The East of England
Priorities Advisory Committee
Hosted by PrescQIPP

GUIDANCE STATEMENT

Severe localised psoriasis

Use of biologic and oral therapies in adult patients with severe localised psoriasis, involving high impact or difficult to treat sites, which does not meet NICE criteria

PAC recommendations

1. Adalimumab is recommended as an option for treating high impact site psoriasis when the following criteria are met:
   - Disease has not responded to standard systemic therapies, including ciclosporin, methotrexate and phototherapy in line with local pathways and there is a
   - Physicians Global Assessment (PGA) of 'severe' or 'very severe' and
   - Dermatology Life Quality Index (DLQI) > 10 and
   - At least one localised, high impact and difficult to treat site, such as the face, scalp, palms, soles, flexures and genitals, assessed by the clinician at baseline (see measures for assessing disease severity).
2. Apremilast can be considered as an alternative for patients where adalimumab is contraindicated or not suitable, e.g. patients who are unable to use a subcutaneous device, or who decline biologic therapy.
3. Treatment should be discontinued if:
   - There is a failure to demonstrate an adequate response to treatment at 16 weeks and at subsequent reviews defined as:
     - » PGA of clear, nearly clear or mild disease OR 50% improvement in an appropriate disease score outlined by the clinician at baseline (see page 7 for further details) and
     - » A 5-point reduction in DLQI score from baseline.
   - Therapy is not tolerated or becomes contraindicated.
4. Routine commissioning of subsequent biologic agents if response to treatment with adalimumab/ apremilast is inadequate, or therapy is not tolerated or becomes contraindicated, is **NOT** recommended.
5. Baseline and outcome data must be submitted to the commissioner for the purposes of auditing this policy.

Background

The updated 2017 NICE clinical guideline (CG153) for assessment and management of psoriasis recommends biologic therapy or apremilast for people with psoriasis requiring systemic therapy, in line with the current individual NICE technology appraisals.[1]

Biologic therapy or oral therapies with apremilast or dimethyl fumarate, are recommended as an option for treating plaque psoriasis if:

- Standard systemic treatments such as methotrexate, ciclosporin and phototherapy have failed, are not tolerated or are contraindicated, and
- The psoriasis has a large impact on physical, psychological or social functioning resulting in a DLQI >10 (DLQI >18 for infliximab), and
- Psoriasis is severe, defined by a total Psoriasis Area and Severity Index or PASI ≥10 (PASI ≥20 for infliximab).[2-14]

Patients with localised psoriasis affecting sensitive or difficult to treat areas such as the face, scalp, palms, nails, soles, flexures and genitals (also known as high impact sites), but with a PASI score < 10 are not eligible for biologic therapy or oral therapy with apremilast or dimethyl fumarate under the current NICE technology appraisals.[2-14]

NICE CG153 recommends topical treatments for the general management of all types of psoriasis.[1] Non-biologic systemic treatments, such as methotrexate and ciclosporin, can be offered to patients with any type of psoriasis which cannot be controlled by topical treatments, and has a significant impact on physical, psychological and social wellbeing, and one or more of the following apply:

- Psoriasis is extensive (for example, more than 10% of body surface area affected or a PASI score of more than 10) or
- Psoriasis is localised and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at high impact sites) or
- Phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within three months).

Severe localised psoriasis affecting sensitive or difficult to treat areas, is associated with significant functional impairment and/or high levels of distress.[15]

Evidence

The British Association of Dermatologists (BAD) recommend that biologic therapy should be offered for treatment of psoriasis in patients with high impact site psoriasis if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated. However, the recommendation does not cover the use of the oral therapies apremilast or dimethyl fumarate. In addition it does not recommend a specific first line biologic for the treatment of any type of psoriasis. However, for adults with psoriasis who also have evidence of psoriatic arthritis, a TNF antagonist, such as adalimumab or an interleukin-17 antagonist antagonist should be offered as first line biologic treatment.[15]

There is limited information on the use of biologic therapy for difficult to treat psoriasis involving high impact or sensitive areas and there appears to be no comparative data.

