Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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apremilast 10mg, 20mg and 30mg film-coated tablets (Otezla®)

SMC No. (1052/15)

Celgene Ltd.

08 May 2015

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

apremilast (Otezla®) is accepted for use within NHS Scotland.

Indication under review: for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA).

In two phase III, randomised, placebo-controlled studies in patients with moderate to severe plaque psoriasis, a significantly greater proportion of patients who received apremilast achieved at least 75% improvement in the Psoriasis Area and Severity Index (PASI) score at 16 weeks compared with those who received placebo.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

For the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA).

Dosing Information

30mg twice daily taken orally, morning and evening, approximately 12 hours apart, swallowed whole, with no food restrictions. An initial titration schedule over 5 days from 10mg daily on day 1 to 30mg twice daily on day 6 is recommended. See the summary of product characteristics (SPC) for details.

If a patient shows no evidence of therapeutic benefit after 24 weeks, treatment should be reconsidered. The patient's response to treatment should be evaluated on a regular basis. Clinical experience beyond 52 weeks is not available.

Treatment with apremilast should be initiated by specialists experienced in the diagnosis and treatment of psoriasis (or psoriatic arthritis).

Product availability date

16 February 2015

Summary of evidence on comparative efficacy

Psoriasis is a chronic, inflammatory skin disease which follows a relapsing and remitting course. The most common form is plaque psoriasis which is characterised by well delineated red, scaly plaques that vary in extent from a few patches to generalised involvement.[1] Apremilast is the first of a new class of treatment, inhibiting phosphodiesterase-4 (PDE4) which leads to increased intracellular cyclic adenosine monophosphate (cAMP) levels. This down-regulates the inflammatory response by modulating the expression of tumour necrosing factor-alpha (TNF-α), interleukin-23, interleukin-17 and other inflammatory cytokines which have been implicated in psoriasis. Apremilast has also been accepted by SMC for restricted use alone or in combination with Disease Modifying Antirheumatic Drugs (DMARDs) for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to at least two prior DMARD therapies.[2]

The evidence to support the efficacy of apremilast in the treatment of plaque psoriasis comes from two randomised, double-blind studies (ESTEEM 1 and 2).[3,4,5] Both studies were of similar design and comprised four treatment phases: a 16-week, randomised, double-blind, placebo-controlled phase (weeks 0 to 16), a 16-week maintenance phase (weeks 16 to 32), a 20-week withdrawal phase (weeks 32 to 52) and an ongoing 4-year long-term extension. Eligible patients were aged ≥18 years with chronic plaque psoriasis for ≥12 months. Their disease was moderate to severe, defined by a Psoriasis Area and Severity Index (PASI) score ≥12, and patients had an affected body surface area (BSA) ≥10%, a static Physician Global Assessment (sPGA) score ≥3 (at least moderate) and were candidates for phototherapy and/or systemic therapy. The PASI is a rating score for measuring the severity of psoriatic lesions based on area coverage

and plaque appearance (erythema, infiltration and desquamation severity) which ranges from 0 to 72 (higher scores indicating more severe disease).[6] Patients were randomised, in a ratio of 2:1, to receive apremilast (30mg twice daily) or placebo for the 16-week placebo-controlled phase. From weeks 16 to 32, all patients received apremilast (30mg twice daily) for the maintenance phase. At week 32, patients initially randomised to receive apremilast who achieved at least PASI-75 (a reduction of at ≥75%) in ESTEEM 1 or PASI-50 (a reduction of at ≥50%) in ESTEEM 2, were re-randomised to either apremilast (30mg twice daily) or placebo for the withdrawal phase (weeks 32 to 52) to determine durability of response on stopping. Patients who were re-randomised to placebo and who lost PASI-75 response (ESTEEM 1) or PASI-50 response (ESTEEM 2) were retreated with apremilast.[3]

The primary outcome in both studies was the proportion of patients who achieved PASI-75 (a reduction of at ≥75%) from baseline to week 16. In both studies, the primary outcome was achieved by significantly more patients in the apremilast than placebo groups. The main secondary outcome was the proportion of patients who achieved a sPGA score of clear (0) or almost clear (1) with at least a 2-point reduction from baseline at 16 weeks, which was also achieved by significantly more apremilast than placebo patients. The table below gives details of primary and secondary outcomes.

