November 2012
No.47

NICE Bites

Crohn's disease

NICE CG152; 2012

This guideline covers the management of Crohn's disease in children, young people and adults.

Definition of terms

BMI	body mass index
BMD	bone mineral density
CDAI	Crohn's disease activity index
CI	contraindication
IV	intravenous
5-ASA	5-aminosalicylic acid
TPMT	thiopurine methyltransferase

Treatment and management

Induction of remission

Monotherapy

- In people with a first presentation, or a single inflammatory exacerbation of Crohn's disease in a 12-month period:
  First-line: **conventional glucocorticosteroids** (prednisolone, methylprednisolone or IV hydrocortisone), ***OR*** in children/young people consider enteral nutrition if there is concern about growth or adverse effects.
- In people who decline, cannot tolerate or have a CI to conventional glucocorticosteroids:
  Second-line: **budesonide*U**children/young people for people with distal ileal, ileocaecal or right-sided colonic disease, **OR**
  5-ASA (aminosalicylates)*
  mesalazine**U,** olsalazine**U,** and balsalazide**U.**
- Explain that budesonide and 5-ASA are less effective than conventional glucocorticosteroids, and 5-ASA is less effective than budesonide but have fewer adverse effects.
- **Do NOT** offer budesonide or 5-ASA for severe presentations or exacerbations.
- **Do NOT** offer azathioprine, mercaptopurine or methotrexate as monotherapy to induce remission.

Add-on treatment to induce remission

- Consider add-on treatment if:
  - there are two or more inflammatory exacerbations in a 12-month period, **OR**
  - the glucocorticosteroid dose cannot be tapered.

  First-line: **ADD azathioprineU or mercaptopurineU** to a conventional glucocorticosteroid or budesonide:
  - assess TPMT activity before offering azathioprine or mercaptopurine,
  - **Do NOT** offer if TPMT activity is deficient (very low or absent),
  - if TPMT activity is below normal but not deficient (according to local laboratory reference values) consider giving azathioprine or mercaptopurine at a lower dose.
- In people who cannot tolerate azathioprine or mercaptopurine, or in whom TPMT activity is deficient.
  Second-line: **ADD methotrexateU**** to a conventional glucocorticosteroid or budesonide.

*See Summary of Product Characteristics for full prescribing information.

Severe active Crohn's disease

- **Clinical definition**: very poor general health and one or more symptoms including weight loss, fever, severe abdominal pain and usually frequent diarrhoeal stools daily (≥3 to 4).
- People with severe active Crohn's disease may or may not develop new fistulae or have extra-intestinal manifestations of the disease.
- Normally (but not exclusively) corresponds to a CDAI score of ≥300 or a Harvey-Bradshaw score of ≥8 to 9.

Infliximab and adalimumab (NICE TA187)

- Give infliximab* or adalimumab*§ to people with severe active Crohn's disease that has not responded to, or who are intolerant of or have a CI to conventional therapy (including immunosuppressive and/or glucocorticosteroid treatments).
- Infliximab is also licensed for people:
  - with active fistulising Crohn's disease which has not responded to, or who are intolerant of or have a CI to conventional therapy (antibiotics, drainage, immunosuppressive treatments),
  - aged 6 to 17 years with severe active Crohn's disease which has not responded to, or who are intolerant of or have a CI to conventional therapy (corticosteroids, immunosuppressives, primary nutrition therapy).
- Use the least expensive drug taking into account drug administration costs, required dose and product price per dose. This may vary for individual patients.
- Give as a planned course until treatment failure (including the need for surgery), or until 12 months after start of treatment, whichever is shorter. Then reassess whether ongoing treatment is still clinically appropriate.
- Only continue treatment if there is clear evidence of ongoing active disease as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary.
- Specialists should discuss the risks and benefits of continued treatment with patients and consider a trial withdrawal for all people in stable clinical remission.
- People continuing treatment should be reassessed at least every 12 months to determine if ongoing treatment is clinically appropriate.
- People whose disease relapses after treatment is stopped should have the option to start treatment again.
- Treatment should only be started and reviewed by clinicians with experience of TNF inhibitors and of managing Crohn's disease.

U unlicensed indication. Obtain and document informed consent.

****Methotrexate is given as a **once-weekly** dose. See BNF and BNFC for important prescribing information

§ Adalimumab is currently **U** in children/young people however, in October 2012 the CHMP issued a positive opinion for use of adalimumab in children aged 6 to 17 years for Crohn's disease.

Produced for healthcare professionals by North West Medicines Information Service,
The Pharmacy Practice Unit, 70 Pembroke Place, Liverpool, L69 3GF.
Editor: Lindsay Banks. Telephone 0151 794 8117. E-mail: nwmedinfo@nhs.net

Crohn's disease continued……

NICE CG152; 2012

Maintaining remission

- Discuss options for managing remission including no treatment or treatment.
- Record person's views in their notes.

