# Clinical Commissioning Policy:
# Abatacept for autoimmune complications of primary immunodeficiencies caused by CTLA-4 or LRBA genetic mutation (aged 2 years and over) [2309]

## Summary

Abatacept is not recommended to be available as a routine commissioning treatment option for autoimmune complications of primary immunodeficiencies caused by CTLA-4 or LRBA genetic mutation within the criteria set out in this document.

The policy is restricted to adults and children aged two years and over in line with licenced indications for abatacept. There is insufficient safety data for use of intravenous abatacept in children under the age of two years old.

## Committee discussion

Clinical Panel considered the evidence base and the decision was made to progress the policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed on the NHS England website.

## What we have decided

NHS England has carefully reviewed the evidence to treat autoimmune complications of primary immunodeficiencies caused by monogenic disorders in CTLA-4 and LRBA gene function with abatacept NHS England recognises that the published evidence identifies that, at present, there is sufficient evidence to commission this treatment. However, following the relative prioritisation process undertaken in May 2024 for funding interventions in 2024/25, NHS England has concluded that, balanced against other relative priorities that were also considered during this process, abatacept for autoimmune complication of primary immunodeficiencies caused by CTLA-4 or LRBA genetic mutation (Aged 2 years and over) will not be funded this time within the resources available.

The evidence review which informs this commissioning position can be accessed on the NHS England website.

## Links and updates tor policies

This document relates to the following policies:

Allogeneic haematopoietic stem cell transplant for primary immunodeficiencies

- HSCT clinical commissioning policy

Immunoglobulin replacement therapy in primary immunodeficiencies

- Immunoglobulin replacement clinical commissioning policy

# Plain language summary

## About primary immunodeficiencies

Primary immunodeficiencies (PID)[1] are rare heritable conditions 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. One of the presentations of PID is of chronic immune dysregulation which may cause autoimmune disease including chronic inflammation. This may be caused by dysfunction of the regulatory T ($T_{Reg}$) cell, an immune cell that is essential for preventing autoimmunity. Genetic causes for these immune deficiencies have been identified in some patients, including single gene (monogenic) mutation of the lipopolysaccharide (LPS)-responsive and beige-like anchor protein (LRBA) or cytotoxic T-lymphocyte associated protein 4 (CTLA-4) genes which lead to the production of faulty LRBA or CTLA-4 proteins. These proteins are responsible for normal regulation of the $T_{Reg}$ cell.

Patients often suffer with complex autoimmune diseases that may affect most organs and the blood as a result of PID. This may include – but is not limited to – autoimmune lung disease that, if untreated, will result in progressive and irreversible lung fibrosis or respiratory failure, a range of skin diseases including psoriasis and vitiligo, arthritis, immune cytopenias, neuro-inflammation, inflammatory bowel disease or enteropathy and granulomatous to fibrotic liver disease.

In severe cases, the autoimmune complications may be life-threatening and the life expectancy of patients with PID who suffer with autoimmune complications is considerably shortened (Bates et al, 2004). Patients are also vulnerable to infection as they are unable to make effective antibodies. As a result, most patients will be established on immunoglobulin (Ig) replacement therapy.

## About current treatment

Currently there are no medications commissioned for the treatment of autoimmune complications of PID, and each complication tends to be managed in isolation by immunology specialists in tertiary centres. This is usually with steroids, sirolimus and non-specific immune suppressant agents, such as azathioprine or mycophenolate mofetil.

Definitive treatment for PID is allogeneic hematopoietic stem cell transplant (HSCT), which NHS England currently commissions. However, HSCT is a difficult and high-risk procedure and transplant related mortality for LRBA deficiency is reported to be higher than that of other PIDs (Tesch et al, 2019). Splenectomy may also be considered in intractable cytopenias; however, effectiveness is variable for sustained recovery.

## About abatacept

Abatacept is a biological drug that specifically targets $T_{Reg}$ cells. It is licensed for rheumatoid and psoriatic arthritis in adults and for polyarticular juvenile idiopathic arthritis in children aged two years and older. Abatacept can be given intravenously or

[1] PIDs may also be described in the literature as:

- Human inborn errors of immunity (IEI)
- Primary immune regulatory disorders (PIRD)
- Primary immune deficiencies

subcutaneously. Steroids may be used prior and/or concomitantly in the acute phase to induce and maintain remission.

Abatacept is proposed to be used as first line long-term treatment for autoimmune or inflammatory complications such as granulomatous inflammatory lung disease, arthritis inflammatory bowel disease and autoimmune cytopenias that arise due to $T_{Reg}$ cell dysfunction. Abatacept is used to maintain remission in this condition. This proposed use of abatacept is off label.

