

Ustekinumab for refractory Crohn's disease in pre-pubescent children (aged < 6 years old) [200404P]

Summary

Ustekinumab is not recommended to be available as a routinely commissioned treatment option for refractory Crohn's disease in pre-pubescent children aged < 6 years old.

The policy is restricted to certain age groups as there is insufficient evidence to confirm safety and it is not recommended to be used in those age groups included in this policy. Ustekinumab may be used according to the criteria specified in NICE technology appraisal (TA) 456 in children aged six years and older via [NHS England's Policy 170001/P Commissioning Medicines for Children in Specialised Services](#). Note that ustekinumab is not licenced in children for Crohn's disease and therefore this is an off-label use.

Committee discussion

Clinical Panel recommended progressing as a not for routine policy proposition.

The evidence base was considered to be sparse in pre-pubertal children with no standard treatment pathways or monitoring. It was agreed that NHS England should await the randomised controlled trial report in 2023 and then review the evidence base.

Clinical Priorities Advisory Group considered the documentation presented.

See the [committee papers](#) for full details of the evidence.

What we have decided

Ustekinumab is licensed for use in adult patients with moderately to severely active Crohn's Disease and access is defined in NICE TA 456 'Ustekinumab for moderately to severely active Crohn's disease after previous treatment'. Ustekinumab is not licensed for this indication in children. Ustekinumab has been licensed for the treatment of moderate to severe plaque psoriasis in children and adolescent patients from the age of 6 years and older. Consequently, the NHS England Commissioning Medicines for Children in Specialised Services policy can be applied to enable off-label use of ustekinumab in children aged 6 years and over with Crohn's disease.

NHS England has carefully reviewed the evidence to treat refractory Crohn's disease with ustekinumab in pre-pubescent children in this policy. We have concluded that there is not enough evidence to make the treatment available at this time for children aged less than six years of age.

Plain language summary

About Crohn's disease

Crohn's disease (CD) is a long-term condition that mainly affects the bowel. Some people may develop symptoms that affect other body parts as well. There are currently at least

115,000 people in the UK with CD. Up to a third of people with CD are diagnosed before the age of 21 years. Common symptoms of CD in children include bloody diarrhoea, weight loss, abdominal (tummy) pain and delayed puberty.

CD has two basic phases: the active phase and the remission (inactive) phase. The active phase involves frequent flares (sudden occurrences of severe symptoms). There are two different treatments depending on the phase of the disease; treatment of active phase of the disease (inducing remission) or prevention of relapse during the remission phase. For this policy, refractory CD is defined as patients whose active disease does not respond or has stopped responding to standard treatment.

About current treatment

Treatment is largely to relieve symptoms rather than cure. For mild disease, two types of therapies are generally used: enteral nutrition or steroids. For severe disease, add on therapy with stronger immunosuppressive medications such as azathioprine and methotrexate are used. Infliximab, a tumour necrosis factor (TNF) alpha inhibitor can be used in severe, active CD.

For children who have failed all the treatment as stated above, there is no alternative licensed therapy. These patients may be dependent on steroids to control the disease. Patients are at risk of complications and repeated surgical interventions if the disease is poorly controlled.

About the new treatment

Ustekinumab is a biological human monoclonal antibody, which inhibits human cytokine interleukins 12 and 23 (which are involved in immune system functions), thereby reducing disease activity (ustekinumab, summaries of product characteristics).

Ustekinumab is licensed for the treatment of moderately to severely active CD in adults and access is defined as per NICE TA 456 'Ustekinumab for moderately to severely active Crohn's disease after previous treatment'.

Ustekinumab is not licensed for this indication in children under 18 years.

The subcutaneous injections are licensed for the treatment of moderate to severe plaque psoriasis in young people from the age of 6 years and older. Access for children aged 6 years and older may be considered in line with the criteria in NHS England's Commissioning Medicines for Children in Specialised Services policy (NHS England 170001/P, 2017). This policy therefore does not commission the use of ustekinumab to treat refractory CD in children less than 6 years old.

Epidemiology and needs assessment

The incidence of CD in CYP is increasing worldwide, ranging from 2.5 to 11.4 per 100,000 population, with an estimated prevalence of 43/100,000 (Benchimol EI et al 2011; Kappelman MD et al, 2007). It is estimated that 8,000 CYP are affected by IBD nationally. It is anticipated that around 30% CYP will require escalation to TNF alpha inhibitor treatment, out of which, 10% will fail the treatment or not maintain a response and require ustekinumab. This approximates to 250 CYP nationally, and 10-15 CYP annually within a large paediatric IBD centre.

In paediatric-onset CD, the genetic component is more dominant and recurrence within the family is more prevalent than in adults (Polito II JM et al, 1996; Griffiths AM, 2004).

Childhood is a time of dynamic physical changes, bone accrual and growth along with emotional maturation. Paediatric IBD is also more often extensive and is associated with a more aggressive disease course, including a greater propensity for disease extension and early immunomodulation (Van Limbergen J, 2008; Vernier-Massouille G et al, 2008; Pigneur B et al 2010).

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Abbreviated paediatric Crohn's disease activity index (PCDAI)	An abbreviated scoring system that evaluates CD disease activity. A score of 0 to 70 with 0 to 10: remission, 10 to 15: mild disease, 16 to 25: moderate disease and greater than 25: severe disease.
Children and young people (CYP)	This refers to children and young people aged 3-18 years.
Pre-pubescent children	A child or young person in the years prior to puberty, as determined by clinical judgement.
Enteral nutrition	This refers to a method of feeding that delivers nutrition and medication directly to the gastrointestinal tract.

Ileocaecal resection	This surgery involves removing the junction of the small and large intestine. The healthy end of the small intestine is then joined directly to the colon.
Immunosuppressive medications	This is a group of medication that acts by suppressing the immune system. Examples are aminosalicylates (5-aminosalicylic acid, 5-ASA) and methotrexate.
Inflammatory bowel disease (IBD)	This refers to Crohn's disease and ulcerative colitis. Both causes inflammation in the bowels.
Refractory Crohn's disease (CD)	This means there is high Crohn's disease activity despite conventional pharmacological treatment, including inadequate response to or loss of response to TNF alpha inhibitor treatment.
Steroids	This includes prednisolone, methylprednisolone or intravenous hydrocortisone.
Stricture	Narrowing of the intestine.
Stool/ faecal calprotectin	A substance that is found in the intestines when there is inflammation present.
Tumour necrosis factor alpha (TNF alpha) inhibitors	This refers to a group of biological medication that blocks a pro-inflammatory molecule, TNF alpha in the body. An example of this is infliximab.

References

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