Health Technology Briefing
October 2025

Obinutuzumab for treating childhood onset idiopathic nephrotic syndrome

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 36273	NICE ID: Not Available	UKPS ID: 675143

Licensing and Market Availability Plans

Currently in phase III clinical development

Summary

Obinutuzumab is being developed for the treatment of childhood onset idiopathic nephrotic syndrome. In nephrotic syndrome, there is a problem affecting the sieve mechanism of the kidney. The holes of the sieve enlarge, causing large amounts of protein to leak from the blood into the urine. Research shows that people with nephrotic syndrome often have differences in certain immune cells called B cells, which help fight infections. Although nephrotic syndrome can affect people of any age, it is usually first diagnosed in children aged between one and six years old. Idiopathic is a medical term that describes a condition with an unknown cause. There are currently limited treatment options for patients with childhood onset idiopathic nephrotic syndrome, and current therapies often fail to stop the condition from returning.

Obinutuzumab is a monoclonal antibody (a type of protein) that has been designed to attach to the protein CD20, which is found on B cells. By attaching to CD20 on B cells, obinutuzumab makes them a target for the body's immune (defence) system, which kills the B cells. Obinutuzumab is administered through an injection into a vein (intravenous). If approved (licensed), obinutuzumab would provide a new treatment option for patients with childhood onset idiopathic nephrotic syndrome.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Treatment of childhood onset idiopathic nephrotic syndrome in patients two years and older.[1]

Technology

Description

Obinutuzumab (Gazyva,[2] Gazyvaro) is a recombinant monoclonal humanised and glycoengineered Type II anti-CD20 antibody of the immunoglobulin G1 isotype. It specifically targets the extracellular loop of the CD20 transmembrane antigen on the surface of non-malignant and malignant pre-B and mature B-lymphocytes, but not on haematopoietic stem cells, pro-B-cells, normal plasma cells or other normal tissue. Glycoengineering of the Fc part of obinutuzumab results in higher affinity for FcγRIII receptors on immune effector cells such as natural killer cells, macrophages and monocytes as compared to non-glycoengineered antibodies.[3]

Obinutuzumab is currently in clinical development for the treatment of childhood onset idiopathic nephrotic syndrome. In the phase III clinical trial (INShore, NCT05627557) participants are administered 1000 mg (or 20 mg/ kg for participants less than 45 kg) of obinutuzumab via intravenous (IV) infusions on days 1, 15, 168 (week 24), and 182 (week 26).[1]

Key Innovation

Idiopathic nephrotic syndrome can be classified on the basis of response to steroid therapy or pattern of relapse.[4] The majority of children respond well to steroids within four weeks (steroid-sensitive nephrotic syndrome); however, most will relapse, with approximately half becoming steroid-dependent or developing frequent relapses.[4] The treatment of steroid-dependent or frequently relapsing nephrotic syndrome is challenging because patients may experience a long-term relapsing disease with prolonged exposure to steroids and immunosuppressive drugs over years.[5]

Obinutuzumab represents a promising treatment option for paediatric patients with steroid-dependent or frequently relapsing nephrotic syndrome. At a low dose, obinutuzumab can induce B-cell depletion and sustain remission in children. Obinutuzumab exhibits strong antibody-dependent cytotoxicity, which can result in greater induction of direct cell death by mechanisms that are largely caspase-independent and a less complement-dependent cytotoxity.[5] In a retrospective single-centre cohort study of children with steroid-dependent or frequently relapsing nephrotic syndrome treated with low-dose obinutuzumab, relapse-free survival was high despite the rapid cessation of all oral treatments. One year after obinutuzumab infusion, 92% of the patients remained in remission.[5]

If licensed, obinutuzumab would provide a new treatment option for patients with childhood onset idiopathic nephrotic syndrome.

