The guidelines for the treatment of severe psoriasis in adults

Relevant NICE documents:

Etanercept TA103
Adalimumab TA146
Infliximab TA 134
Brodalumab TA 511
Ustekinumab TA 180
Secukinumab TA 350
Apremilast TA 419
Guselkumab TA 521
Ixekizumab TA442
Management of psoriasis CG 151
Dimethyl Fumarate TA475

Severe Psoriasis: **PASI ≥ 10 and DLQI > 10 and failed previous systemic therapies or these treatments are CI or not tolerated** (e.g ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation),

Apremilast (TA419) or Dimethyl Fumarate (TA475)

For dosing see - appendix 2
Adequate response* within 16 weeks

Yes

Maintain same treatment and monitor patient (adequate response time 16

No

Yes – consider alternative biologic agent – (local agreement)

Use one of the following treatment options:

- Adalimumab (TA146) or
- Etanercept (TA103) or
- Ustekinumab (TA180) or
- Secukinumab (TA 350)
- Ixekizumab (TA 442)
- Brodalumab (TA 511)
- Guselkumab (TA 521)

Or

- **Infliximab (TA134)**
  if disease is very severe as defined by PASI ≥ 20 and DLQI > 18

Yes – maintain treatment and monitor patient at appropriate intervals

Has the biologic been withdrawn because of an adverse effect?

- If no adequate response* at specified time (see appendix 1) - the patient is a **primary non-responder or**
- **secondary non-responder** (initially responds, but subsequently loses response), proceed as per local guidance below

The CCG will **only commission 3 switches per patient** – this includes 1 for treatment failure and 2 for intolerance (including intolerance to apremilast and dimethyl fumarate.

Reassess PASI and DLQI if the patient fails to respond to the first biologic.
Proceed to second biologic if:

- **PASI >15 and DLQI>15 and**
- **the patient has had a 6 week trial of topical treatment and**
- **there is a risk of admission within the 6 weeks and**
- **Prior approval form is sent to medicines management clinical effectiveness team**

Previous drug treatment an interleukin mediated biologic:

- Ustekinumab non responder
- Secukinumab non-responder
- Ixekizumab non responder
- Guselkumab
- Brodalumab

Second drug option:

- Etanercept
- Adalimumab
- Infliximab (very severe psoriasis)

Previous drug treatment with:

- Etanercept non responder
- Adalimumab non responder
- Infliximab non responder

Second drug option:

- Ustekinumab
- Secukinumab
- Ixekizumab
- Guselkumab
- Brodalumab

In exceptional circumstances some patients may not show adequate response to a second biologic, **and** the psoriasis may have worsened (PASI>25 and DLQI>20, measured 4 weeks apart) **and** there may be a risk of readmission; under these circumstances it may be appropriate to request the use of a third biologic through an IFR.

NICE approved treatment

Local variation to NICE

Adequate response 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 the DLQI score from when treatment started.

Date reviewed: October 2018
Review due: September 2020

Appendix 1

	Dose	*Adequate response times (weeks)	Further information
Infliximab	5-mg/kg intravenous infusion over a 2-hour period followed by additional 5-mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter	10	Infliximab is a chimeric human-murine IgG1 monoclonal antibody
Etanercept	Subcutaneous injection at a dose of 25 mg twice weekly. Alternatively, 50 mg given twice weekly may be used for up to 12 weeks followed, if necessary, by a dose of 25 mg twice weekly	12	Etanercept is a recombinant human tumour necrosis factor (TNF) receptor fusion protein that inhibits the activity of TNF
Adalimumab	Subcutaneous injection of an initial 80 mg dose, followed by 40 mg given subcutaneously every other week starting 1 week after the initial dose	16	Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α)
Secukinumab	Subcutaneous injection at a dose 300 mg at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4	12	Secukinumab is a high-affinity, fully human monoclonalantibody that binds to and neutralises interleukin-17A
Ixekizumab	By subcutaneous injection; 160 mg at week 0, followed by 80 mg every 2 weeks until week 12. After week 12, 80 mg every 4 weeks	12	Ixekizumab) is an antibody that inhibits IL-17A (interleukin-17A, a pro-inflammatory cytokine)
Ustekinumab	The recommended dose of ustekinumab is 45 mg for people who weigh 100 kg or less, and 90 mg for people who weigh over 100 kg. An initial dose of ustekinumab is administered subcutaneously at week 0, followed by another dose at week 4, and then a further dose every 12 weeks	16	Ustekinumab is a fully human monoclonal antibody that targets interleukin-12 (IL-12) and IL-23
Brodalumab	The recommended dose is 210 mg administered by subcutaneous injection at weeks 0, 1 and 2, followed by 210 mg every 2 weeks	12	Brodalumab is a recombinant fully human monoclonal immunoglobulin IgG2 antibody that binds with high affinity to human IL-17RA and blocks the biological activities of the pro-inflammatory cytokines IL-17A, IL-17F, IL-17A/F heterodimer and IL-25
Guselkumab	The recommended dosage of guselkumab is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a 100 mg maintenance dose every 8 weeks. Consideration should be given to stopping treatment in people whose disease has shown no response after 16 weeks of treatment	16	Guselkumab is a human IgG1λ monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity

Appendix 2

Dose titration for Dimethyl Fumarate

To improve tolerability, it is recommended to begin treatment with a low initial dose with subsequent gradual increases. The maximum daily dose allowed is 720 mg (3 x 2 tablets of dimethyl fumarate 120 mg).

Week	Number of tablets			Total daily dose (mg) of dimethyl fumarate
	Morning	Midday	Evening	
Dimethyl fumarate 30 mg				
1	0	0	1	**30**
2	1	0	1	**60**
3	1	1	1	**90**
Dimethyl fumarate 120 mg				
4	0	0	1	**120**
5	1	0	1	**240**
6	1	1	1	**360**
7	1	1	2	**480**
8	2	1	2	**600**
9+	2	2	2	**720**

Dose titration for apremilast

- Day 1 - 10mg am
- Day 2 - 10mg am & pm
- Day 3 - 10mg am, 20mg pm
- Day 4 - 20mg am & pm
- Day 5 - 20mg am & 30mg pm
- Day 6 and thereafter - 30mg am & pm

NB: reduce dose 30mg od in severe renal impairment (CrCl <30ml/min, estimated using Cockcroft-Gault equation)

MHRA warning - apremilast

MHRA, Jan 2017, have issued a warning regarding risk of suicidal thoughts and behavior associated with apremilast use.