaques.

### 09 THERAPEUTIC USE

Like other potent topical corticosteroids, BETESIL is a first-line treatment in plaque psoriasis, with the exception of sensitive areas (face and skin folds). BETESIL is an alternative to these, and to the betamethasone/calcipotriol combination.

BETESIL is a second-line treatment in other inflammatory skin disorders. It should only be used when a previous corticosteroid treatment has failed or where there is a specific clinical aspect that the physician feels will not respond to a moderate topical corticosteroid. It should not be used on the face or in skin folds.

Whatever the disorder, because of its plaster form, BETESIL is beneficial for well-localised skin disorders or plaques in difficult-to-treat places. It enables the dose of topical corticosteroid administered to be controlled.

Treatment with BETESIL should not exceed 30 days. As soon as an appreciable improvement is observed, it should be replaced with another topical corticosteroid, which should be applied at progressively less frequent intervals.

In psoriasis, this treatment can also be followed with a vitamin D analogue.

As with any topical corticosteroid, the prescription should be accompanied with an explanation of how to use the product and information about progressively stopping treatment, as well as warnings regarding possible resumption of treatment.

### 010 TRANSPARENCY COMMITTEE CONCLUSIONS

Taking into account all of this information, and following discussion and a vote, the Committee concludes:

#### 010.1 Actual benefit

Plaque psoriasis is a chronic, non-infectious, non-contagious and usually benign disorder, which can have a significant psychosocial impact in some forms.
The other inflammatory skin disorders – eczema, lichenification, lichen planus, granuloma annulare, palmoplantar pustulosis and mycosis fungoides – are variable in appearance, site and severity.

BETESIL is intended as symptomatic treatment.

The efficacy/adverse effects ratio of BETESIL is high.

BETESIL is a first-line treatment in plaque psoriasis and a second-line treatment in other inflammatory skin disorders that do not respond to less potent topical corticosteroids.

There are treatment alternatives.

### Public health benefit

The public health burden from the population of patients with psoriasis presenting as localised plaques on the knees and elbows (the target population of BETESIL) is low.

Management of psoriasis is not a public health need.

In view of the available data, no impact on morbidity or on patients’ quality of life is expected.

The applicability of the trial results to use in real-life situations seems to be acceptable.

In the current state of knowledge and in view of the fact that other therapies are already available, it is not expected that BETESIL will benefit public health in this indication.

Consequently, the Committee considers that:

The actual benefit of BETESIL 2.25 mg medicated plaster in the Marketing Authorisation indication is substantial.

The Committee recommends inclusion on the list of medicines reimbursed by National Insurance and on the list of medicines approved for use by hospitals in the indication “inflammatory skin disorders which do not respond to treatment with less potent corticosteroids” and at the dosage in the Marketing Authorisation.

### Proposed reimbursement rate: 65%

#### 010.2 Improvement in actual benefit (IAB)

BETESIL 2.25 mg medicated plaster does not offer any improvement in actual benefit (non-existent IAB V) in the treatment strategy for psoriasis and other inflammatory skin disorders that do not respond to less potent corticosteroids.

#### 010.3 Target population

BETESIL 2.25 mg plaster is indicated in inflammatory skin disorders that do not respond to less potent corticosteroids when the location of the lesions is appropriate for a plaster form (well localised with surface area < 75 cm²).

The most common of these situations is plaque psoriasis. The other disorders involved are rarer and their number, which is difficult to evaluate, is low in comparison with the number of patients whose psoriasis could be treated with BETESIL.

In the UK, an epidemiological study¹² conducted in 2005 involving 8 million people evaluated the prevalence of treated psoriasis as 1.5% of the general population. If we extrapolate this data to the French population, 950,000 adults are being treated for psoriasis.

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According to experts, 85% of patients with psoriasis have plaque psoriasis.

Of these, the number of patients with some difficult-to-treat plaques is impossible to quantify with precision.

The target population of BETESIL is impossible to quantify precisely but is fewer than 800,000 patients.

011 TRANSPARENCY COMMITTEE RECOMMENDATIONS

- **Packaging**
  Depending on the surface area to be treated and number of plaques, it is appropriate for the prescription conditions.
  It would be preferable for the pharmaceutical company to also apply for inclusion of other existing forms of packaging (B4 and B16 plasters) to adapt to the expected duration of treatment and extent of lesions to be treated.