Table: Psoriasis area and severity index (PASI) and static Physician's Global Assessment (sPGA) outcomes at week 16 in ESTEEM 1 and 2 studies [2,3]

	ESTEEM 1		**ESTEEM 2**	
	Apremilast (n=562)	**Placebo (n=282)**	**Apremilast (n=274)**	**Placebo (n=137)**
Primary outcome: Proportion of patients with PASI-75 at week 16	33% (186/562)	5.3% (15/282)	29% (79/274)	5.8% (8/137)
Difference versus placebo (95% CI), p-value	28% (23 to 32), p<0.0001		23% (16 to 30), p<0.0001	
Proportion of patients with sPGA of clear or almost clear at week 16	22% (122/562)*	3.9% (11/282)	20% (56/274)*	4.4% (6/137)
Mean PASI score at baseline	18.7	19.4	18.9	20.0
Mean % change in PASI score from baseline	-52%*	-17%	-51%*	-16%
Proportion of patients who achieved PASI-50	59% (330/562)*	17% (48/282)	56% (152/274)*	20% (27/137)
Proportion of patients who achieved PASI-90	9.8% (55/562)*	0.4% (1/282)	8.8% (24/274)**	1.5% (2/137)

PASI = psoriasis area and severity index; PASI-50, PASI-75 and PASI-90 correspond to reduction of 50%, 75% and 90% respectively, in PASI score compared to baseline. sPGA (0/1) = static physician's global assessment score of 0 or 1 with at least a 2-point reduction from baseline. CI = confidence interval
* = p<0.0001 versus placebo; ** = p=0.0042 versus placebo

There were also significantly greater improvements in patients treated with apremilast compared with placebo in terms of reductions in BSA affected and pruritus visual analog scale (VAS) score at week 16. Quality of life was assessed by the Dermatology Life Quality Index (DLQI)

questionnaire score which measures how much a skin problem has affected a patient's life over the last week (range 0 to 30, with scores of 11 to 20 indicating a very large effect on patient's life and of 21 to 30 an extremely large effect on patient's life). At week 16, the DLQI score improved from baseline by -6.6 in the apremilast group versus -2.1 in the placebo group in ESTEEM 1 ($p<0.0001$) and by -6.7 versus -2.8 respectively in ESTEEM 2 ($p<0.0001$). In both studies, the mean change in DLQI score was more than the minimal clinically important difference of at least 5-points. [2,3]

The clinical benefit of apremilast was noted across subgroups defined by baseline demographics and baseline clinical disease characteristics (including psoriasis disease duration and patients with a history of psoriatic arthritis) and regardless of prior use of psoriasis medication and response to previous treatments. [7] The response to apremilast was rapid with significantly greater improvements in the signs and symptoms of psoriasis evident by week 2. [2]

During the maintenance phase of both studies (weeks 16 to 32), the effect of apremilast on PASI and sPGA was maintained and patients who continued on treatment had a significantly longer time before loss of PASI-75, PASI-50 or sPGA during the withdrawal phase (weeks 32 to 52).

In an ongoing phase 3b, randomised, double-blind study (PSOR-010), 250 patients with moderate to severe plaque psoriasis were treated with apremilast (30mg twice daily), etanercept (50mg subcutaneously once weekly) or placebo for a 16-week double-blind, controlled period. At week 16, all patients were switched to receive apremilast to week 104. The primary objective of the study was the comparison of apremilast and placebo at week 16 in terms of PASI-75.[8] [9]

*Other data were also assessed but remain commercially confidential.**

Summary of evidence on comparative safety

During the 16-week placebo-controlled phase of the ESTEEM 1 and 2 studies (pooled analysis), adverse events were reported in 70% (573/832) of apremilast patients and 57% (239/418) of placebo patients and these were mild to moderate in severity in most patients. Severe adverse events were reported in 3.8% (32/832) and 3.6% (15/418) of patients respectively. Adverse events were considered treatment-related in 40% (330/832) of apremilast patients and 21% (87/418) of placebo patients. Adverse events led to discontinuation in 5.4% of apremilast and 3.8% of placebo patients during the 16 weeks controlled phase and in 8.4% of apremilast patients overall, including the treatment to 52 weeks.[3,4,5]

In the pooled analysis of the 16-week, placebo-controlled phase of ESTEEM 1 and 2, the most frequently reported adverse events in the apremilast and placebo groups respectively were diarrhoea (18% versus 6.7%), nausea (17% versus 6.7%), upper respiratory tract infection (8.4% versus 6.5%), nasopharyngitis (7.3% versus 6.9%) and tension headache (7.3% versus 3.3%). The gastro-intestinal adverse reactions generally occurred within the first 2 weeks of treatment and usually resolved within 4 weeks.[3]

