East Lancashire Health Economy Medicine Management Board

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Psoriasis: LMMG Biologic and High Cost Drug Commissioning Pathway

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Lancashire & South Cumbria Medicines Management Group NHS

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1.0		David Prayle	12 April 2016
1.1		David Prayle	3 August 2016
1.2	Post LMMG minor accuracy changes made	David Prayle	14 September 2016
1.3	Addition of Ixekizumab	David Prayle	March 2018
1.4	Addition of brodalumab and nonbiologic high cost drugs, title updated to include reference to nonbiologic drugs	David Prayle	May 2018
1.5	Addition of guselkumab	David Prayle	November 2018
1.6	Addition of tildrakizumab and risaknizumab	Sharon Andrew, David Prayle	September 2019
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Acknowledgments

The Greater Manchester Medicines Management Group's guideline on the treatment of psoriasis was used as a reference in the development of this guideline.

Psoriasis: LMMG Biologic Commissioning Pathway

Biologic agents may only be initiated if the patient's psoriasis has not responded to standard systemic therapies including, for example, ciclosporin, methotrexate and PUVA/UVB; or the person is intolerant of, or has a contraindication to, these treatments

Biosimilars

Biosimilar versions of biologics are becoming available, usually with a lower cost than the originator product.

The prescribing of biosimilar preparations should be by brand name, followed by the concentration and recommended daily dose in units and a statement of the formulation.

The preparation with the lowest acquisition cost (taking into account administration costs, dosage and price per dose) should normally be used. However, it is recognised that biosimilar prices may vary over time and that other factors such as the availability of stability data may influence the choice of treatment.

It may not always be appropriate for organisations to switch formulary choice in response to minor price variations.

PASI ≥ 10 and DLQI ≥ 10

PASI ≥ 20 and DLQI ≥ 18

Adalimumab (TA146) Ustekinumab (TA180) Guselkumab (TA521) Risankizumab (TA596) Certolizumab pegol (TA574)	Etanercept (TA103) Secukinumab (TA350) Ixekizumab (TA442) Brodalumab (TA511)	Tildrakizumab (TA575)	Infliximab (TA134)
Review at 16 weeks	Review at 12 weeks	Review at 12-28 weeks, discontinue at 28 weeks if criteria below not met	Review at 10 weeks

Discontinue if the biologic is not tolerated or becomes contraindicated.
Discontinue if response is not adequate at the above review dates or the psoriasis initially responds adequately but subsequently loses this response. Adequate response is defined as either:

- a 75% reduction in the PASI score (PASI 75) from when treatment started **or**
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from start of treatment

Second line treatment: NICE CG153 supports the use of an alternative biologic as second line treatment if the initial biologic is discontinued for the criteria listed above

Third line treatment: For adults in whom there is an inadequate response to a second biological drug, NICE CG153 recommends seeking supra-specialist advice from a clinician with expertise in biological therapy. Choose alternative third biologic with supra-specialist advice.

Disease Background

Psoriasis is an inflammatory skin disease that typically follows a relapsing and remitting course. The prevalence of psoriasis is estimated to be around 1.3–2.2% in the UK. Psoriasis can occur at any age, although is uncommon in children (0.71%) and the majority of cases occur before 35 years.[1] Plaque psoriasis is characterised by well-delineated red, scaly plaques that vary in extent from a few patches to generalised involvement.[1]

Psoriasis for many people results in profound functional, psychological, and social morbidity, with consequent reduced levels of employment and income.[1]

First-line therapy includes traditional topical therapies such as corticosteroids, vitamin D and vitamin D analogues, dithranol and tar preparations.

Second-line therapy includes the phototherapies (broad or narrow band ultraviolet B light and psoralen plus UVA light [PUVA]) and systemic non-biological agents such as ciclosporin, methotrexate and acitretin.

Systemic biological therapies are reserved for **third line use**.

Apremilast is a Phosphodiesterase type-4 inhibitor, Dimethyl Fumarate is an oral fumaric acid ester (FAE) and both should be reserved for **fourth line use** (third line use if systemic therapy is contraindicated or not tolerated).

