Plaque Psoriasis High Cost Immune Modulator Treatment Pathway

Approved by Surrey Heartlands Integrated Care System Area Prescribing Committee October 2023

Patient must have failed to respond to standard systemic therapies such as ciclosporin, methotrexate, acitretin and phototherapy (as per individual NICE guidance) the patient is intolerant to or has a contraindication to these treatments.

See page 3 of pathway

Psoriasis Area & Severity Index (PASI) ≥ 10 AND Dermatology Life Quality Index (DLQI) > 10

OR

Patient does not qualify for treatment within this pathway.

Consider IFR if clinically exceptional to the cohort

1st LINE

START TREATMENT

Monitor patient for initial treatment period as defined by NICE TA.

For primary intolerance/adverse effects, see notes below.. Withdraw treatment if **response** is not maintained (secondary failure).

Monitor patient every 6 months ongoing

NO

Primary failure

YES

Continue treatment & monitor patient every **6 months.** For primary intolerance/adverse effects, see notes below.

Withdraw treatment if **response** is not maintained (secondary failure).

Initial Treatment Period

The initial treatment length varies as per NICE TA's. See following page for details of expected clinical review

2nd LINE

Start treatment & monitor patient for initial treatment period as defined by NICE TA.

For primary intolerance/adverse effects, see notes below.. Withdraw treatment if **response** is not maintained (secondary failure).

Monitor patient every 6 months ongoing.

Primary failure

Secondary failure or secondary intolerance—see notes below

3rd LINE

Start treatment & monitor patient for initial treatment period as defined by NICE TA.

For primary intolerance/adverse effects, see notes below.. Withdraw treatment if **response** is not maintained (secondary failure).

Monitor patient every 6 months ongoing.

Primary failure

Secondary failure or secondary intolerance—see notes below

4th LINE and beyond

Requests must be considered at an external MDT via the Dermatology clinical network application form and process

Secondary failure or secondary intolerance—see notes below

ADEQUATE RESPONSE

A 75% reduction in the **PASI** score from when treatment started (**PASI 75**)

OR

A 50% reduction in the **PASI** score (**PASI 50**) and a five point reduction in the **DLQI** from when treatment started

	Definition	Action
Primary Failure	Occurs when the response criteria (as defined within the NICE TA) is **not fully met** when response to treatment is assessed at the time interval defined within the NICE TA	Move to the NEXT treatment line/mode of action (if one is available)
Secondary Failure	Occurs when the response to treatment (as defined within the NICE TA) is **no longer met**	Move to the NEXT treatment line/mode of action (if one is available)
Primary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side-effects of that treatment that occurs **during the initial time period defined by the NICE TA**	Use another option from the SAME treatment line
Secondary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side effects of that treatment that occurs **after the initial time period defined by the NICE TA**	Move to the NEXT treatment line OR discuss at Dermatology Clinical Network.
Conception	If conception plans or pregnancy indicate a change of drug is advisable, it is agreed that this **does not constitute a change in line of treatment**	Please update Blueteq accordingly

Initiate treatment at 1st line with the least costly treatment option which currently is

Biosimilar adalimumab. (treatments highlighted are the least costly preparation in class)

Mode of action (Note: different colour denotes oral or subcutaneous treatment)	Drug	NICE TA & date of publication	Expected clinical review below and then every 6 months:	Points to consider when initiating
Fumaric Acid ester	Dimethyl Fumarate (ORAL)	***NICE TA475***	16 weeks	www.nice.org.uk Place in therapy as an alternative to biological therapies and apremilast
Phosphodiesterase (PDE4) inhibitor	Apremilast (ORAL)	***NICE TA419***	16 weeks	www.nice.org.uk Apremilast was less effective but also less costly than biological therapies.
TYK2 enzyme (TYK2 belongs to the JAK family) **NHS resources- Information from Bristol Myers Squibb (NICE committee papers)** As a small molecule medication, it is anticipated that deucravacitinib will not develop immunogenicity and it therefore presents patients with an option for a treatment with good durability and less need for switching.	Deucravacitinib (ORAL)	***NICE TA907***	24 weeks	www.medicines.org.uk It is not known whether TYK2 inhibition may be associated with the adverse reactions of JAK inhibition. www.nice.org.uk **Clinical effectiveness:** Less effective and more expensive than adalimumab, bimekizumab and tildrakizumab. Clinical trial evidence shows that deucravacitinib improves symptoms of plaque psoriasis compared with placebo and apremilast.
TNF alpha inhibitor • *Adalimumab is the least costly TNF alpha inhibitor* • *Note that by using SC infliximab administration costs will be reduced and capacity released in infusion suites*	Adalimumab	***NICE TA146***	16 weeks	Adalimumab is the least costly systemic biologic treatment available (August 2023)
	Etanercept	***NICE TA103***	12 weeks	Biosimilars available
	Infliximab	***NICE TA134***	10 weeks	IV biosimilars available Subcutaneous (SC) biosimilar available SC injection licensed for use in Psoriasis. Consider SC route over Infusion to release capacity in infusion suites
	Certolizumab	***NICE TA574***	16 weeks	In conception or pregnancy if change of drug is advisable, this does not constitute a change in line of treatment.
Interleukin 17A/RA inhibitor	Secukinumab	***NICE TA350***	12 weeks	www.nice.org.uk **Clinical effectiveness:** Secukinumab appears to be more clinically effective than etanercept and adalimumab, and to have similar clinical effectiveness to ustekinumab and infliximab, the only direct trial evidence was for secukinumab compared with etanercept. NB: 2 x 150mg (300mg) injections required for each dose
	Ixekizumab	***NICE TA442***	12 weeks	www.nice.org.uk **Clinical effectiveness:** Direct trial evidence was for ixekizumab compared with etanercept.
	Brodalumab	***NICE TA511***	12 weeks	www.nice.org.uk **Clinical effectiveness:** The committee concluded that brodalumab was more clinically effective than placebo and ustekinumab.
	Bimekizumab	***NICE TA723***	16 weeks	www.nice.org.uk **Clinical effectiveness:** Results of trials showed that bimekizumab was more effective than adalimumab, secukinumab and ustekinumab. NB: 2 x 160mg (320mg) injections required for each dose
Interleukin (IL)23 protein	Tildrakizumab	***NICE TA575***	12-28 weeks then at 28 weeks	www.nice.org.uk **Clinical effectiveness:** NICE concluded that tildrakizumab was more clinically effective than placebo and etanercept www.nice.org.uk **&** www.medicines.org.uk **I**n patients with certain characteristics (e.g. high disease burden, body weight ≥ 90 kg) 200 mg may provide greater efficacy.
	Risankizumab	***NICE TA596***	12 weeks	www.nice.org.uk **Clinical effectiveness:** Evidence from clinical trials shows that risankizumab is more effective than adalimumab and ustekinumab.
	Guselkumab	***NICE TA521***	16 weeks	www.nice.org.uk **Clinical effectiveness:** Evidence from clinical trials and indirect comparisons show that guselkumab is more effective than TNF-alpha inhibitors (that is, adalimumab, etanercept and infliximab) and ustekinumab. It also suggests that guselkumab is likely to provide similar health benefits to ixekizumab and secukinumab.
Interleukin 12/23 inhibitor	Ustekinumab	***NICE TA180***	16 weeks	www.nice.org.uk **Clinical effectiveness:** Demonstrated to be more clinically effective than etanercept