Pooled data from longer-term safety data up to 52 weeks found that adverse events were the same as those reported during the controlled period and that there was no increase in incidence on longer term use. [3]

Summary of clinical effectiveness issues

Apremilast is the first of a new class of treatment for psoriasis. Four biologic therapies are licensed for the treatment of moderate to severe plaque psoriasis in adults, including the tumour necrosis factor (TNF) antagonists, infliximab, etanercept and adalimumab and an antagonist of interleukin (IL)-12 and IL-23, ustekinumab. These have been reviewed by SMC and have been accepted for use within NHS Scotland mainly for patients with severe disease with some restrictions relating to response. A fifth biologic therapy, secukinumab, which inhibits interleukin-17A, has been accepted by SMC for restricted use for the treatment of moderate to severe plaque psoriasis for patients who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contra-indication to these treatments.

The primary outcome in the ESTEEM 1 and 2 studies was PASI-75 which is a relevant and well recognised measure of symptom severity in psoriasis. The difference over placebo was statistically significant in both studies at 16 weeks and the treatment effect was evident from week 2. The European Medicines Agency considers that PASI alone is not sufficient to evaluate psoriasis severity at baseline and on treatment and strongly recommends the use of a validated, standardised global score in conjunction with PASI.[6] The sPGA score, a recognised measure of psoriatic symptoms, was the key secondary outcome in both studies. The duration of the controlled phase of the ESTEEM studies was limited to 16 weeks which is short for a chronic condition with a relapsing remitting course. However, uncontrolled data to 52 weeks suggest that the treatment effect is maintained.[3] The Summary of Product Characteristics notes that if a patient shows no evidence of therapeutic benefit after 24 weeks, treatment should be reconsidered.[2]

Both studies enrolled a range of patients including those naive to all systemic therapies or phototherapy, treatment-experienced patients and those who had failed a number of treatments. However, a proportion of patients from the study do not represent the licensed population. Approximately one third (35 to 36%) of study patients were naive to treatment with systemic therapies and/or phototherapy and the previously-treated study patients were not required to have failed on systemic therapy or have a contraindication or be intolerant to it. These patients would not be eligible for treatment with apremilast within its licensed indication. [3]

There are no comparative data with other agents and although the ongoing PSOR-010 study included etanercept as an active control, the study was not designed to compare the relative efficacy or safety of apremilast with etanercept.[8,9] The European Public Assessment Report notes that it was difficult to rank apremilast with other first-line systemic conventional therapies since the available evidence did not include an active comparator study. Therefore apremilast was approved for second-line use.[3]

The company presented results of an indirect comparison of apremilast with biologic therapies (adalimumab, etanercept, infliximab and ustekinumab) using a Bayesian network meta-analysis which included 22 studies. The target population included patients with moderate to severe plaque psoriasis. The analysis compared efficacy measured by PASI-50, PASI-75 and PASI-90. The results cannot be shared as they remain commercially confidential. There was heterogeneity among the studies with differences in study populations (including severity of disease and previously used treatments) and the observed differences in PASI responses in the placebo groups of the studies.

The introduction of apremilast would offer patients with severe psoriasis (PASI ≥10 and DLQI ≥10) an alternative oral treatment to biologic therapies. In patients with psoriasis not severe enough to be eligible for biologic therapies (PASI ≥10 and DLQI ≤10), apremilast offers an alternative to BSC.

*Other data were also assessed but remain commercially confidential.**

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis which compared treatment sequences with and without apremilast in severe psoriasis patients with a PASI≥10 and DLQI>10, who had failed to respond to, or had a contraindication to, or were intolerant to other systemic non-biologic therapies. The analysis evaluated apremilast as an additional line of therapy before a sequence of biological therapy and BSC. The treatment sequences used in the analysis were apremilast followed by adalimumab, etanercept and BSC versus adalimumab etanercept and BSC.

A Markov modelling approach was adopted for the analyses based on the University of York Assessment Group Model adapted to enable an evaluation of sequential treatments. In terms of model structure, patients in the apremilast sequence entered the model and received a trial of apremilast (trial period) and then proceeded to a continued use period if they achieved a response to treatment at the end of the trial period. Patients who did not achieve a response at the end of the trial period proceeded to the trial period of the first biologic treatment and to continued use if they achieved a response; or to the trial period of a second biologic treatment if they did not achieve response. Patients who failed to respond to a second biologic progressed to BSC. During the continued use phases, patients could withdraw from treatment due to loss of efficacy or other causes. In the comparator sequence, the same model structure was applied, except patients were initiated to the first biologic therapy instead of apremilast. Response to treatment was defined as achieving a PASI-75 and mortality was also included throughout the model.