In 2017 and 2020, the BAD published recommendations for the use of biologic therapy in the treatment of psoriasis, supported by meta-analyses on short term efficacy of biologics.[16,17] The results showed that for some biologics, there is evidence of efficacy at some high impact sites including:

- Palmoplantar pustulosis (PPP)/nail psoriasis - adalimumab, etanercept, guselkumab, infliximab, ixekizumab, ustekinumab
- Palmoplantar psoriasis (non-pustular) – secukinumab
- Nail psoriasis – secukinumab (Note: Included trial did not include patients with PPP).
- Genital psoriasis – ixekizumab.

Adalimumab

The 2020 BAD meta-analysis included a phase 3, randomized, placebo-controlled trial which evaluated the safety and efficacy of adalimumab (ADA) in patients with moderate-to-severe fingernail psoriasis and moderate to severe plaque psoriasis. In the initial 26-weeks (Period A), 217 patients were

randomized in a 1:1 ratio to 40mg ADA (n=109) every other week or to placebo (n=108) from week 1. All patients assigned to ADA had an 80mg dose at week 0. Patients continued with or switched to 40mg ADA every-other-week treatment in the subsequent 26-week open-label extension (OLE) period. The main efficacy evaluations were ≥ 75% improvement in total-fingernail modified nail psoriasis severity index (mNAPSI 75), and achievement of Physicians Global Assessment for Fingernail Psoriasis (PGA-F) score of clear (0) or minimal disease (1) with a ≥ 2-grade improvement from baseline, across the trial for patients who continued ADA from Period A through the OLE (Continuous-ADA Population). Of the 217 patients initially randomized in Period A, 188 entered the OLE period; (n=94 from both placebo and ADA groups). For the Continuous-ADA Population (n=109), the rate of achievement of total-fingernail mNAPSI 75 was 25.9% at week 16, increased to 47.4% at week 26 and to 54.5% at week 52. The rate of achievement of PGA-F 0/1 with ≥2 grades of improvement from baseline was 29.4% at week 16, increased to 51.1% at week 26 and to 55.6% at week 52. The majority of adverse events were mild (22.7%) or moderate (31.5%) in severity. The most common events were nasopharyngitis (12.3%) and upper respiratory tract infection (8.4%). The rates of serious adverse events and of serious infections were 6.9% and 3.4%, respectively.[18,19]

A 16 week, multicentre, randomized, double-blind, placebo-controlled study with an added 12-week open label period (excluded from the 2017 meta-analysis due to too few patients in placebo arm), enrolled 81 patients with moderate (75%) to severe (25%) chronic plaque psoriasis involving hands and/or feet. Seventy two patients were randomised in a 2:1 ratio to receive either ADA 40mg (n=49) every other week (80mg at week 0) or placebo (n=23) for 16 weeks. Patients continued or switched to ADA in the subsequent 12-week period. Those who switched to ADA from placebo were given an 80mg dose at week 16. The primary end point was the proportion of patients with a Physician's Global Assessment of hands and/or feet (hfPGA) score of "clear" or "almost clear" at week 16. Other efficacy measures included the Erythema, Scaling, Induration, Fissuring (ESIF) scale for characterizing palmoplantar disease, Nail Psoriasis Severity Index (NAPSI), and psoriasis/psoriatic arthritis pain scores measured by visual analog scale (VAS). At week 16, 31% and 4% of patients randomized to ADA and placebo respectively, achieved an hfPGA score of clear or almost clear (p = 0.01). The percentages of patients achieving greater than 75% improvement in ESIF (ESIF 75) at week 16 were 29% and 4% (p = 0.03) for ADA and placebo treated patients respectively. Fifty percent of patients in ADA group achieved significantly higher mean percentage NAPSI improvement compared with 8% in placebo group. The majority of adverse events in both groups were mild to moderate. In both periods combined, nasopharyngitis (27% and 13% for ADA and placebo treated patients, respectively) was most frequently reported.[20]

