NHS England

Clinical Commissioning Policy: Infliximab for the treatment of hidradenitis suppurativa

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Clinical Commissioning Policy: Infliximab for the treatment of hidradenitis suppurativa

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Contents

Policy Statement

NHS England will not routinely commission infliximab for the treatment of hidradenitis suppurativa in accordance with the criteria outlined in this document. In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources. This policy document outlines the arrangements for funding of this treatment for the population in England.

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

Plain Language Summary

About Hidradenitis Suppurativa (HS)

Hidradenitis Suppurativa (HS) is a painful skin disease.

- It causes abscesses - a painful collection of pus under the skin.
- It also causes scars on the skin - usually around the groin, buttocks, breasts and armpits.

It is not clear what causes the bumps and spots - they may be the result of blocked sweat glands (holes in the skin where sweat comes from) and hair follicles (holes in the skin that the hair grows out of).

HS usually starts around the age of 11 to 12 years.

- However, it can appear at any age.

- It lasts for most of someone's life and will always need treatment.

If the illness is bad, it can seriously affect a person's social life and levels of activity. Patients may need to go to hospital often.

About the new treatment

Infliximab is a medicine used for 'auto-immune' illnesses - like Crohn's disease. This is where the body's immune system doesn't work properly. Infliximab dampens down the body's immune response and reduces inflammation (swelling). This means it might work for patients with HS.

What we have decided

NHS England has carefully reviewed the evidence treat HS with infliximab. We have decided that there is not enough evidence to make the treatment available at this time.

1 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission infliximab for patients with hidradenitis suppurativa (HS).

Hidradenitis suppurativa (HS) is a chronic skin disease that causes abscesses and scarring on the skin, usually around the groin, buttocks, breasts and armpits. The disease tends to start in one area with the formation of a single, firm lesion. If the condition is not diagnosed or adequately controlled with medication, lesions are likely to become increasingly more common, spread to other areas of the body and grow in size. As the disease progresses, patients may also develop fistulas or sinus tracts, channels that form under the skin and break out on the surface and constantly discharge pus. Lesions, fistulas and sinus tracts are all prone to secondary infection which will usually require antibiotic treatment.

The condition can have a very significant impact on quality of life, requiring hospital admissions and resulting in major physical impairment, e.g. preventing sitting, mobilising or sexual function, causing scarring or permanent swelling (lymphoedema) of involved sites within the armpits and anogenital skin. Longstanding uncontrolled disease is occasionally associated with skin cancer. The condition can have a significant impact on the patients' social functioning, such as their ability to work or have intimate relationships.

The exact cause of HS is unclear; however the lesions appear to be the result of blocked hair follicles linked to sweat glands. There are indications that genetic factors play a role in up to a third of patients, meaning the condition is more likely in those with relatives who are affected. The British Association of Dermatologists has also suggested that HS may be linked to Crohn's disease.

Onset of HS is most common in late teens and early 20s. HS outbreaks may persist for years with interspersed or continuous periods of inflammation. Early diagnosis is important as a successful combination of treatments can often help manage the condition and prevent the need for multiple surgeries. Due to the relative lack of

attention in the medical literature and often embarrassing nature of the disease, many patients are either misdiagnosed or do not seek medical diagnosis.

Infliximab is a biologic therapy known to reduce the body's inflammatory response. There is substantive clinical evidence and experience of its effectiveness in other autoimmune disorders such as Crohn's disease and rheumatoid arthritis. For this reason, there is clinical interest in whether it may alleviate symptoms and improve quality of life among patients with HS. Infliximab is not currently licensed for this indication and it is unlikely that an extension will be sought as the patent for infliximab has now expired and biosimilar products are now available.

2 Definitions

Hidradenitis suppurativa (HS) is a chronic skin disease characterised by clusters of abscesses or subcutaneous boil-like infections that most commonly affect sweat gland bearing areas such as the underarms, under the breasts, inner thighs, groin and buttocks.

Hurley's staging system is used for the classification of patients with skin/dermatologic diseases. It separates patients into three groups based largely on the presence and extent of diseased tissue:

Hurley Stage I: Solitary or multiple isolated abscess formation without scarring or sinus tracts.
Hurley Stage II: Recurrent abscesses, single or multiple widely separated lesions with sinus tract formation. (Frequent restriction of movement, which may require minor surgery such as incision or drainage.)
Hurly Stage III: Diffuse or broad involvement across a regional area with multiple interconnected sinus tracts and abscesses, which impact on the ability of the patient to function.

Infliximab is an antibody administered intravenously that is licensed for treating a number of chronic inflammatory diseases. It works by blocking the effects of tumour

necrosis factor alpha, a substance made by cells of the body which has an important role in promoting inflammation.

3 Aims and Objectives

This policy proposition aims to define NHS England's commissioning position on infliximab as part of the treatment pathway for adult and adolescent patients with hidradenitis suppurativa.

The objective is to ensure an evidence based approach in considering the use of infliximab for adult and adolescent patients with hidradenitis suppurativa.

4 Epidemiology and Needs Assessment

While diagnosis of hidradenitis suppurativa is rare, the estimated prevalence is approximately 90,000 patients in England. Prevalence of HS is proportionally higher in women who are more frequently affected than men at a ratio of 2.7 (NICE, 2015).

Due to a lack of research and licensed interventions for HS, the patient pathway is complex and it is difficult to estimate what proportion of patients fail to respond to standard treatment. Based on expert clinical opinion, it is estimated that this would be up to 100 HS patients per annum in England.

5 Evidence Base

NHS England has concluded that there is currently not sufficient evidence to support a proposal for the routine commissioning of infliximab for patients with hidradenitis suppurativa. Opportunities for additional high quality research should be considered to provide further insight into the likely benefits and risks of using infliximab in the management of HS.

