WORCESTERSHIRE PATHWAY
for use of CYTOKINE MODULATORS in Adults with SEVERE PLAQUE PSORIASIS
September 2019

Inadequate response (including intolerance or contra-indication) to 2 standard systemic therapies (such as ciclosporin and methotrexate) and phototherapy (further definition overleaf)

AND

SEVERE DISEASE defined as: **PASI > 9 AND DLQI > 10**

Choose most appropriate agent giving consideration to clinical circumstances (see below); where no clear indication, **use least expensive**:

Preferred Agents:	Alternative Agents:
1. **Adalimumab** (TNFα) TA 146	- Certolizumab (TNFα) TA 574 or
2. Tildrakizumab (IL-23) TA 575	- Guselkumab (IL-23) TA 521 or
3. Brodalumab (IL-17A/25) TA 511	- Ixekizumab (IL-17A) TA 442 or
4. Secukinumab (IL-17A) TA 350	- Risankizumab (IL-23) TA 596 or
	- Ustekinumab (IL-12/23) TA 180

Notes:

a. For Very Severe Plaque Psoriasis (PASI > 19 & DLQI > 18) consider Infliximab (TNFα) TA 134

b. For patients with psoriatic arthritis consider licensed agents such as TNF alpha antagonists (adalimumab, certolizumab) or IL-17 antagonists (secukinumab, ixekizumab)

Blueteq initiation form

Intolerable adverse effect - consider alternative agent (see notes overleaf)#

OR

- **Apremilast** TA 419 **or**
- **Dimethyl fumarate** TA 475

Consider when:
- Patient preference
- Needle phobia
- Contra-indication/ intolerance of other agents

Blueteq initiation form

Assessment within 10-28 weeks[i]

Switch to alternative agent

Blueteq Discontinuation

Adequate response:
PASI 75% ↓
OR
PASI 50% ↓ AND DLQI 5 point ↓

YES

Continue & review 6-12 monthly
Blueteq Continuation Form

NO

Dose Escalation[ii]
(adalimumab, tildrakizumab)

Consider referral to Rheumatology
If significant arthritis symptoms
(PEST score ≥ 3)

Failure of up to 4 cytokine modulator treatments (including small molecules apremilast & dimethyl fumarate) constitutes the end of the commissioned pathway

Specific circumstances that may suggest the use of a specific agent:

Adalimumab: Co-existent conditions such as: RA (TA 375), AS (TA383), uveitis[iii], IBD (TA 187/329), PsA (TA 199)
Apremilast: Infection risk, TB, malignancy, needle phobia
Brodalumab: Contraindication in active Crohn's disease. Caution where history of depression and/or suicidal ideation or behaviour
Certolizumab: Women contemplating pregnancy
Infliximab: IBD (TA 187/329), uveitis[iii], PsA (TA199), high body mass index, compliance issues/severely impaired manual dexterity
Ixekizumab/Secukinumab: Avoid in patients prone to candida infections; use with caution in IBD as this may worsen existing disease
Tildrakizumab: Weight ≥ 90kg
Ustekinumab: Weight > 100kg
Etanercept: Consider when other biologics have failed or cannot be used, or where short half-life is important

i. see overleaf for initial assessment period required
ii. dose escalation for other agents is not supported by NICE
iii. there are known associations between uveitis and central demyelinating disorders; a neurological examination is recommended before initiation and at every review

* See overleaf

Prepared by Consultant Dermatology Team at Worcestershire Acute Hospitals NHS Trust
Approved by Worcestershire Area Prescribing Committee September 2019

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Inadequate Response to Standard Systemic Therapies, defined as:

- Treatment with at least 2 oral agents including ciclosporin and methotrexate AND
- Phototherapy (UVA or UVB)
- Maximum doses reached or treatment or further titration limited by contraindication or intolerance respectively
- Each agent to be trialled at maximum tolerated dose for a period of at least 6 months before assessing effect

Reference: NICE TA for each agent and consensus opinion

Preferred Pathway:

	Psoriasis	***Psoriatic arthritis (where psoriasis predominates)***
Recommended Agent:	*adalimumab*	*adalimumab*
	tildrakizumab	*secukinumab*
	brodalumab	*ixekinumab*

Note: the choice of agent also depends on co-morbidities, balancing onset of action, safety and relative efficacy

Rationale:

a. *The recommended agents target different cytokines (where available); it is likely that an individual's disease will be driven by 1 of these cytokines, so if 1 agent fails then another is likely to work*
b. *Within their class, each of these agents offer the most cost-effective option*
c. *All agents have demonstrated a PASI 75 of around 70% or higher*
d. *Apremilast, an inhibitor of phosphodiesterase 4 (PDE4), modulates the expression of cytokines and mediators including TNF-alpha and IL-23, and is available as an oral agent. It is less efficacious than the biologics and is therefore NOT recommended as a 1st line agent; there are safety concerns with an active MHRA Drug Safety Update (January 2017). Apremilast offers an alternative option for patients who prefer an oral agent, those with needle phobia and patients with contra-indications/intolerance of other agents (significant infection risk e.g. indwelling catheter, leg ulcers; recent malignancy; TB)*
e. *Dimethyl fumarate:*
    a. *offers an alternative oral agent to apremilast, particularly when other treatments are not suitable. Indirect evidence suggests it is less effective than apremilast or other agents, but it is less costly*
    b. *is not a cytokine modulator but is recommended at the same stage of treatment by NICE*

Initial Assessment (as per NICE TAs):

Tildrakizumab	*- 28 weeks*
Adalimumab/Apremilast/Certolizumab/Dimethyl fumarate/Guselkumab/Risankizumab/Ustekinumab	*- 16 weeks*
Brodalumab/Etanercept/Ixekizumab/Secukinumab	*- 12 weeks*
Infliximab	*- 10 weeks*

#Intolerable Adverse Effect/Investigations (including use of apremilast & dimethyl fumarate):

i. *If this occurs within the initiation review period, evidence of clinical benefit is unnecessary for a switch to an alternative agent at the same level of the pathway*
ii. *If this occurs beyond the initiation period, patients need to demonstrate required clinical response in order to switch to an alternative agent at the same level of the pathway*
iii. *For patients not meeting the specific clinical response criteria for continuation, this is deemed treatment failure and patients progress to the next level of the treatment pathway*

Commissioning Arrangements

1. Use of any agents outside of the commissioning pathway will not be reimbursed by commissioners under the excluded PbR arrangements; this includes re-introduction of agents after prior failure.
2. Any proposed changes to the pathway require an application to and consideration by Worcestershire Area Prescribing Committee.
3. This pathway currently excludes patients with hand & foot psoriasis & pustular psoriasis & a further application to APC is required.
4. For patients who fall outside of this pathway but where there is demonstrable evidence that the patient has exceptional clinical circumstances, an Individual Funding Request may be submitted for consideration.

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