Another phase IIIb, multicentre, randomized, double-blind, vehicle-controlled study (excluded from the 2017 meta-analysis due to inappropriate comparison) reported the efficacy and safety of ADA with and without calcipotriol/betamethasone topical treatment in patients with moderate to severe psoriasis (BELIEVE study). A total of 730 patients received either ADA with topical calcipotriol/betamethasone (C/B) (n=366) or ADA with drug-free vehicle (n=364). The primary endpoint was the proportion of patients in each treatment group who achieved a 75% improvement in the PASI (PASI 75 response) at week 16. Secondary endpoints, measured throughout the study, included PASI 75 (other than week 16), 90% and 100% improvement in the PASI (PASI 90 and PASI 100 responses, respectively), mean PASI score, PGA of 'clear' or 'minimal', and patient-reported outcomes, using VAS for pruritus and pain, and the DLQI. At week 16, a PASI 75 response was achieved by 64.8% of patients treated with ADA + C/B vs. 70.9% treated with ADA + vehicle, but results were not statistically different (p = 0.086). More patients on monotherapy achieved PASI 90 and PASI 100 responses [PASI 90: 38.8% for ADA + C/B vs. 50% for ADA + vehicle (p = 0.002); and PASI 100: 15.3% for ADA + C/B vs. 24.2% for ADA + vehicle (p = 0.003)]. Mean PASI scores decreased for both groups over time, and at week 16, were 4.7±6.2 and 3.9±7.1 for ADA + C/B and ADA + vehicle, respectively (p = 0.110). Improvements in PGA were seen in both treatment groups, with a total of 60.5% of patients overall having a score of 'clear' or 'minimal' at week 16.[21]

In 2015, the same author published a sub-analysis of effects on scalp and nails in the BELIEVE study. Of the 730 enrolled patients, 663 (91.3%), 457 (63.1%) and 433 (60.1%) had psoriasis of the scalp, nails, or both, respectively. Similar proportions of patients with (68.2%) and without (63.5%) scalp involvement achieved a PASI 75 response at week 16 [adjusted odds ratio (OR) 1.34; p = 0.320]. PASI 75 response rates were lower in patients with nail psoriasis compared with patients without nail psoriasis at week 8 (53.0% vs. 62.9%; OR, 0.68; p = 0.019) and week 16 (65.0% vs. 73.0%; OR 0.70; p = 0.052). PASI 75 response rates were 66.1% in patients with scalp and nail involvement and 70.8% in patients without both scalp and nail involvement at week 16 (OR 0.87; p = 0.423). Patients in all scalp and nail subgroups reported improvements in DLQI and Visual Analog Scale (VAS) pain scores throughout the study. Patients with scalp psoriasis exhibited improvements in scalp symptoms demonstrated by a median (mean ± SD) decrease from baseline Psoriasis Scalp Severity Index (PSSI) at week 16 of 100% (77.2 ± 96.9%). Patients with nail psoriasis improved, demonstrated by a median (mean ± SD) decrease from baseline NAPSI at week 16 of 39.5% (9.4 ± 164.5%).[22]

In a recent small observational prospective study, 39 patients with difficult to treat psoriasis received adalimumab 40mg every two weeks for 24 weeks. Four (10%) patients were children with a mean age of 15 years old (the youngest patient was 12 years old). Nails psoriasis affected 16 (41%) patients, palmoplantar psoriasis affected three (7%) patients, while scalp psoriasis was diagnosed in 34 (87%) patients, of which four were children. Genital psoriasis affected seven (18%) patients, one of whom was a child. Safety and efficacy were assessed at weeks 0, 6, 12, and 24 using PASI, Visual Analogue Scale for Pain (PAIN VAS), Visual Analogue Scale for Itch (ITCH VAS), DLQI, NAPSI, Static PGA of Genitalia (sPGA-G), hfPGA, and PSSI. Thirty (88.24%) patients achieved PASI 75 at week 16 (p = 0.004), 29 (87.88%) patients achieved PSSI 75 at week 16 (p = 0.05). A total of 62.5% of patients achieved NAPSI 75 at week 24 (p = 0.001) while 97% of patients achieved hfPGA (0-1) at week 24, but without any significant result (p = 0.585). PSSI (week 0 mean value = 22.09, SD = 13.95) showed improvement at the 4-week visit (mean value = 4.45, SD = 4.74, p < 0.001). hfPGA also presented improvement, starting from a mean value of 3.67 at week 0 (SD = 0.58) and achieving a mean value of 1.67 (SD = 0.58) at week 4 (p < 0.001). NAPSI (week 0 mean value = 19.94, SD = 13.23, p < 0.001), instead, decreased slower (week 4 = 15.56, SD = 11.87; week 24 = 7.93, SD = 10.69, p < 0.001). sPGA-G (week 0 mean value = 3.75, SD = 0.50) showed an improvement until week 16 (mean value =1, SD = 1.15,p = 0.01), while at week 24 it increased (mean value = 1.50, SD = 2.07, p = 0.114). This study comments that most studies describing difficult to treat psoriasis are post-hoc analysis of clinical trials, however this is a real life evaluation of adalimumab efficacy in all difficult to treat areas in both adults and children. The pace of improvement is different in each difficult to treat area. Scalp psoriasis reached a complete fast healing in the first month of treatment, while nail psoriasis took more time to improve, although a constant improvement was seen over time, unlike other areas.[23]