The source of the data used to populate the economic model included pooled data from the ESTEEM 1 and ESTEEM 2 studies, the published literature and a network meta-analysis. The ESTEEM 1 and ESTEEM 2 data were used to inform baseline characteristics, the published literature supplied information such as withdrawal rates and trial duration, while the network meta-analysis was used to estimate the comparative efficacy of the treatments.

Baseline utility estimates were derived from the published literature and improvements in utility were generated through achieving a PASI-50, 75 and 90 response. Medicine costs were included in the analysis as were the costs associated with administration, physician visits, hospitalisation for non responders, and monitoring and laboratory tests.

The base case results indicated that the apremilast sequence dominated the comparator sequence (i.e. it was more effective and less costly). This result was based on an incremental quality adjusted life year (QALY) gain of 0.14 QALYs and savings of £3,226. The results indicated that apremilast was associated with a QALY gain over the comparator sequence and this was because apremilast sequence patients spent more time on active therapies and less time on BSC than in the comparator sequence, owing to the additional active therapy

(apremilast) in the sequence. In addition, from the model outputs provided by the company it appeared that due to the model design apremilast mainly displaced time on BSC as opposed to time on biologic therapies. The apremilast sequence was therefore associated with a QALY gain since it was more effective than BSC.

The company provided univariate and scenario sensitivity analysis which also reported that the apremilast sequence dominated the comparator sequence. The exception being a one year time horizon which resulted in a QALY loss of 0.01 QALYs and a saving of £241 (£45,100 saved per QALY lost). A cost-effectiveness acceptability curve displayed that the apremilast sequence had a 100% probability of being cost-effective for all willingness to pay thresholds.

The company also provided an additional analysis which evaluated apremilast as an additional line of therapy before BSC for patients with a PASI≥10 and DLQI≤10 who are ineligible for biological therapy. The comparators in this subgroup were apremilast followed by BSC versus BSC alone and the analysis reported that apremilast followed by BSC was dominant versus BSC only.

The main issues with the analysis were:

- The cost of BSC was estimated to be £887.90 per cycle which implied a yearly cost of £11,543 per year. The results indicated that since patients in the apremilast sequence spend less time in the costly BSC health state, the apremilast sequence was less expensive than the comparator sequence despite the presence of an additional therapy in the sequence. However, the source which informed many of the assumptions regarding BSC referenced that the cost of BSC has been reported as £5,328 per year at most in other technology assessments. The company provided an analysis where the cost of BSC was £5,328 per year. The results of this analysis generated an incremental cost effectiveness ratio (ICER) of £15,922 per QALY gained for the apremilast sequence versus the comparator sequence. For the subgroup of patients with PASI≥10 and DLQI≤10 who are ineligible for biological therapy, the use of an alternative estimate for BSC of £511 per cycle increased the ICER to £22,824. SMC clinical expert response regarding the assumptions that made up BSC in the base case analysis was mixed. One expert did suggest that the assumptions sounded reflective of current practice and experience. However, another two experts did query some of the assumptions used in the model and thought that the cost of BSC may have been overestimated.
- Infliximab was mentioned by the SMC clinical experts as a potential treatment option. However, infliximab was not included in the base case analysis or any sensitivity analysis despite efficacy data being reported in the network meta-analysis. The cost of infliximab was also included in the budget impact estimates of displaced medicines. The company provided two analyses which included infliximab in the treatment sequences. In the first analysis, infliximab replaced etanercept in the treatment sequences, while in the second analysis, infliximab was added to the sequences after etanercept and before BSC. The results of both analyses reported that the apremilast sequence remained dominant versus the comparator sequence.

Despite these issues, the economic case has been demonstrated.

Summary of patient and public involvement

The following information reflects the views of the specified Patient Groups.

- Submissions were received from The Psoriasis and Psoriatic Arthritis Alliance (PAPAA), Psoriasis Association, Psoriasis Scotland Arthritis Link Volunteers (PSALV) and the Skin Conditions Campaign Scotland (SCCS). All four are registered charities.

- The Psoriasis Association, PSALV and SCCS have received pharmaceutical company funding in the past two years, with the Psoriasis Association and PSALV receiving funding from the submitting company. PAPAA has not received any pharmaceutical company funding.