References:

1. NICE Technical Appraisals. Available at: www.nice.org.uk
2. Drug Safety Update April 2023. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality. Available at: Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality

Clinical contraindications and considerations for pre-biologics

www.medicines.org.uk & www.nice.org.uk & Clinical Guideline: Psoriasis (assessment & management) CG153. *(Developed: January 2018 Updated November 2021)*

Clinical contraindications

Phototherapy (TLO1 or PUVA)	Ciclosporin	Methotrexate	Acitretin
	• Hypersensitivity to the active substance or to any of the excipients • Combination with products containing Hypericum perforatum (St John´s Wort) • Combination with medicines that are substrates for the multidrug efflux transporter P-glycoprotein or the organic anion transporter proteins (OATP) and for which elevated plasma concentrations are associated with serious and/or life-threatening events, e.g. bosentan, dabigatran etexilate and aliskiren	• Presence of severe/significant renal or significant hepatic impairment. • Liver disease including fibrosis, cirrhosis, recent or active hepatitis; active infectious disease; and overt or laboratory evidence of immunodeficiency syndrome(s). • Serious cases of anaemia, leucopenia or thrombocytopenia. • Methotrexate should not be used concomitantly with drugs with antifolate properties (eg co-trimoxazole). • Methotrexate is teratogenic and should not be given during pregnancy or to mothers who are breast feeding. • Patients with a known allergic hypersensitivity to methotrexate should not receive methotrexate	• **PREGNANCY:** Acitretin, the active substance of Acitretin, is highly teratogenic and must not be used during pregnancy. The same applies to all women of childbearing potential, unless strict contraception is practiced 4 weeks before, during and for 3 years after treatment • **LACTATION:** Acitretin is contraindicated during the period of breast-feeding. • Acitretin is not indicated in hepatic and renal dysfunction (liver and kidney failure), severe hyperlipaemia, concurrent use of vitamin A or other retinoids and during co-medication with methotrexate. Since Acitretin and tetracyclines can cause an increase in intracranial pressure, they must not be given concurrently. • Acitretin must not be used concomitantly with low dose progesterone-only products (minipills) • Acitretin must not be used in patients with hypersensitivity to the active substance "acitretin" or other retinoids or to any of the excipients.

Cautions

Phototherapy (TLO1 or PUVA)	Ciclosporin	Methotrexate	Acitretin
• People at risk of skin cancer • People with lighter skin types I or II on Fitzpatrick Scale	Lymphomas or other malignancies • Related to degree and duration of immunosuppression • Excess unprotected sun exposure • Concomitant UVB/PUVA not recommended Infections • Short-term reversible, dose reduction • Long-term – Structural changes Hepatotoxicity • Dose-dependent, reversible Hypertension, blood lipids increased, hyperkalaemia, hypomagnesaemia, hyperuricaemia.	• Acute or chronic interstitial pneumonitis • Blood dyscrasia (leucopenia, thrombocytopenia) Hepatotoxicity – risk factors • Alcohol abuse • Increased LFTs • Hereditary hepatopathy • Diabetes Mellitus • Adiposity • Exposure to hepatotoxic drugs • Diarrhoea, ulcerative stomatitis with risk of haemorrhagic enteritis and intestinal perforation (death) • Decreased fertility • Inactive chronic infections • Pleural effusions, ascites	

Other considerations for phototherapy: * Physical limitations – patients cannot stand for treatment

*Severe psoriasis that won't respond—pustular & erythrodermic presentations

* Position of disease—scalp, flex joints, lower leg, nail

* Manifestation of disease—thick plaques