The BAD meta-analyses did not include the oral therapies; apremilast or dimethyl fumarate. As part of this EoE PAC review, an additional literature search was undertaken for evidence to support the use of oral therapies in the treatment of high impact site psoriasis.

Apremilast

The main studies evaluating the efficacy and safety of apremilast for psoriasis are ESTEEM-1 and ESTEEM-2. These are multi-centre, randomised, double-blind, placebo-controlled studies that enrolled patients with chronic plaque psoriasis who had a body surface area involvement of 10% or over, PASI score ≥12, static PGA of ≥3 (moderate or severe), and who were candidates for phototherapy or systemic therapy. Both studies had a similar design through to week 32. A total of 1255 patients were randomised to treatment, with 836 taking apremilast and 394 receiving placebo. In both studies, patients were randomised 2:1 to apremilast 30mg twice daily or placebo for 16 weeks (placebo-controlled phase) and from weeks 16-32, all patients received apremilast 30mg twice daily (maintenance phase). During the randomised treatment withdrawal phase (weeks 32-52), patients originally randomised to apremilast who achieved at least a 75% reduction in their PASI score (PASI 75) (ESTEEM 1) or a 50% reduction in their PASI score (PASI-50) (ESTEEM 2) were re-randomised at week 32 to either placebo or apremilast 30mg twice daily. Patients who were re-randomised to placebo and

who lost PASI 75 response (ESTEEM 1) or lost 50% of the PASI improvement at week 32 compared to baseline (ESTEEM 2) were retreated with apremilast 30mg twice daily. Patients who did not achieve the designated PASI response by week 32, or who were initially randomised to placebo, remained on apremilast until week 52.

The primary endpoint was the proportion of patients achieving PASI 75 at week 16. The secondary efficacy end point was the proportion of patients achieving sPGA score of 0 (clear) or 1 (almost clear) with a point reduction of 2 or more from baseline at week 16. In both studies at week 16, more patients in apremilast group achieved PASI 75 compared to placebo (ESTEEM 1: 33.1% vs 5.3%, p<0.0001; ESTEEM 2: 28.8% vs 5.8%, p<0.001). The sPGA score of 0 or 1 at week 16 was also achieved by significantly more patients receiving apremilast vs. placebo (ESTEEM 1: 21.7% vs 3.9%; ESTEEM 2: 20.4% vs 4.4%; p < 0.001). Most adverse effects were mild to moderate in severity; the most common were nausea, diarrhoea, upper respiratory tract infection, nasopharyngitis, tension headache and headache.[24,25]

A post hoc analysis of data pooled from phase IIb (PSOR-005) and phase III (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1 and 2) clinical studies was conducted to determine the effect of apremilast 30mg twice daily versus placebo at week 16 in a subset of patients with moderate to severe plaque psoriasis with active palmoplantar psoriasis (baseline Palmoplantar Psoriasis Physician Global Assessment [PPPGA] score ≥1). PSOR-005 was a multicentre, randomized, placebo-controlled, dose-ranging study of apremilast in patients with moderate to severe plaque psoriasis.

