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Psoriasis: LSCMMG Biologic and High Cost Drug Commissioning Pathway

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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
1.7	Lines of biologic increased to six options. Position of Apremilast and dimethyl fumarate clarified.	David Prayle	July 2020
Date of next review: July 2023			

Psoriasis: LSCMMG 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

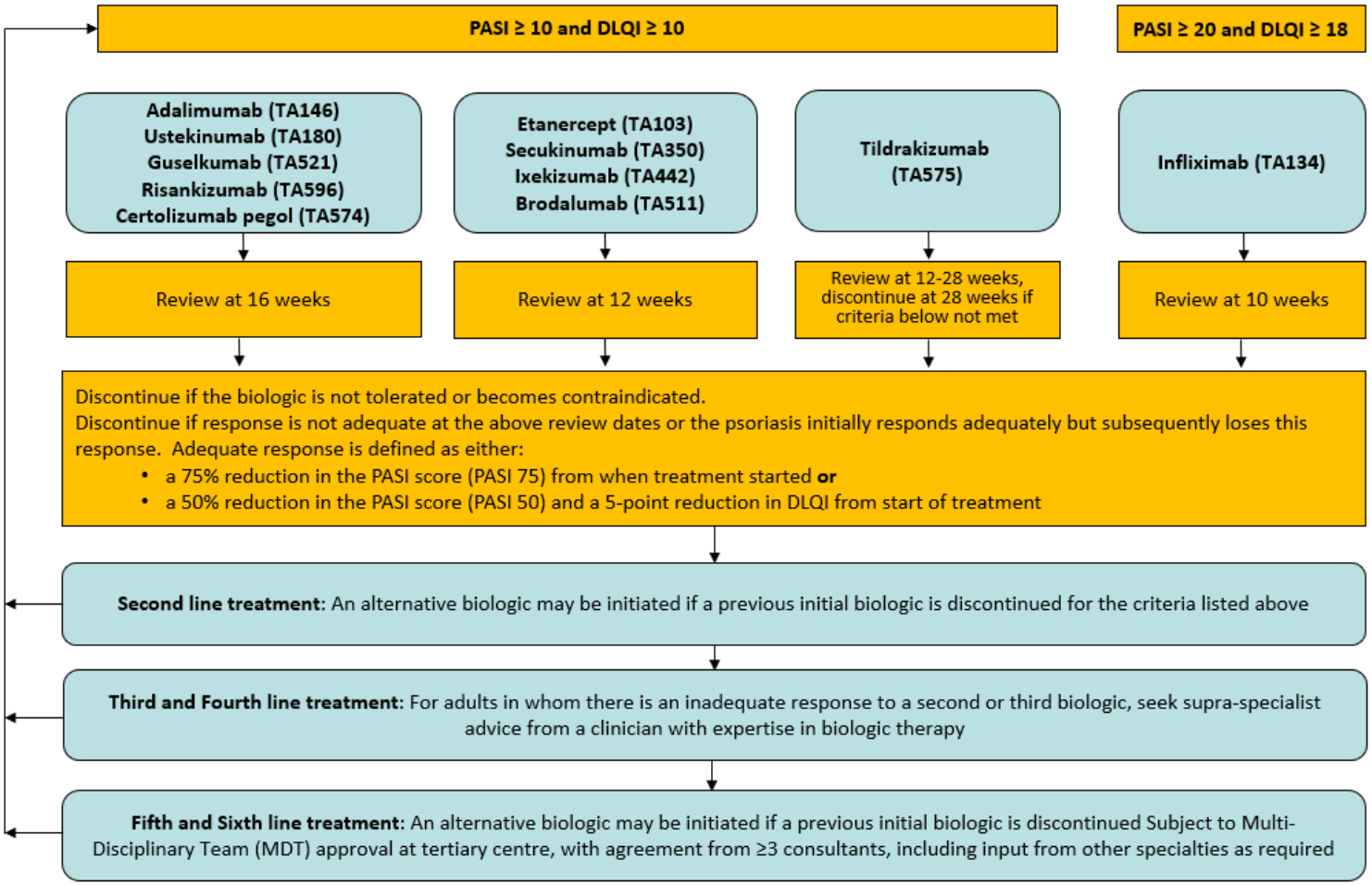
Biosimilars

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.