- Chronic plaque psoriasis (CPP) is a lifelong condition. For sufferers the condition can be extremely embarrassing. The symptoms include widespread itchy flaky skin, which sheds continuously. Owing to the highly visible nature of psoriasis, patients often avoid social situations and it can affect employability. The psychological effects combined with the physical discomfort impact on all aspects of their lives. Amongst long-term conditions, moderate to severe CPP produces some of the greatest reductions in Quality of Life indices.

- Current therapies have limitations: topical treatments work but are time consuming and messy, UV light therapy can be inconvenient, DMARDs and biologic agents do not appear to help everyone or may stop working.

- As an oral tablet, apremilast is convenient, allowing patients to self-manage their condition. It does not require repeated monitoring at clinics. Apremilast is a new treatment option, targeting a chemical pathway not covered by other agents and provides patients with a further treatment option.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published clinical guideline 121 "Diagnosis and management of psoriasis and psoriatic arthritis in adults" in 2010.[10] Although the guideline recommends choice of treatment should be made on the basis of individual factors, comorbidity including the presence of psoriatic arthritis, geographic factors affecting access to phototherapy and considerations of adverse effects, methotrexate and ciclosporin are the preferred options for systemic therapy. Recommendations include:

- Patients with severe or refractory psoriasis should be considered for systemic therapy with ciclosporin, methotrexate or acitretin, following discussion of benefits and risks.
- Methotrexate is recommended for longer term use and where there is concomitant psoriatic arthritis.
- Ciclosporin is recommended for short term intermittent use.
- Acitretin can be considered as an alternative.
- Fumaric acid esters can be considered as an alternative maintenance therapy for patients who are not suitable for other systemic therapies or have failed other therapies.
- Hydroxycarbamide can be considered as an alternative maintenance therapy for patients who are not suitable for other systemic therapies or have failed other therapies.

Biologic therapy (unless they have contraindications or are at increased risk of hazards from these therapies) should be offered to patients with severe psoriasis who fail to respond to, or have a contraindication to, or are intolerant of phototherapy and systemic therapies including ciclosporin and methotrexate. Recommendations include:

- Adalimumab loading regimen followed by 40mg every other week is recommended in the treatment of severe psoriasis.
- Etanercept 25mg twice weekly or 50mg weekly is recommended in the treatment of severe psoriasis.
- Infliximab 5mg/kg at weeks 0, 2, 6 and repeated as maintenance treatment every two months is recommended in the treatment of severe psoriasis, especially when rapid disease control is required.
- Ustekinumab 45mg for patients weighing under 100 kg and 90 mg for patients weighing over 100 kg given at weeks 0 and 4 then every 12 weeks as maintenance is recommended in the treatment of severe psoriasis.

The National Institute for Health and Care Excellence (NICE) published clinical guideline 153 "Psoriasis: the assessment and management of psoriasis" in October 2012.[1] This advises that the choice of systemic therapy should take into account the individual's needs, preferences and disease severity and recommends that:

- Methotrexate should be offered as the first choice for systemic therapy in individuals who are not at increased risk of liver damage and who do not meet the criteria for ciclosporin as a first choice treatment option.
- Ciclosporin should be offered as the first choice for systemic therapy in individuals who
    - need rapid or short-term disease control
    - have palmoplantar pustulosis or
    - are considering conception (both men and women)
- there should be consideration on changing from methotrexate to ciclosporin (or vice-versa) when response to the first-choice systemic treatment is inadequate
- acitretin may be considered as treatment option in individuals
    - where methotrexate and ciclosporin are not appropriate or have failed or
    - who have pustular forms of psoriasis

The clinical guideline makes recommendations for biologic therapy from existing NICE technology appraisals, recommending that:

- Adalimumab, etanercept, infliximab and ustekinumab may be considered as treatment options when the disease is severe and psoriasis has not responded to, or the patient is intolerant to, standard systemic therapies
- Treatment should be discontinued in people whose psoriasis has not responded adequately at 16 weeks for adalimumab and ustekinumab, and at 12 and 10 weeks for etanercept and infliximab respectively.
- Switching to a alternative biologic drug should be considered if there is no adequate or sustained response or if the first biological drug cannot be tolerated
- Specialist advice should be sought if an individual fails to respond to a second biologic drug.