## Epidemiology and needs assessment

PID is estimated to affect 4,200 people in the UK and may present at any age, although PID associated with $T_{Reg}$ cell deficiency generally presents in childhood (NHS England, 2018). The incidence of $T_{Reg}$ cell dysfunction is estimated to be <1 per million and has only been described in the literature in the last decade.

Based on estimations from immunology centres in England, the current prevalence of PID associated with $T_{Reg}$ cell dysfunction is estimated to be 60 patients with a new diagnosis of one patient per annum in England.

## 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

| | |
|---|---|
| Allogeneic Haematopoietic stem cell transplantation (HSCT) | A procedure which replaces the patient's own blood stem cells and immune system with those from a healthy donor, enabling the establishment of normal immune system functions. |

| | |
|---|---|
| Autoimmunity | A misdirected immune response that occurs when the immune system goes awry and attacks the body itself. |
| CTLA-4 | Cytotoxic T-lymphocyte-associated protein 4 |
| LRBA | Lipopolysaccharide (LPS)-responsive and beige-like anchor protein |
| Primary immunodeficiency (PID) | A group of rare inherited disorders of the immune system which cause serious, debilitating and often life-threatening diseases. Although many patients with Primary Immunodeficiency will have a clearly defined genetic aetiology, others will remain genetically undefined. |

# References


Bates CA, Ellison MC, Lynch DA, Cool CD, Brown KK, Routes JM. Granulomatous-lymphocytic lung disease shortens survival in common variable immunodeficiency. J Allergy Clin Immunol. 2004 Aug;114(2):415-21. doi: 10.1016/j.jaci.2004.05.057. PMID: 15316526.

Kiykim, A. et al. (2019) 'Abatacept as a long-term targeted therapy for LRBA deficiency', The Journal of Allergy and Clinical Immunology: In Practice, 7(8). doi:10.1016/j.jaip.2019.06.011.

Lo, B. et al. (2015) 'Patients with LRBA deficiency show CTLA4 loss and immune dysregulation responsive to abatacept therapy', Science, 349(6246), pp. 436–440. doi:10.1126/science.aaa1663.

Rodina, Y. et al. (2021) 'Rituximab and abatacept are effective in differential treatment of interstitial lymphocytic lung disease in children with primary immunodeficiencies', Frontiers in Immunology, 12. doi:10.3389/fimmu.2021.704261.

Tesch, V.K. et al. (2020) 'Long-term outcome of LRBA deficiency in 76 patients after various treatment modalities as evaluated by the immune deficiency and dysregulation activity (IDDA) score', Journal of Allergy and Clinical Immunology, 145(5), pp. 1452–1463. doi:10.1016/j.jaci.2019.12.896.

Vignali, D.A., Collison, L.W. and Workman, C.J. (2008) 'How regulatory T cells work', Nature Reviews Immunology, 8(7), pp. 523–532. doi:10.1038/nri2343.

# Appendix

## Paediatrics (<18 years old)

By subcutaneous injection (child 2-17 years old)

Subcutaneous abatacept should be given without an intravenous loading dose.

For children weighing 50kg or more, a dose of 125mg once a week should be used. For children weighing <50kg, please use intravenous abatacept or obtain abatacept 50mg, if 10kg to less than 25kg, or 87.5mg subcutaneous pre-filled syringes, if 25kg - 50kg, via Clinigen on a named patient basis, at the agreed Patient Access Scheme (PAS) Price.

By intravenous infusion (child 6-17 years old)[2]

| **Body weight of child** | **Dose** |
|---|---|
| up to 75 kg | 10mg/kg every four weeks |
| 75 kg to 100 kg | 750mg every four weeks |
| 101 kg or more | 1g every four weeks |

## Adults (≥18 years old)

By subcutaneous injection

Abatacept should be given at a maintenance dose of 125 mg per week via subcutaneous injection, regardless of weight.

This can be given with or without a 30-minute intravenous loading dose, as per the intravenous dosing table (adults) below. If a single IV infusion loading dose is given to initiate treatment, the first 125 mg abatacept subcutaneous injection should be administered within a day of the intravenous infusion, followed by the weekly 125 mg abatacept subcutaneous injections.

By intravenous infusion

| **Body weight of adult** | **Dose** |
|---|---|
| Body weight up to 60 kg | 500 mg every 4 weeks |
| Body weight 60–100 kg | 750 mg every 4 weeks |
| Body weight 101 kg and above | 1 g every 4 weeks |

[2] Use of a loading dose for children treated with intravenous abatacept is at the clinical discretion of the treating consultant and should be used in accordance with the recommended dose in the SmPC