Adult (age≥18 years) excluded high cost drug treatment pathway for active Crohn's disease- based on NICE TAs 187, 352, 456, 888 & 905

Note 1: Severe Active Crohn's Disease
- Severe active Crohn's disease is defined as very poor general health and one or more symptoms such as weight loss, fever, severe abdominal pain and usually frequent diarrhoeal stools (≥3 daily).
- People with Severe Active Crohn's Disease may or may not develop new fistulae or have extra-intestinal manifestation of the disease.
- This clinical definition normally, but not exclusively, corresponds to:
  - Crohn's disease activity index (CDAI) score ≥300
  - Harvey-Bradshaw (HBI) score of ≥ 8-9.

Where HBI/CDAI is not a relevant indicator of disease severity specialist judgement confirmed with alternative objective measures (e.g. colonoscopy, MRI, stoma output, CRP, ESR, faecal calprotectin) to be provided that demonstrate severe active Crohn's Disease. These will also be used to monitor treatment response.

Note 2: Conventional immunosuppressive therapy
Usual Adult maintenance treatment dose ranges:
- Azathioprine - 2 mg/kg/day to 2.5 mg/kg/day.
- Mercaptopurine - 0.75 mg/kg/day to 1.5 mg/kg/day
- Methotrexate - 15 mg to 25 mg once weekly.

Note 3: Less expensive drug
The choice of treatment should be made on an individual basis after discussion between the patient and their clinician about the advantages and disadvantages of the treatments available. **If more than 1 treatment is suitable, the least expensive should be chosen** (taking into account administration costs, dosage and price per dose).
Cost order: 1. Adalimumab biosimilar (least costly) 2. Infliximab biosimilar 3. Ustekinumab biosimilar 4. Upadacitinib 5. Vedolizumab SC 6. Risankizumab 7. Vedolizumab IV (most costly)
If least expensive choice not selected rationale to be provided

Note 4: Response definitions
Severe Active Crohn's Disease
- Response - decrease in HBI ≥3 points
- No response - decrease in HBI ≤2
- *Where HBI is not a relevant indicator of disease severity the 'on treatment' alternative objective measures will be used (compared to baseline) to demonstrate response.*

Active fistulising Crohn's
- Response - ≥50% improvement in fistula drainage
- No response - <50% improvement in fistula drainage

'On treatment' HBI scores or alternative objective measures can also be used (compared to baseline) to demonstrate response.

Note 5: Disease reassessment
At 12 months after the start of treatment, people should have their disease reassessed to determine whether ongoing treatment is still clinically appropriate.
Treatment should only be continued if there is clear evidence of ongoing adequate response (Note 4) and active disease. This should be determined by:
- Clinical symptoms and
- Biological markers (eg CRP, ESR) and
- Investigation, including endoscopy if necessary.

Note 6: Dose Escalation
For patients who have responded to induction and maintenance treatment regime of a TNF inhibitor or ustekinumab biosimilar but then lost response an attempt to recapture response with a temporary period of increased dose / shortened interval between doses may be made: one infliximab dose of 10mg/kg or 3 doses of Infliximab 5mg/kg given 4-6 weekly and then stretch back to 8 weekly; or up to 8 weeks on weekly adalimumab 40mg then stretch back to every other week; or 2 doses of ustekinumab biosimilar given 8 weekly then back to 12 weekly.

Note 7: Ustekinumab:
After initial intravenous loading dose first subcutaneous dose is given at week 8. After this dosing every 12 weeks is recommended.
Consideration should be given to discontinuing treatment in patients who show no evidence of therapeutic benefit by week 16 or 16 weeks after switching to the 8-weekly dose (i.e. after 2 doses). De-escalate from 8 weekly maintenance schedule to 12 weekly if patient in stable clinical remission.

Does the adult have Severe Active Crohn's Disease (See note 1)? → Yes → Has there been lack/loss of response, intolerance or contraindication to optimised conventional therapy (Note 2) taken for an adequate period, including;
- Immunosuppressive and/or
- Corticosteroid treatments? (includes steroid dependence or requirement for regular repeat courses)

Does the adult have active **Fistulising** Crohn's disease? → Yes → Has there been lack/loss of response, intolerance or contraindication to conventional therapy (Note 2) taken for an adequate period, including;
- Antibiotics and
- Drainage and
- Immunosuppressive treatments?

