NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 17th January 2024

Intervention: abatacept

Indication: autoimmune complications of primary immunodeficiencies caused by CTLA-4 or LRBA genetic mutation (aged 2 years and over)

URN: 2309

Gateway: 2, Round 1

Programme: Blood and Infection

CRG: Immunology and Allergy

Information provided to the Panel

Policy Proposition

Evidence Review completed by Solutions for Public Health

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision (EtD) Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq™ Form

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the off-label use of abatacept as a treatment option for patients with autoimmune complications of primary immunodeficiencies (PID) caused by CTLA4 or LRBA genetic mutation (aged 2 years and over). PID is a rare heritable condition where the body's immune system does not work properly and in some cases attacks itself (autoimmunity). The illness can affect one or many parts of the immune system and the genetic causal mechanisms can vary greatly. There is no current standard of care pathway, and each autoimmune complication of PID associated with loss of immune function tends to be managed in isolation. The current prevalence is estimated to be 60 people, with one new diagnosis per annum. Abatacept is a biological medicine that specifically targets regulatory T cells and can be given intravenously or subcutaneously.

The proposition and the supporting evidence review were presented to Panel members. Four non-comparative studies were included in the evidence review - three retrospective case series and one prospective case series, including between 18 and 29 patients treated with abatacept. No cost-effectiveness studies were identified.

The critical outcomes for clinical effectiveness were disease remission, organ specific disease activity/response and symptom alleviation. Important outcomes identified were treatment failure, radiographic changes, steroid use reduction, and quality of life (QoL). The presentation to Panel members covered all elements of the evidence. The evidence presented across all critical and

important outcomes was reported as very low using modified GRADE. Limitations of the studies presented were discussed including the lack of comparison with standard of care and, in one of the studies, some patients received other treatments.

It was highlighted that one study reported statistically significant improvement in the median score used to assess disease burden and treatment responses in both children and adults. Two studies provided evidence that most children and adults experienced full or partial response or remission of organ specific disease. Evidence was also reported in symptom improvement. In one study it was reported that 1/23 patients stopped treatment due to inadequate response. Very few non-severe adverse events were experienced.

Panel members agreed that clinical benefit and improvement in patient outcomes from using this treatment was clearly evidenced across critical and important outcomes.

The proposition and supporting documents were considered and some amendments requested.

Panel members discussed that many patients would be treated with steroids and rituximab. The order of treatment was discussed. It is not clear where this treatment would be considered in the pathway or the anticipated duration of treatment.

EHIA – a point to be considered for inclusion. PIA
– no amendments required.

Recommendation

Clinical Panel agreed with the proposition and recommended this proceeds as a routine commissioning proposition once the amendments requested had been completed and approved via Chair's action.

Why the panel made these recommendations

Clinical Panel acknowledged the challenges of conducting robustly designed research in conditions that have small patient populations. Although limited and of very low certainty, Clinical Panel considered the available evidence showed clear clinical benefit for patients for all critical outcomes and that these would outweigh the harms of the very few non-severe adverse effects identified.

Documentation amendments required Policy Proposition:

- The proposition needs to outline what is commissioned treatment and what is not as this is currently unclear.
- The Summary of Product Characteristics advise caution of use in patients prone to infection, which is this group. Careful consent and monitoring is needed and this should be made clear in the proposition.
- Inclusion criteria – ○ It is not clear where this treatment would be considered in the pathway or the anticipated duration of treatment. Clarification required.
    - The term 'organ dysfunction' needs definition as not currently clear what this means.
- Starting criteria –

    - multidisciplinary team – this requires defining further as it is not clear what the definition of a credible expert in this situation is.
- Monitoring – Policy Working Group to look at the six-month review requirement as this was considered too late by Panel members and should happen earlier.
- Dosing – although the information is taken from the SmPC, it is confusing to understand. The national specialised services Pharmacy Lead should support how to present this more effectively in the proposition.
- Audit section – ○ There is an expectation to participate in a registry – does this already exist and therefore in use?
    - states rituximab rather than abatacept. This requires amending.

EHIA:

- Genetic testing may not be easily accessible to all hospitals. Does this need to be highlighted or a form of words to address/mitigate in the EHIA?

Declarations of Interest of Panel Members: One received due to clinical practice.

Panel Chair: Anthony Kessel, Deputy Medical Director, Specialised Services

Actioned amendments

Required action	Response
Policy Proposition	
The proposition needs to outline what is commissioned treatment and what is not as this is currently unclear.	**Actioned – written more clearly**
The Summary of Product Characteristics advise caution of use in patients prone to infection, which is this group. Careful consent and monitoring is needed and this should be made clear in the proposition.	**Actioned – this has been made clear in the starting criteria**
Inclusion criteria	
It is not clear where this treatment would be considered in the pathway or the anticipated duration of treatment. Clarification required.	**Actioned – the section 'about abatacept' and the inclusion criteria have both been updated to make it clear that abatacept is a first line treatment option for those eligible**
The term 'organ dysfunction' needs definition as not currently clear what this means.	**Actioned – examples of what this means have been added. This is not an extensive list as organ dysfunction may present differently for each patient**
Starting criteria	
multidisciplinary team – this requires defining further as it is not clear what the definition of a credible expert in this situation is.	**Actioned – this has been changed to reflect that immunologists should be starting treatment with abatacept**
Monitoring	
Policy Working Group to look at the six-month review requirement as this was considered too late by Panel members and should happen earlier.	**The PWG felt that six months was the earliest that response to treatment could be monitored. Additional information was added to the monitoring section to demonstrate how response may be assessed. The monitoring section also states a medical review at 3 months should be done to assess tolerability to treatment.**
Dosing	
Although the information is taken from the SmPC, it is confusing to understand. The national specialised services Pharmacy Lead should support how to present this more effectively in the proposition.	**Actioned – the dosing section has been moved to an appendix and split into adults and paediatrics to make things clearer.**
Audit section	
There is an expectation to participate in a registry – does this already exist and therefore in use?	**The registry already exists and the PWG were keen that clinicians using abatacept**

	should be encouraged to populate the registry.
states rituximab rather than abatacept. This requires amending.	**Actioned**
EHIA	
Genetic testing may not be easily accessible to all hospitals. Does this need to be highlighted or a form of words to address/mitigate in the EHIA?	**The policy states 'genetic testing of blood by a sensitive PCR based method and/or laboratory confirmation of LRBA deficiency or CTLA-4 insufficiency must have occurred prior to initiating treatment' to mitigate for when genetic testing may not be available. All hospitals should have access to tests that will allow laboratory confirmation of the condition, even if genetic testing is not available.**