The British Association of Dermatologists (BAD) published a guideline on biological interventions in psoriasis in 2009.[11] The guideline recommends that adalimumab, etanercept, infliximab and ustekinumab may be considered in individuals with severe disease who meet at least one of the following criteria:

- Phototherapy and alternative standard systemic therapy are contraindicated or cannot be used due to the development of, or risk of developing, clinically important treatment related toxicity
- Intolerant to standard systemic therapy
- Unresponsive to standard systemic therapy

The guideline also recommends that methotrexate may be considered as a co-medication with adalimumab, etanercept and infliximab.

Additional information: comparators

The biologic therapies (etanercept, infliximab, adalimumab and ustekinumab) are the main comparators for patients with severe disease.

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Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)*
Apremilast	**30mg orally twice daily**	**7,150**
Infliximab[¥]	5 mg/kg intravenously at weeks 0, 2 and 6 weeks, then every 8 weeks	First year: 12,088 - 13,424 Subsequent years: 9,066 - 10,071
Ustekinumab	45mg (or 90mg[**]) subcutaneously at weeks 0 and 4 then every 12 weeks	First year: 12,882 Subsequent years: 8,588
Adalimumab	80mg subcutaneously then 40 mg alternate weeks*	First year: 9,860 Subsequent years: 9,156
Etanercept	25mg subcutaneously twice weekly; or 50mg subcutaneously weekly***	9,295

Doses are for general comparison and do not imply therapeutic equivalence. Costs for apremilast, adalimumab and etanercept from eVadis on 3 March 2015 and costs for ustekinumab and infliximab from MIMs March 2015. Costs based on a bodyweight of 70kg. * costs are based on one year of treatment but this will be shorter if there is no response. ** ustekinumab 90mg given if bodyweight >100kg.*** etanercept 50mg twice weekly may be given for 12 weeks if necessary then 25mg twice weekly or 50mg weekly. Costs do not take any patient access schemes into consideration.[¥] Costs for infliximab reflect the range of list prices for the reference product and biosimilar products.

Additional information: budget impact

The submitting company estimated there to be 12,413 patients eligible for treatment with apremilast in year 1 and year 5 respectively. Treatment uptake was estimated at 0.10% in year 1, rising to 2.10% in year 5. The discontinuation rate was estimated to be 20%. This resulted in 10 patients assumed to be treated in year 1 rising to 209 patients in year 5.

The submitting company estimated the gross medicines budget impact to be £71k in year 1 and £1.5m in year 5. As other medicines were assumed to be displaced, the net medicines budget impact was estimated to be £18k in year 1 and savings of £250k in year 5. These estimates were based on patient numbers in the severe disease population only and according to SMC clinical experts may underestimate the budget impact.

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

1. National Institute for Health and Care Excellence (NICE). Clinical Guideline 153. Psoriasis: the assessment and management of psoriasis. October 2012.

2. Celgene Ltd. Otezla® summary of product characteristics 23 January 2015

3. European Medicines Agency. Public Assessment Report: apremilast, procedure number EMEA/H/C/003746. www.ema.europa.eu [accessed 16 February 2015].

4. NCT01194219. Study to evaluate safety and effectiveness of oral apremilast (CC-10004) in patients with moderate to severe plaque psoriasis (ESTEEM 1) www.clinicaltrials.gov [accessed 16 February 2015]

5. NCT01232283. Study to evaluate safety and effectiveness of oral apremilast (CC-10004) in patients with moderate to severe plaque psoriasis (ESTEEM 2) www.clinicaltrials.gov [accessed 16 February 2015]

6. European Medicines Agency. Guideline on clinical investigation of medicinal products indicated for the treatment of psoriasis, CHMP/EWP/2454/02 . www.ema.europa.eu [accessed 16 February 2015]..

7. **Commercial in Confidence*

8. NCT01690299. Phase 3b safety and efficacy study of apremilast to treat moderate to severe plaque-plaque psoriasis. www.clinicaltrials.gov [accessed 5 March 2015]

9. **Commercial in Confidence*

10. Scottish Intercollegiate Guidelines Network (SIGN). Guideline number 121. Diagnosis and management of psoriasis and psoriatic arthritis in adults. October 2010.

11. The British Association of Dermatologists guidelines for biological interventions in psoriasis. British Journal of Dermatology 2009;161:987-1019.

12. Scottish Intercollegiate Guidelines Network (SIGN). Guideline number 121. Diagnosis and management of psoriasis and psoriatic arthritis in adults. October 2010.

This assessment is based on data submitted by the applicant company up to and including 18 April 2015.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy_Statements/Policy_Statements*

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.