In the three studies, a total of 427 patients had palmoplantar psoriasis at baseline (29.8% of the 1431 participants), with 153 receiving placebo and 274 taking aprelimast. Of the 427, 144 had moderate to severe disease (PPPGA of ≥3). In the studies, 52 of the 144 patients with moderate to severe disease received placebo and the remaining 92 received apremilast. At 16 weeks, patients with moderate to severe disease treated with apremilast were more likely to have a PPPGA of 0 or 1 compared with placebo (48% (44/92) vs 27% (14/52); p = 0.021). Common adverse events occurring in 5% or more of patients receiving apremilast included diarrhoea, nausea, upper respiratory tract infection, nasopharyngitis, vomiting, tension headache, and headache. None of the apremilast studies assessed the percentage of psoriasis body surface area involvement or localization of lesions on the palms and soles in patients with palmoplantar psoriasis, nor did they note pustular versus non-pustular forms.[26]

A separate analysis of the ESTEEM trials on the efficacy of apremilast in difficult to treat nail and scalp psoriasis was published in 2016. At baseline, out of 1255 patients, 824 had nail psoriasis (target nail NAPSI score ≥1), and 832 had moderate to very severe scalp psoriasis (Scalp Physician Global Assessment (ScPGA) score ≥3). In both ESTEEM-1 and ESTEEM-2, the mean percent change in NAPSI score at 16 weeks was −22.5% (p < 0.0001) and −29.0% (p = 0.0052) with apremilast versus +6.5% and −7.1% with placebo. At week 16, the proportion of patients who achieved a NAPSI-50 was 33.3% and 44.6% with apremilast versus 14.9% and 18.7% with placebo (p < 0.0001). Among patients with moderate to very severe scalp psoriasis (ScPGA score ≥3) at baseline, achievement of ScPGA score of 0 (clear) or 1 (minimal) at week 16 was 46.5% and 40.9% with apremilast versus 17.5% and 17.2% with placebo (p < 0.0001).[27]

A randomised, double-blind, placebo-controlled trial on the effectiveness of apremilast for palmoplantar psoriasis was published in 2018. In this study, 100 participants with moderate to severe palmoplantar psoriasis (PPPGA of ≥3) were randomized to either apremilast 30mg twice a day or placebo for 16 weeks. At week 16, all patients received apremilast 30mg twice a day until week 32. The primary endpoint was the proportion of patients who achieved a PPPGA score of 0 or 1 at week 16. Secondary endpoints included change from baseline in mean PPPGA, palmoplantar PASI (PPPASI) and palmoplantar psoriasis surface area (PPPSA) at week 16, change from baseline in PPPASI at week 32 for patients randomized to apremilast, and proportion of patients achieving a PPPGA of 0 or 1 after 32 weeks of treatment with apremilast.

At week 16, the proportion of participants achieving a PPPGA of 0 or 1 was greater in the apremilast group compared to placebo, however this did not reach clinical significance (14% vs 4%; p = 0.16). By week 32, 24% of participants had a PPPGA of 0 or 1. For other secondary endpoints, the proportion of patients achieving a 75% in PPPASI was greater in apremilast than placebo and just reached clinical significance (22% vs. 8%; p = 0.0499). The average improvement score of PPPASI was greater with apremilast than placebo (-7.4 ±7.1 vs. -3.6 ± 5.9; p = 0.017). Exploratory end points showed an improvement in DLQI score with apremilast compared to placebo (−4.3 ± 5.1vs. −0.8 ± 4.5; p = 0.0004) and in reducing activity impairment with apremilast compared to placebo (−11.0 ± 22.3 vs. 2.5 ± 25.5; p = 0.0063).[28]

In a phase 3b, double-blind, placebo-controlled study, 303 adults with moderate to severe scalp psoriasis who had inadequate response/intolerance to at least one topical scalp psoriasis therapy were randomised 2:1 to apremilast (n=201) 30mg twice daily or placebo (n=102) for 16 weeks. At week 16, patients initially randomized to placebo were switched to apremilast [placebo/apremilast (P/A) group] and patients initially randomized to apremilast continued active treatment [apremilast/apremilast (A/A) group] through to week 32. The primary endpoint was the proportion of patients who achieved ScPGA response, defined as score of 0 (clear) or 1 (almost clear), with at least a 2-point reduction, at week 16. Secondary endpoints included at least a 4-point improvement from baseline in whole body itch and scalp itch Numeric Rating Scales (NRSs) and mean improvement in DLQI at week 16.