Regulatory & Development Status

Obinutuzumab has Marketing Authorisation in the EU/UK for the following indications:[3]

- in combination with chlorambucil for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia and with comorbidities making them unsuitable for full dose fludarabine based therapy
- in combination with chemotherapy, followed by obinutuzumab maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma

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Obinutuzumab is also in phase II and III clinical development for:[6]

- membranous nephropathy
- lymphoma
- chronic lymphocytic leukaemia
- graft vs. host disease
- Richter syndrome
- lupus nephritis

Patient Group

Disease Area and Clinical Need

Nephrotic syndrome is a condition that causes the kidneys to leak large amounts of protein into the urine.[7] B cells are suggested to play an important role in the pathogenesis of nephrotic syndrome.[8] Although nephrotic syndrome can affect people of any age, it is usually first diagnosed in children aged between one and six years old. Most children with nephrotic syndrome have times when their symptoms are under control (remission), followed by times when symptoms return (relapses). In most cases, relapses become less frequent as they get older and often stop by their late teens. Main symptoms include swelling (oedema), infections, urine changes, and blood clots.[7] Idiopathic conditions do not have a known cause.[9] Nephrotic syndrome tends to be more common in those with an Asian background, although it is unclear why.[7]

There are approximately 10,000 cases of nephrotic syndrome in the UK each year.[10] Idiopathic nephrotic syndrome has an annual incidence of 2 per 100, 000 children in UK.[11] In England, 2024-25, there were 7,881 finished consultant episodes (FCEs) and 6,185 admissions for nephrotic syndrome (ICD-10 code N04) which resulted in 16,593 FCE bed days and 3,452 day cases.[12]

Recommended Treatment Options

There is no treatment option recommended by National Institute for Health and Care Excellence (NICE) for nephrotic syndrome.

Treatment options for nephrotic syndrome in children include:[7]

- steroids (prednisolone)
- diuretics
- penicillin
- albumin infusions
- other medications which may be used alongside or in place of steroids if the child's remission cannot be maintained with steroids or they experience significant side effects, include:
    - Levamisole
    - Cyclophosphamide
    - Ciclosporin
    - Tacrolimus
    - Mycophenolate
    - Rituximab

Clinical Trial Information

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Trial	**INShore,** NCT05627557, EudraCT-2022-000369-42, CTIS-2023-505140-19-00; A Phase III, International, Multicentre, Randomised Open Label Study to Evaluate the Efficacy and Safety of Obinutuzumab Versus Mycophenolate mofetil in Patients With Childhood Onset Idiopathic Nephrotic Syndrome **Phase III** – Active, not recruiting **Locations:** Five EU countries, USA and other countries **Primary completion date (estimated):** September 2025
Trial Design	Randomised, parallel assignment, active-controlled, open-label
Population	N = 85 (actual); subjects with a diagnosis of frequently relapsing nephrotic syndrome or steroid dependent nephrotic syndrome before the age of 18 years, with at least one relapse in the six months prior to screening, after discontinuation of or while receiving oral corticosteroids and/or immunosuppressive therapy to prevent relapses; aged 2 to 25 years
Intervention(s)	1000 mg (or 20 mg/kg for participants less than 45 kg) obinutuzumab via IV infusion on days 1, 15, 168 (week 24) and 182 (week 26), with premedication of the following prior to infusions: • 80 mg (or 1.5 mg/kg if </=45 kg) methylprednisolone IV • 15 mg/kg acetaminophen orally • 0.5-1 mg/kg diphenhydramine hydrochloride orally or IV
Comparator(s)	600 mg/m^2 mycophenolate mofetil (oral) twice a day (target 1200 mg/m2/day in divided doses, maximum 2 g/day) to week 52
Outcome(s)	Primary outcome measure: Percentage of participants with sustained complete remission at 1 year [time frame: week 52] See trial record for full list of all outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Obinutuzumab is already marketed in the UK. The NHS indicative cost of one 1000 mg/40 ml solution for infusion vial of obinutuzumab (25 mg/1 ml) is £3,312.00.[13]

Relevant Guidance

NICE Guidance

There are no NICE guidelines for nephrotic syndrome.

NHS England (Policy/Commissioning) Guidance

NHS England. Clinical Commissioning Policy: Rituximab for the treatment of Steroid Resistant Nephrotic Syndrome in paediatric patients. E03/P/c. July 2015.

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Other Guidance

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

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