In summary:

- There are predominantly level 2/3 studies that report on the clinical effectiveness of infliximab in patients with moderate to severe HS, with one small (n=38) RCT. The RCT found non-significant difference at the initial primary endpoint however significant benefit was found in post hoc analysis.

- Infliximab appears not to be associated with significant adverse effects in the majority of patients, noting that there is a lack of long term studies. Hypersensitivity reactions to infliximab are not uncommon.
- There is insufficient evidence to identify subgroups of patients with moderate to severe HS who may benefit more from infliximab.
- To date, no studies have been identified which evaluate the cost effectiveness of infliximab in the treatment of HS.

Research question 1: Is infliximab clinically effective in limiting the frequency and severity of flares and avoiding sequential surgery to affected areas in patients who have moderate (Hurley stage II) or severe (Hurley stage III) hidradenitis suppurativa, despite optimised treatment with multiple conventional therapies?

The evidence on clinical effectiveness of infliximab in the treatment of patients with HS is limited to a small, single-centre RCT and (predominantly) level 3 studies. This is not unexpected given the rarity of this condition.

The majority of patients who received infliximab were not in remission and had failed to respond to conventional treatments (systematic antibiotics, steroids and/or retinoid). Grant et al. (2010) in a double blinded, randomised control trial (level 1-) (n=38) found non-significant benefit in patients receiving infliximab at initial primary end point analysis when compared to placebo. Post-hoc analysis however showed a significant benefit, with reduction in the HS severity index score of 25-50% ($p<0.001$). These findings are consistent with several systematic reviews (Brunasso et al., 2011 and Blok et al., 2013, level 2- and 3 respectively) that consist predominately of case series and case studies, and have shown a significant to moderate response in up to 90% of the patients. All of the systemic reviews evaluated have incorporated the RCT conducted to date (Grant et al., 2010), with duplication of evidence.

The baseline scores of both dermatology life quality index (DLQI) and visual analogue scale (VAS) that assesses pain, in HS is high. Grant et al. (2010) observed a significant improvement in the DLQI ($P=0.003$), VAS ($P<0.001$) and physicians global assessment score ($p<0.001$) in the infliximab treatment group at 8 weeks.

They also found a reduction in inflammatory markers, erythrocyte sedimentation rate and C-reactive protein in the infliximab group. These findings are consistent with other reported case series and case studies (level 3), with majority of follow-up to one year.

Van Rappard (2012), a small (n=20) retrospective cohort study, compared treatment outcomes of infliximab with another biological therapy and found that at one year, infliximab was more effective than adalimumab. There is insufficient evidence to compare other biological therapies with infliximab in treating severe to moderate HS.

The majority of studies have used 5mg/kg of intravenous infliximab, induction therapy (0, 2 and 6 weeks), and if continued then maintenance therapy at 8 weekly cycles. Moriarty et al., (2014) (level 3) described in three patients a weaning of response at 4 weeks during maintenance therapy, and were subsequently changed to 4 weekly cycles with an improvement in symptoms. It is widely recognised that infliximab can potentially lead to a loss of response long-term, attributed to immunogenicity and development of drug antibodies. Paradela et al. (2012) (level 3) assessed long-term efficacy of infliximab in HS in 10 patients and observed that relapse occurred in 50% of patients after a median period of 37 weeks with a median disease free period of 16 weeks.

Research question 2: Is infliximab a safe and well tolerated drug to use in patients with hidradenitis suppurativa (Hurley stage II-III)?

In the majority of patients, infliximab appears not to be associated with significant adverse effects. It has been associated with infusion reactions, and Grant et al. (2010) (level 1-) reported hypersensitivity reactions in up to 22% of patients (4 patients). Cases of opportunistic infections, hepatitis, lupus, peripheral neuropathy and pulmonary embolism have also been reported. Scheinfeld et al. (2014) reported a case (level 3) of a patient with severe HS developing metastatic squamous cell carcinoma (SCC) during induction therapy with infliximab. It remains controversial whether infliximab promotes the development of SCC in HS.

The paradoxical effects of infliximab have been reported. Gori et al. (2012) reported a patient developing acne and Nuno et al. (2012) (level 3) describe a patient developing flexural psoriasis. Acaquacalda et al. (2015) described 3 patients out of 11 developing an acute and painful polyarthritis without a systematic reaction during treatment with infliximab, resolution of arthritic symptoms following cessation of two patients and one following treatment with another biological therapy. There is a lack of long-term studies evaluating the tolerance of infliximab in HS patients

Research question 3: Are there any particular subgroups of patients with hidradenitis suppurativa (indicated by severity, co-morbidities and demographic factors) who are likely to benefit more from the use of infliximab?

HS is associated with other inflammatory conditions, such as inflammatory bowel disease, SAPHO syndrome, psoriasis and pyoderma gangrenosum. A systemic review (level 3) evaluated the efficacy of infliximab in patients with HS and other inflammatory disease (Machet et al., 2013) and reported infliximab to be efficacious in 72% of the cohort (16/22 patients), with statistically insignificant higher failure rates when compared to patients with HS alone (27% vs 13%, p=0.1).

There is insufficient evidence to identify subgroups of patients with HS who may benefit more from infliximab. However, infliximab has been administered to patients with moderate to severe HS in all studies.

Research question 4: Is infliximab cost effective in the treatment of hidradenitis suppurativa (Hurley stage II-III)?

To date no studies have been identified which evaluate the cost effectiveness of infliximab in the treatment of HS.

6 Documents which have informed this Policy

NICE Single Technology Appraisal- Adalimumab for treating moderate to severe hidradenitis suppurativa. Final scope (October 2015)

7 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

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