No maintenance treatment

- When people choose not to receive maintenance treatment:
  - discuss and agree with them and their parents/carers follow-up plans including frequency of follow-up and who they should see,
  - ensure they know which symptoms suggest a relapse and should prompt an appointment with their healthcare professional (e.g. unintended weight loss, abdominal pain, diarrhoea, general ill-health) and how to access the healthcare system,
  - discuss the importance of not smoking.

Maintenance treatment

- Offer **azathioprineU** or **mercaptopurineU:**
  - as monotherapy to maintain remission when previously used with a conventional glucocorticosteroid or budesonide to induce remission,
  - to maintain remission in people who have not previously received these drugs (particularly those with adverse prognostic factors such as early age of onset, perianal disease, glucocorticosteroid use at presentation and severe presentation).
- Consider **methotrexateU** to maintain remission only in people who:
  - needed methotrexate to induce remission, **OR**
  - have tried but did not tolerate azathioprine or mercaptopurine for maintenance, **OR**
  - have CIs to azathioprine or mercaptopurine (e.g. deficient TPMT activity or previous episodes of pancreatitis).
- **Do NOT** offer a conventional glucocorticosteroid or budesonide to maintain remission.

Surgery

Consider surgery as an alternative to medical treatment early in the course of the disease in:

- Children and young people whose disease is limited to the distal ileum and who have growth impairment despite optical medical treatment, and/or refractory disease.
- Adults whose disease is limited to the distal ileum. Take into account:
  - benefits and risks of medical treatment and surgery,
  - risk of recurrence after surgery,
  - individual preferences,
  - record the person's views in their notes.

Managing strictures – see full guideline

Maintenance treatment after surgery

To maintain remission after surgery;

- Consider **azathioprineU** or **mercaptopurineU** in people with adverse prognostic factors such as:
  - more than one resection, **OR**
  - previously complicated or debilitating disease (e.g. abscess, involvement of adjacent structures, fistulising or penetrating disease).
- Consider **5-ASA.**
- **Do NOT** offer budesonide or enteral nutrition.

Conception and pregnancy

- Give information about the possible effects of Crohn's disease on pregnancy, including potential risks and benefits of medical treatment and possible effects of Crohn's disease on fertility.
- Effective contraception is required during and for at least 3 months after immunosuppressive treatments in men and women (see individual product SPCs).
- Ensure effective communication and information-sharing across specialties (primary care, obstetrics and gastroenterology) in the care of pregnant women with Crohn's disease.

Monitoring

- Monitor drug treatments as advised in the current BNF or BNFC (consult chapter one and other relevant sections).
- Ensure there are documented local safety policies and procedures (including audit) for adults, children and young people receiving treatment that needs monitoring.
- Nominate a staff member to act on abnormal results; to communicate with GPs and people with Crohn's disease and/or their parents/carers.

5-ASA (aminosalicylates)

- Monitor renal function before treatment starts, at 3 months then annually (more frequently if renal impairment).
- If there is suspicion of a blood dyscrasia do a blood count and stop the drug immediately.

Azathioprine and mercaptopurine*

- Do a full blood count weekly for the first 4 weeks of treatment (more frequently with higher doses or if severe hepatic or renal impairment present). Then monitor at least every 3 months.
- Monitor for neutropenia even if the person has normal TPMT activity.

Methotrexate

- Do a full bood count, renal and liver function tests before starting treatment and repeat every 1 to 2 weeks until treatment is stabilised. Then monitor every 2 to 3 months.

Osteopenia

- Crohn's disease is a cause of secondary osteoporosis.
- Assess the risk of fragility fracture in adults: see NICE CG146.
- **Do NOT** routinely monitor for changes in BMD in children and young people.
- Consider monitoring BMD in children and young people with risk factors including low BMI, low trauma fracture or continued/repeated glucocorticosteroid use.

Colonoscopic surveillance – see NICE CG118.

Counselling

- Give information, advice and support on; smoking cessation, medicines adherence, and fertility.
- Provide additional information on the following when appropriate:
  - possible delay of growth and puberty in children and young people,
  - diet and nutrition,
  - fertility and sexual relationship,
  - prognosis,
  - adverse effects of their treatment,
  - cancer risk,
  - surgery,
  - care of young people in transition between paediatric and adult services,
  - contact details for support groups.
- Give age-appropriate, multidisciplinary support if there are concerns about the disease and its treatment, including body image, living with a chronic illness, and attending school and higher education.
- Advise patients to report symptoms such as bruising, purpura, sore throat, mouth ulcers, fever or malaise during treatment with 5-ASA or immunosuppressives (see BNF).

Visit the NICE Pathway: Crohn's disease

*See Summary of Product Characteristics for full prescribing information.