NICE have estimated that a benchmark rate for the number of people with psoriasis eligible for and receiving treatment with biologic drugs is 0.045%, or 45 per 100,000 adults aged 18 years or older per year.[2]

NICE Guidance - Biologics

NICE have produced individual Technology Appraisals for each of the eight currently available biological drugs for the treatment of plaque psoriasis.

The Technology Appraisals were published incrementally, between 2006 and 2018, as evidence for the newly available drugs became available. The NICE pathway lists the following options for the treatment of 'severe psoriasis', defined as exhibiting a Psoriasis Area and Severity Index (PASI) of ≥10 and Dermatology Life quality Index (DLQI) of >10:

- Etanercept (TNFα inhibitor) - TA103 (2006)[3]
- Adalimumab (TNFα inhibitor) - TA146 (2008)[4]
- Ustekinumab (Interleukin 12/23 inhibitor) - TA180 (2009)[5]
- Secukinumab (Interleukin 17A inhibitor) - TA350 (2015)[6]
- Ixekizumab (Interleukin 17A inhibitor) – TA442 (2017)[7]
- Brodalumab (Interleukin 17A inhibitor) – TA511 (2018)[8]
- Guselkumab (Interleukin 23 inhibitor) – TA521 (2018)[9]
- Tildrakizumab (Interleukin 23 inhibitor) – TA575 (2019)[10]
- Risankizumab (Interleukin 23 inhibitor) – TA596 (2019)[11]

The following is listed for the treatment of 'very severe psoriasis', defined as exhibiting a PASI ≥20 and DLQI >18:

- Infliximab (TNFα inhibitor) - TA134 (2008)[12]

The biological agents listed above can only be initiated if the patient's psoriasis has not responded to standard systemic therapies including ciclosporin, methotrexate and PUVA; or the person is intolerant of, or has a contraindication to, these treatments.

In Clinical Guideline 153, Psoriasis: assessment and management,[1] which was produced in 2012 before secukinumab was reviewed, NICE recommends that clinicians should consider changing to an alternative biological drug in adults if:

- the psoriasis does not respond adequately to a first biological drug as defined in NICE technology appraisals (at 10 weeks after starting treatment for infliximab, 12 weeks for etanercept, and 16 weeks for adalimumab and ustekinumab; primary failure) **or**
- the psoriasis initially responds adequately but subsequently loses this response, (secondary failure) **or**
- the first biological drug cannot be tolerated or becomes contraindicated.

For adults in whom there is an inadequate response to a second biological drug, seek supra-specialist advice from a clinician with expertise in biological therapy.[1]

An adequate response is defined as either:

- a 75% reduction in the PASI score (PASI 75) from when treatment started or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from start of treatment.

A second biologic increases the likelihood of people responding to treatment, avoiding an onward referral to best supportive care.[16] NICE estimate that if the proportion of patients who do not respond to a first-line biological drug, but are prescribed a second-line biologic were to increase from 70% to 90%, it is estimated that this would lead to a cost saving of approximately £730 per 100,000 population.[16]

Apremilast and Dimethyl Fumarate

The use of Apremilast and Dimethyl Fumarate in the treatment of severe plaque psoriasis are recommended as fourth line options, after the use of systemic biologics.

If systemic biologic therapies are contraindicated or not tolerated then Apremilast and Dimethyl Fumarate may be used as alternative third line therapies.

Apremilast and dimethyl fumarate should be used as described in their respective NICE Technology Appraisals.

NICE TA 419 - **Apremilast** for treating moderate to severe plaque psoriasis[13] states: Apremilast is recommended as an option for treating chronic plaque psoriasis in adults whose disease has not responded to other systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and ultraviolet-A light), or when these treatments are contraindicated or not tolerated, only if:

- the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10
- treatment is stopped if the psoriasis has not responded adequately at 16 weeks; an adequate response is defined as:
    - a 75% reduction in the PASI score (PASI 75) from when treatment started or
    - a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from start of treatment
- the company provides apremilast with the discount agreed in the patient access scheme.