At week 16, significantly more patients in the apremilast group achieved the primary endpoint - 43.3% (95% confidence interval (CI) 36.2-50.5) vs. 13.7% (95% CI 6.6-20.8) on placebo, p<0.0001. For the secondary endpoints, more patients on aprelimast achieved a 4 point or greater improvement in scalp itch Numeric Rating Scale (NRS) was - 47.1% (95% CI 39.5-54.7) vs. 21.1% (95% CI 11.8-30.3), and whole body itch NRS - 45.5% (95% CI 38.1-52.9) vs. 22.5% (95% CI 13.7-31.3), and significantly greater DLQI improvement was observed versus placebo (-6.7 vs -3.8; all p < 0.0001). Common adverse events with apremilast were diarrhoea (30.5%), nausea (21.5%), headache (12.0%), and vomiting (5.5%). At week 32, ScPGA response was sustained in the A/A group (45.5%) and occurred in the P/A group (63.1%). 49.3% of patients in both groups (A/A and P/A), achieved NRS-Scalp Itch response, and 45.7% (A/A) and 59.7% (P/A) achieved NRS-Whole Body Itch response. The mean change (improvement) in DLQI total score was −6.8 in the A/A group and −8.0 in the P/A group.[29,30]

Dimethyl fumarate

In 2015, Cochrane published a systematic review of oral fumaric acid esters (FAEs) in psoriasis. Six studies with a total of 544 participants were included in the review; five compared FAEs with placebo and one used methotrexate as an active comparator. Participants in the included studies had chronic plaque psoriasis in two studies; various psoriasis subtypes in two studies (chronic plaque, guttate, pustular and erythrodermic) and unreported psoriasis subtype in two studies. PASI score at baseline was reported in only three studies, and was required to be ≥10 in one study, ≥12 in one study and 16–24 in one study. The review found limited evidence to suggest that FAEs, containing dimethyl fumarate as active component, are superior to placebo in the treatment of psoriasis and very low-quality evidence to determine the relative efficacy of FAEs compared with methotrexate. Commonly reported adverse effects associated with FAEs include gastrointestinal symptoms (58% of participants in one study), flushing (42%, 48% and 95% in three studies), eosinophilia (19% and 38% in two studies) and reversible proteinuria (30% in one study). However, the evidence was limited due to a lack of full reports and inconsistencies of reporting. No long-term studies were identified to comment on the long-term efficacy and safety of FAEs in psoriasis. Some studies included participants with various types of psoriasis, but the outcomes reported did not indicate whether the response to FAEs varied between different subgroups.[31]

Commissioning criteria

The North Central London and South East London Area Prescribing Committees have separately agreed local Psoriasis Biologic Drug treatment pathways which include specific recommendations and clinical threshold criteria for treating high impact site psoriasis.[32,33]

As there is a lack of robust data, but a clear clinical need in this patient group for use in all forms of severe localised disease, PAC have agreed to recommend commissioning of a trial of adalimumab or apremilast for this patient group, broadly in line with these recommendations as follows.

Eligibility criteria for therapy

Adalimumab (the best value product) is recommended as first line treatment option for high impact site psoriasis in patients when the following criteria are met:

- Disease has not responded to other systemic therapies, including ciclosporin, methotrexate and phototherapy in line with local pathways and
- Physicians Global Assessment (PGA) of 'severe' or 'very severe' and
- DLQI >10 and
- At least one localised, high impact and difficult to treat site, such as the face, scalp, palms, soles, flexures and genitals assessed by the clinician at baseline.

Apremilast can be considered as an alternative for patients where adalimumab is contraindicated or not suitable, e.g. patient is unable to use a subcutaneous device, or who decline biologic therapy.

