HEREFORDSHIRE AND WORCESTERSHIRE CYTOKINE MODULATOR PATHWAY FOR MANAGEMENT OF ULCERATIVE COLITIS* IN ADULTS

November 2020

* This pathway excludes management of acute exacerbations of ulcerative colitis (see note 7. overleaf)

Failure of conventional therapy (including immunosuppressive & corticosteroid treatment)

FIRST LINE

Choose the most appropriate agent and if no clear indication for a specific agent then use the least expensive agent:

- **Adalimumab** (TA 329) OR
- **Infliximab**# (TA 329) *particularly where acute presentation and rapid response required*

For patients contra-indicated or intolerable adverse effect, consider:

- Tofacitinib (TA 547) **OR** Ustekinumab (TA 633) **OR** Vedolizumab# (TA 342)

 # Sub-cutaneous and intravenous versions of these products are approved for use (see overleaf)

Blueteq approval required

Intolerable adverse effect

Relapse After Withdrawal: Re-introduction Of Original Agent (NICE)

3-6 month & annual review: Assessment of CLINICAL RESPONSE/BENEFIT

No Clinical Benefit
Blueteq discontinuation required

Consideration of drug level and antibody status

SECOND and SUBSEQUENT LINE

Preferred order*:

- Adalimumab **OR** Infliximab# **OR** Golimumab (TA 329) *(Only where positive antibody status)*
- Ustekinumab (TA 633) **OR** Vedolizumab# (TA 342)
- Tofacitinib (TA 547)

Blueteq approval required

** Unless clinically inappropriate e.g. due to contra-indications or intolerable adverse effects*

 # Sub-cutaneous and intravenous versions of these products are approved for use (see overleaf)

Failure of up to 4 cytokine modulators constitutes the end of the commissioned cytokine modulator pathway

Clinical Benefit
Blueteq continuation required (annual)

Ongoing Active Disease
Or
Other Indication
(see notes overleaf)

No Active Disease
> 6 consecutive months clinical remission with standard dosing

Continue with Annual Review
Blueteq approval required

Consider Attempting a Trial Withdrawal of Treatment
Blueteq discontinuation for successful withdrawals

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

Adalimumab: Co-existent conditions such as: RA (TA 375), AS (TA383), Psoriasis (TA146).
Golimumab: Consider if patient over 100kg (patient access to double dose). Compliance issues/Patient convenience (monthly dosing).
Infliximab: Compliance issues, severely impaired manual dexterity.
Tofacitinib: Needle phobia, severely impaired manual dexterity
Vedolizumab: Contra-indication to TNF alpha inhibitors

Prepared and agreed by Consultant Gastroenterology Teams across Herefordshire and Worcestershire
Approved by Medicines and Prescribing Committee November 2020

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Notes:

1. Where TNF alpha inhibitors are not clinically appropriate tofacitinib, ustekinumab OR vedolizumab may be used at an earlier stage in the pathway.
2. Infliximab may be used at any stage for acute presentation where rapid response required.
3. Second line TNF alpha inhibitor use is only indicated for non-responders to TNF alpha inhibitors with positive antibody status.
   Rationale: The evidence suggests that other patient cohorts are unlikely to respond to further TNF alpha inhibitor treatment.
4. Sub-cutaneous and intravenous presentations of infliximab and vedolizumab are approved for use, providing they are used within the licensed dosing regime, without either dosage or administration frequency escalation.
5. A recent safety update currently restricts use of tofacitinib administered at a dose of 10mg twice daily in patients at high risk of pulmonary embolism; risk factors are outlined in the MHRA Drug Safety Update (May 2019).
6. A trial withdrawal of treatment, for patients in stable clinical remission for more than 6 consecutive months on standard dosing regimes, may be inappropriate for the following groups:
   - *Patients receiving tofacitinib, ustekinumab or vedolizumab, due to absence of evidence*
   - *Patients in whom there are no alternative immunosuppressive maintenance options (e.g. prior failure or intolerance)*
   - *Patients receiving second or subsequent lines of treatment, following prior relapse (direct or indirect)*
7. The pathway excludes management of acute exacerbations of ulcerative colitis, which is covered by NICE Technology Appraisal 163. The APC have considered this indication separately and determined:
   - The requirement for ciclosporin to be contraindicated or clinically inappropriate is not necessary within Herefordshire and Worcestershire.
   - Beyond the 3 dose induction course, patients may be transitioned onto long-term maintenance treatment.

Intolerable Adverse Effect:

I. If this occurs within the initiation review period, evidence of clinical benefit is unnecessary.
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 Herefordshire and Worcestershire Medicines and Prescribing Committee.**
3. **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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