The guidelines for the treatment of severe psoriasis in adults

Relevant NICE documents:

Etanercept TA103	Ustekinumab TA 180	Ixekizumab TA442
Adalimumab TA146	Secukinumab TA 350	Management of psoriasis CG 151
Infliximab TA 134	Apremilast TA 419	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

No

Use one of the following treatment options:

- Adalimumab (TA146) or
- Etanercept (TA103) or
- Ustekinumab (TA180) or
- Secukinumab (TA 350)
- Ixekizumab (TA 442)

Or

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

Yes

Maintain same treatment and monitor patient (adequate response time 16

- 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

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

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

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.

Key

Local variation to NICE

As per NICE guidance

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.

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.

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.