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 phototherapy and systemic non-biological agents such as ciclosporin, methotrexate and acitretin.

Biologics

Systemic biological therapies are reserved for **third line use**. 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 have produced individual Technology Appraisals for each of the eleven currently available biological drugs for the treatment of plaque psoriasis. The following agents have been appraised by NICE 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 receptor antagonist) – TA511 (2018)[8]
- Guselkumab (Interleukin 23 inhibitor) – TA521 (2018)[9]
- Certolizumab pegol (TNFα inhibitor) – TA574 (2019)[10]
- Tildrakizumab (Interleukin 23 inhibitor) – TA575 (2019)[11]
- Risankizumab (Interleukin 23 inhibitor) – TA596 (2019)[12]

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)[13]

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 initially produced in 2012 and last updated in 2017, 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 (…*examples of drugs and time periods given*[a]…; 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.

[a] The NICE guideline lists the biologics available at the time of its last update in 2017

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.

NICE Clinical guideline 153 also advises that, for adults in whom there is an inadequate response to a second biological drug, to seek supra-specialist advice from a clinician with expertise in biological therapy.[1]

Lines of Biologics

Guidance on additional lines of biologic treatment after third line has not been produced by NICE. An advisory statement produced by the Regional Medicines Optimisation Committee states:

> *A policy adopted by a commissioner that would serve to limit patients' access to appropriate treatments based on a number of prior treatments being attempted would be counter to the provisions of the NHS Constitution*[14]

And:

> *When a treatment fails, guidance from specialist bodies suggests switching to a biologic with a new mechanism of action is more effective than switching within class, although it should be noted that this is based on low quality evidence.*[15] *The exception to this is secondary failure of anti-TNF treatment due to formation of anti-drug-antibodies, in which case switching within class may be a valid treatment option*.[14,16]
>
> *In situations where the appropriateness of further treatment options is undecided, a peer multidisciplinary team discussion is likely to be helpful*[14]

Based on these principles, **this guideline supports the use of a total of six lines of biologic treatment**, taking into account the mechanisms of action of the available biologics and accounting for the potential for secondary failure due to anti drug antibodies in the case of anti TNF agents.

Supra-specialist advice from a clinician with expertise in biologic therapy should be sought for treatment **beyond second** line biologic.

Fifth and **sixth** line biologic treatment may be initiated subject to Multi-Disciplinary Team approval at tertiary centre, with agreement from at least 3 consultants, including input from other specialties as required.

Apremilast and Dimethyl Fumarate

Apremilast is a Phosphodiesterase type-4 inhibitor and Dimethyl Fumarate is an oral fumaric acid ester (FAE); both are approved by NICE for the treatment of moderate to severe plaque psoriasis and either may be used where a biologic is considered inappropriate. Use will not be regarded as one of the sequential treatment options in the patient's pathway.

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

NICE TA 419[17] and NICE TA475[18] respectively allow Apremilast or Dimethyl fumarate to be used for treating moderate to severe 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

For Apremilast the drug's manufacturer must provide the drug with the discount agreed in the patient access scheme.

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[5] NICE TA180 Ustekinumab for the treatment of adults with moderate to severe psoriasis https://www.nice.org.uk/guidance/ta180 [Accessed online on 12 April 2016]

[6] NICE TA350 Secukinumab for treating moderate to severe plaque psoriasis https://www.nice.org.uk/guidance/ta350 [Accessed online on 12 April 2016]

[7] NICE TA442 Ixekizumab for treating moderate to severe plaque psoriasis https://www.nice.org.uk/guidance/ta442/resources/ixekizumab-for-treating-moderate-to-severe-plaque-psoriasis-pdf-82604781265093 [Accessed online 27 February 2018]

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[17] NICE TA419 Apremilast for treating moderate to severe plaque psoriasis. https://www.nice.org.uk/guidance/ta419 [Accessed online on 13 May 2020]

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