NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: September 2020

Intervention: Abatacept

Indication: refractory idiopathic inflammatory myopathies (adults and children over the age of 2 years)

URN: 1925

Gateway: 2, Round 1

Programme: Internal Medicine

CRG: Specialised Rheumatology

Information provided to the Panel

Policy Proposition

Evidence review completed by Solutions for Public Health

Equality and Health Inequalities Assessment (EHIA) Report

Clinical Priorities Advisory Group (CPAG) Summary Report

Patient Impact Form

Key elements discussed

This policy proposition has been developed as a for routine commissioning proposition recommending the use of abatacept for refractory idiopathic inflammatory myopathies (IIM) in adults and children over the age of 2 years old. IIM are chronic inflammatory conditions characterised by muscle inflammation. This leads to weakness which has significant impact on patients' mobility and quality of life. Both adults and children may experience damage to skin, joints, lungs, heart, stomach and gut. Use of Abatacept is proposed as third line treatment ahead of intravenous immunoglobulin (IVIg) when there is an intolerance or inadequate response to glucocorticoids and at least two other immunosuppressive or immunomodulatory agents.

Panel were presented with the evidence review which comprised of a small multi-centre randomised controlled trial comparing immediate treatment with abatacept and delayed treatment with abatacept. It was not clear if the study was powered to demonstrate efficacy due to the trial being a feasibility study. Some self-reported outcomes, such as quality of life, may have created bias and standard treatment given to the delayed treatment group was not described. It was not clear whether some patients also received IVIg during the trial. The study provides evidence of treatment benefit at 3 months in comparison to standard treatment. The evidence suggested there was some improvement in disease activity and Total Improvement Score. However, it was noted there was no evidence available for children, yet the proposition includes children aged over 2 years. The PWG should review this and amend policy title accordingly. Two relevant sub-populations, drug induced myositis and malignancy associated myositis, were excluded from the available evidence. The PWG should consider how

generalisable the available data are to support inclusion of these sub-populations within the eligibility criteria in the proposition.

Overall Clinical Panel considered the size of desirable effect did not translate into clinical benefit and that the clinical effectiveness of abatacept in comparison to IVIg was unclear. As such, Panel requested examination of the evidence underpinning the existing IVIg provision to assess whether abatacept should replace IVIg as 3rd line treatment and requested Panel were presented with a summary to assist with determining the commissioning decision. The PWG were advised to liaise with an IVIg specialist to seek an opinion as to whether the reported abatacept treatment effects might represent clinical benefit and might represent greater benefit than treatment with IVIg than abatacept. Panel considered that access to abatacept may preserve stock of IVIg but agreed the decision to commission should be evidence based. It was suggested that abatacept could considered at the same line as treatment as IVIG dependent on what was most clinically suitable.

Panel noted that the proposition may have benefits in relation to the COVID pandemic as it would allow treatment access facilitated by a virtual multi-disciplinary team, and this may particularly benefit patients in remote locations.

The EHIA was considered. It was noted that implementation of this proposition could advance equality by providing a treatment option for a rare disease and provide access to patient in remote areas.

Recommendation

Clinical Panel does not recommend that this proposition progresses as a for routine commissioning policy proposition at this time as evidence of effectiveness in comparison to IVIg needs to be explored further prior to recommending a commissioning position.

Why the panel made these recommendations

The Panel considered that the evidence base presented was limited and of low quality.

Documentation amendments required

Policy Proposition:

- Paediatric dose to be cross checked with SmPC.

Declarations of Interest of Panel Members: None.

Panel Chair: Anthony Kessel, Clinical Director, National Clinical Policy Team, Specialised Services.

Post panel note

The clinical panel report has been discussed with the policy working group (PWG) and the Chair of the Blood and Infection Programme of Care.

Issue 1 raised by Clinical Panel:

PWG to review inclusion of a paediatric population (children over the age of 2 years), amend policy title accordingly, and cross check the paediatric dose with SmPC.

PWG response:

The PWG wish to keep the policy proposition available to children over the age of 2 years. There is often limited data available for medication efficacy in children and there are concerns that restricting access to the drug in children may lead to inequity in treatment. Abatacept is licensed in over 2 year olds according to the SmPC, in subcutaneous form between the ages of 2-6 years and intravenously after 6 years. Children can suffer from a more severe form of the condition and may have added benefit from receiving the medication. As a precedent, the 1921 abatacept in localised scleroderma policy has recommended abatacept for use in over 2 year olds previously. This has been discussed with and approved by the Pharmacy Lead and CRG Lead Pharmacist.

Issue 2 raised by Clinical Panel:

Two relevant sub-populations, drug induced myositis and malignancy associated myositis, were excluded from the available evidence. The PWG should consider how generalisable the available data are to support inclusion of these sub-populations within the eligibility criteria in the proposition.

PWG response:

The PWG have discussed that statin-induced immune-mediated necrotising myopathy (the drug induced myositis referred to in the report) and dermatomyositis associated with cancer (malignancy associated myositis) should remain included within the policy proposition. The clinical commissioning policy for rituximab in the treatment of dermatomyositis and polymyositis (adults), which looks at an earlier line of treatment in the same group of patients, does not specifically exclude those populations and the PWG wish to follow that precedent. Treatment with immunosuppressants is sometimes indicated in these patients and the same pathway is followed.

Issue 3 raised by Clinical Panel:

Panel requested examination of the evidence underpinning the existing IVIg provision to assess whether abatacept should replace IVIg as 3rd line treatment and requested Panel were presented with a summary to assist with determining the commissioning decision.

PWG Response:

As per the clinical panel request, an evidence summary table of evidence underpinning IVIg provision has been provided. Please also see PWG response to issue 4; abatacept is **not** being recommended to rigidly replace IVIg as 3rd line treatment in all cases.

Issue 4 raised at Clinical Panel:

The PWG were advised to liaise with an IVIg specialist to seek an opinion as to whether the reported abatacept treatment effects might represent clinical benefit and might represent greater benefit than treatment with IVIg. It was suggested that abatacept could considered at the same line as treatment as IVIG dependent on what was most clinically suitable.

PWG response:

The PWG have liaised with the Chair of the Blood and Infection Programme of Care and have reached the following consensus:

Patients with refractory disease (see eligibility criteria in policy proposition draft for definition) will have all treatment decisions including the order of treatment discussed on a case-by-case basis with an expert multidisciplinary team. This includes prescribing abatacept, IVIg and/or cyclophosphamide. Treatment lines may be given sequentially or concurrently depending on clinical status. The patient pathway diagram has been updated to reflect this.

Abatacept is to be considered before IVIg on a case-by-case basis in the new treatment pathway through discussion with the expert multidisciplinary team, unless patients have presented with rapidly deteriorating disease involving major organ involvement including severe lung/respiratory muscle/skin/cardiac involvement and dysphagia. Here IVIg is to be commenced initially as a bridging therapy before prescribing abatacept. Both are to be prescribed concomitantly whilst IVIg is then weaned down over a period of 6 months, which can be modelled after the Improving Values Scheme for switching rituximab and IVIg (attached as Appendix A in the policy proposition document). The PWG have stated that this would be in line with the rituximab policy, current clinical practice, and would be cost saving.