Yes:
- **Adalimumab biosimilar or**
- **Infliximab biosimilar** see Note 3 for guidance on choice

Yes: ***Ustekinumab biosimilar or Risankizumab ONLY if TNF inhibitor not suitable (****see Note 3 for guidance on choice)*** ***Upadacitinib or* Vedolizumab *Subcutaneous (SC) / Intravenous (IV) ONLY if TNF inhibitor contraindicated***

Yes: **Infliximab biosimilar** *Adalimumab may be considered if preference for s/c administration*

BOX 1 — **Give as a planned course of treatment until treatment failure (including the need for surgery), or until 12 months after the start of treatment, whichever is shorter.**

Response (Note 4) within 12 weeks infliximab, adalimumab, upadacitinib & risankizumab, or 16 weeks ustekinumab (see note 7) or 14 weeks vedolizumab SC/IV treatment?

No → Consider switch to alternative TNF inhibitor or a drug from a different class if no response or intolerance to initial TNF inhibitor (If more than 1 treatment is suitable, the least expensive should be chosen, see note 3) → GO TO BOX 1

Yes → Continue maintenance dose.
Where a trial withdrawal at 12 months is likely, from 8 months consider the establishment of an optimised dose of conventional immunosuppressive therapy (Note 2) unless intolerant/contraindicated. **At any point before 12 months of treatment has passed, has treatment failed (including the need for surgery)?**

Yes → Where available, consider TNF inhibitor drug and antibody levels to support a decision to dose escalate or switch

Consider switch to alternative TNF inhibitor or a drug from a different class *(If more than 1 treatment is suitable, the least expensive should be chosen, see note 3)* → GO TO BOX 1

BOX 2 — Consider dose escalation or interval reduction of TNF inhibitor and ustekinumab biosimilar to recapture response (Note 6)

Response to escalated dose?
- **No** → GO TO BOX 1
- **Yes** → De-escalate to standard dose. **Response on return to standard dose?**
  - **Yes** → Discuss the risks & benefits of continued treatment. **Trial withdrawal of patients in stable clinical remission.** *If intolerance/contraindication to maintenance immunosuppressive treatment & only maintenance treatment option is a biologic, a trial withdrawal does not need to be attempted*
    - Patients whose disease has relapsed after treatment is stopped may restart treatment **(go to box 1)**
    - *Patients whose disease has relapsed on previous trial withdrawal may continue maintenance treatment without further trial withdrawal even if in stable clinical remission*
  - **No** → *Consider trial of maintenance escalated dose for patients with clear objective evidence of response to escalated dose & loss of response on de-escalation to standard dose.* Consider alternative treatment (go to box 1) (If more than 1 treatment is suitable, the least expensive should be chosen, see note 3)
    - *Reassess patient after 6 months and then at least every 12 months to determine if ongoing escalated dose is still clinically appropriate (see Note 5).*
    - *Trial of de-escalation in patients without active disease in stable clinical remission*
    - *Patients whose disease has relapsed after trial de-escalation may continue escalated dose*

No → At 12 months after start of treatment reassess the disease (Note 5). **Where there is an ongoing adequate response is there evidence of ongoing active disease?**

Yes → Discuss the risks and benefits of continued treatment. **Maintain treatment.** → Reassess patient at least every 12 months to determine if ongoing treatment is still clinically appropriate.

If loss of response at any time, consider:
(where available, consider TNF inhibitor drug and antibody levels to support a decision to dose escalate or switch):
- trial dose escalation of current TNF inhibitor or ustekinumab biosimilar to recapture response (go to box 2)
- switch to alternative TNF inhibitor (go to box 1)
- switch to ustekinumab biosimilar (go to box 1)
- switch to upadacitinib (go to box 1)
- switch to risankizumab (go to box 1)
- switch to vedolizumab SC/IV (go to box 1)

Patients without active disease in stable clinical remission should have trial withdrawal

Note that a maximum of 6 sequential biologics per patient (including 2 lines of anti-TNF) are routinely commissioned.

Refer to individual SPC's for full prescribing information including dose restrictions, adverse drug reactions, contraindications and cautions; and to Drug Safety Updates for latest drug safety notices.
Note: dose escalation is not routinely commissioned unless specified in the pathway.

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Superseded versions	Adult (age≥18 years) biologics treatment pathway for active Crohn's disease- based on NICE TAs 187, 352 & 456. HMMC, Oct 2020 Adult (age≥18 years) biologics treatment pathway for active Crohn's disease- based on NICE TAs 187, 352 & 456 update Feb 2020. West Essex CCG MOPB, Feb 2020 Addition of price change or biosimilar wording for pathway updates agreed at June 24 APC Addition of ustekinumab biosimilar and corresponding adjustment of order of choice according to cost Nov 2024

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NICE recommends if patients and their clinicians consider a medicine to be one of a range of suitable treatments, the least expensive treatment should be chosen, taking into account administration costs, dosage, price per dose and commercial arrangements. Therefore, in line with this recommendation and HWE APC agreed principles the order of preference of treatments within this pathway will be updated accordingly as prices change or biosimilar medicines become available.