NICE TA475 - **Dimethyl fumarate** for treating moderate to severe plaque psoriasis[14] states: Dimethyl fumarate is recommended as an option for treating plaque psoriasis in adults, only if the disease:

- is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 **and**
- has not responded to other systemic therapies, including, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated.
- Stop dimethyl fumarate treatment at 16 weeks if the psoriasis has not responded adequately. An adequate response is defined as:

- a 75% reduction in the PASI score (PASI 75) from when treatment started or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

Guideline Development

Other areas' psoriasis guidelines were reviewed as part of the development of the Lancashire guideline. Guidelines reviewed include those of the Greater Manchester Medicines Management Group[15] the Pan Mersey Area Prescribing Committee[16] and the Prescribing Clinical Network.[17] Of these, the Greater Manchester Medicines Management Group's work was of most relevance as Lancashire patients are often referred to Manchester for psoriasis treatments and the Greater Manchester Pathway was the most current available, being updated in July 2015 and containing the most recent NICE Technology Appraisals.

Biologic Pathway Principles

The psoriasis pathway in Greater Manchester allows a second or third biological therapy to be tried after a first has failed.[13] Patients requiring biological therapy should fulfil the NICE criteria for initiation and continuing therapy.

The group considered the evidence base for use of a second biologic after a first had failed and noted that the data was limited with varying response rates; however it was also noted that response to one biologic agent is not predictive of a patient's response to a second agent. Costs of all agents are similar (annual cost: £9,282-£10,228) and use of a second agent would be in place of the first so would be cost neutral. It was also noted that alternative treatments would be similarly priced with varying results. NICE Clinical Guideline 153[1] on the assessment and management of psoriasis recommends switching people to a second biologic after the first has failed.

NICE do not prioritise the biologic agents to be used for psoriasis and feedback from local clinicians has indicated that this lack of prescriptiveness is valued and should be reflected in any guideline developed by the LMMG. There are generally agreed principles such as switching from TNF inhibitors to another class of drug in case of drug failure which would be followed, however there are situations where this may not be the best course of action and this is based on specialist clinical decision making.

All drugs are highly efficacious initially, however biologic drugs have an attrition rate year on year of approximately 15%, therefore if switches are not allowed longer term disease control will be lost. The guideline allows three lines of treatment with a biologic as patients will usually be within the supra-specialist advice setting and any third line treatment will be recommended by such a specialist. The guideline does not cover the use of a subsequent biologic after a third has failed due to a lack of available data in this situation (however the use of the nonbiologics apremilast and dimethyl fumarate is covered). If requested this would need to be reviewed by commissioners on a case by case basis to assess affordability.

Financial Impact of Providing a Biologic

Biologics for the treatment of psoriasis are perceived to be expensive, however NICE have provided some cost estimates that show biologics will be effectively cost neutral when compared to best supportive care. Allowing a third choice of biologic, at which point NICE recommend seeking supra-specialist opinion,[1] will be cost neutral. The costing report from NICE Clinical Guideline 153 provides costings for best supportive care, which on average will cost £10,980 for one year, as follows:[18]

Treatment Type	Resource components	Costs per treatment	Proportion receiving treatment	Average cost
Drug related costs				
Methotrexate		£404	45%	£182
Ciclosporin		£2,372	45%	£1,068
No drug	5 outpatient visits	£300	10%	£30
Other treatment				
Day Care Centre	5 visits	£1,813	100%	£1,813
Narrow-band UVB	1 course	£1,882	16%	£301
Inpatient care				
High need	1 admission	£5,876	82%	£4,819
Very high need	2.55 admissions	£14,985	18%	£2,697
Total				**£10,908**
Health economic treatment costs based on the NHS Electronic Drug Tariff for October 2012, and BNF 64 where this was unavailable. Full references are available in the Costing template				

The average cost of a biologic is £10,527 for one year, as follows:[16]

Biologic	Annual drug and administration costs[ab]
Etanercept	£9,643
Infliximab	£13,310
Adalimumab	£9,503
Ustekinumab	£9,651
Unweighted Average	£10,527
[a] Based on a flat, unweighted average, as used by the healthcare economic model [b.] Drug costs based on BNF 64	

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