Measures for assessing disease severity

Disease severity must be assessed at baseline using an appropriate scoring system. The following scoring systems may be considered:

- Severe scalp disease: must be confirmed by documenting ≥30% of scalp surface area affected and a PGA of severe. A Psoriasis Scalp Severity Index (PSSI) score of ≥20 (0-72 scale) may also be used.
- Severe palm/sole disease or other high impact sites: utilise an adjusted PASI score to assist with assessing response from baseline.
- Severe nail disease: a NAPSI score may be used for severe nail disease or a PPPASI >20 for palmoplantar pustulosis.
- Physicians Global Assessment (PGA) classified as clear, nearly clear, mild, moderate, severe or very severe.
- Dermatology Life Quality Index (DLQI).

Assessment of response

Treatment should be stopped in people whose high impact site psoriasis has not responded adequately at 16 weeks or following a review, at least annually.

An adequate response is defined as:

- PGA of clear, nearly clear or mild disease OR 50% improvement in an appropriate disease score outlined by the clinician at baseline AND
- A 5-point reduction in DLQI score from baseline.

Discontinuation criteria

Treatment with biologic or oral therapy should be discontinued if:

- Therapy is not tolerated or becomes contraindicated or
- Response is not adequate as defined above.

Patient numbers and cost impact assessment

Patient numbers at time of publication were unknown. Uptake will be monitored via Bluteq.

Comments sought from: East of England clinicians via PAC members

Author: Monika Wojtowicz

Document history

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Assessment against ethical and commissioning principles

Treatment assessed	Adalimumab and apremilast in adult patients with severe localised psoriasis, involving high impact or difficult to treat sites, which does not meet NICE criteria.

East of England Priorities Advisory Committee recommendation	1. Adalimumab is recommended as an option for treating high impact site psoriasis when the following criteria are met: • Disease has not responded to standard systemic therapies, including ciclosporin, methotrexate and phototherapy in line with local pathways and there is a • Physicians Global Assessment (PGA) of 'severe' or 'very severe' and • Dermatology Life Quality Index (DLQI) >10 and • At least one localised, high impact and difficult to treat site, such as the face, scalp, palms, soles, flexures and genitals, assessed by the clinician at baseline (see measures for assessing disease severity). 2. Apremilast can be considered as an alternative for patients where adalimumab is contraindicated or not suitable, e.g. patients who are unable to use a subcutaneous device, or who decline biologic therapy. 3. Treatment should be discontinued if: • There is a failure to demonstrate an adequate response to treatment at 16 weeks and at subsequent reviews defined as: » PGA of clear, nearly clear or mild disease OR 50% improvement in an appropriate disease score outlined by the clinician at baseline (see page 7 for further details) and » A 5-point reduction in DLQI score from baseline. • Therapy is not tolerated or becomes contraindicated. 4. Routine commissioning of subsequent biologic agents if response to treatment with adalimumab/apremilast is inadequate, or therapy is not tolerated or becomes contraindicated, is NOT recommended. 5. Baseline and outcome data must be submitted to the commissioner for the purposes of auditing this policy.
Clinical effectiveness	Data from meta-analyses and clinical trials indicate that adalimumab and apremilast can be effective in the management of moderate to severe palmoplantar, scalp and nail psoriasis.
Cost effectiveness	There is no cost effectiveness data on the use of adalimumab or apremilast in severe localised psoriasis but the cost of treatment might be offset by a significant improvement in patients' QoL, physical, social or psychological function.
Equity	No issues identified.
Needs of the community	The exact number of patients who would be eligible for treatment remains unclear, but is expected to be low as the vast majority of patients would reach a PASI score of >10 and would therefore be eligible for treatment under the appropriate NICE Guidance and Technology Appraisals.
Need for healthcare (incorporates patient choice and exceptional need)	A small group of patients who do not meet the NICE criteria would benefit from this treatment.

Policy drivers	Decisions from other bodies North Central London. High Cost Drug Treatment Pathway for Psoriasis. June 2020 South East London Area Prescribing Committee. Psoriasis: Biologic Drug Treatment Pathway. Published June 2018, last reviewed July 2020
Disinvestment	None