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Health Technology Briefing
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Glofitamab for treating relapsed or refractory mantle cell lymphoma

Company/Developer	Roche Products Ltd.

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 41010	NICE ID: Not Available	UKPS ID: 675272

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Glofitamab is in clinical development for the treatment of relapsed or refractory mantle cell lymphoma (MCL). MCL is a rare type of blood cancer that affects white blood cells called B cells, which normally help fight infection. MCL develops when abnormal B cells build up in the body forming tumours, resulting in problems within the lymphatic system (part of the immune and circulatory systems) or the organ where they are growing. MCL can be difficult to treat because it often comes back after treatment (relapsed) or does not respond well to treatment (refractory). The outcome for patients with relapsed or refractory MCL remains poor, so there is a need to develop additional treatment options.

Glofitamab is an antibody (a type of protein) designed to recognise and attach to CD20, a protein present on the surface of B cells (including the cancer cells), and to CD3, a protein found on the surface of healthy T cells. T cells are another type of white blood cell that are part of the immune system (the body's natural defences) and can destroy cancer cells. By binding to CD20 and CD3, glofitamab acts as a bridge to bring together the cancer cells and T cells. This encourages the T cells to destroy the cancer cells and helps control the cancer. Glofitamab is injected into the vein (intravenous). If approved (licensed), glofitamab would offer an additional treatment option for patients with refractory or relapsed MCL.

Proposed Indication

Treatment of relapsed or refractory (r/r) mantle cell lymphoma (MCL).[1]

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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Technology

Description

Glofitamab (Columvi) is a bispecific monoclonal antibody that binds bivalently to CD20 expressed on the surface of B cells and monovalently to CD3 in the T-cell receptor complex expressed on the surface of T cells. By simultaneous binding to CD20 on the B cell and CD3 on the T cell, glofitamab mediates the formation of an immunological synapse with subsequent T-cell activation and proliferation, secretion of cytokines and release of cytolytic proteins that results in the lysis of CD20-expressing B cells.[2]

Glofitamab is currently in clinical development for r/r MCL. In the phase III trial (GLOBRYTE, NCT06084936), glofitamab is administered via intravenous injection for 12 cycles (cycle length - 21 days) after two intravenous obinutuzumab pre-treatments.[1]

Key Innovation

The 2:1 configuration of glofitamab enables bivalent binding to CD20 on B cells and monovalent binding to CD3 on T cells. Its CD3-binding region is fused to one of the CD20-binding regions in a head-to-tail manner via a flexible linker for improved target-effector cell binding.[3] This leads to profound antitumour efficacy in preclinical models. CD20 bivalency preserves this potency in the presence of competing anti-CD20 antibodies, providing the opportunity for pre- or co-treatment with these agents.[3]

In pre-clinical studies, glofitamab demonstrated an average 40-fold increase in ex vivo tumour lysis compared to alternative 1:1 configurations.[3] This allows for activity even in the presence of prior or concurrent CD20-directed antibody therapy.[4] This is important, as current marketed CD20 antibodies have a long half-life and many patients with relapsed disease will have CD20 antibody present at the time of salvage treatment. Furthermore, this property allows the use of CD20-depleting agents to mitigate cytokine release syndrome without compromising efficacy.[3] In a phase I/II trial, fixed-duration treatment with off-the-shelf glofitamab monotherapy achieved high cytokine release rates in heavily pretreated patients with r/r MCL.[5,6] If licensed, glofitamab would offer an additional treatment option for patients with r/r MCL.

Regulatory & Development Status

Glofitamab currently has Marketing Authorisation in the EU/UK for the following indications:[2]

- in combination with gemcitabine and oxaliplatin for treatment of adult patients with r/r diffuse large B-cell lymphoma (DLBCL) not otherwise specified who are ineligible for autologous stem cell transplant
- as monotherapy for the treatment of adult patients with r/r DLBCL, after two or more lines of systemic therapy

Glofitamab was awarded an orphan drug designation in the EU in 2022 for the treatment of MCL.[7]

Glofitamab is in phase II or III clinical development for Large B-cell lymphoma.[8]

Patient Group

Disease Area and Clinical Need

MCL is a rare type of B cell non-Hodgkin lymphoma which develops when the body makes abnormal B lymphocytes in the part of the lymph node called the mantle zone.[9] Non-Hodgkin lymphoma is a type of blood cancer that affects white blood cells.[10] The lymphatic system is an important part of the immune

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system, consisting of tubes (lymph vessels) that branch through all parts of the body and carry a straw coloured liquid called lymph, which contains a high number of white blood cells (lymphocytes) which help fight infection.[9] In MCL, the abnormal lymphocytes build up in the lymph nodes or in other organs and do not function correctly so are unable to fight infection, thereby forming tumours which affect the lymphatic system or the organ where they are growing.[9] The most common symptom of MCL is a lump, or lumps, which often develop in several parts of the body such as the neck, armpit and groin. Some people also experience unexplained weight loss, night sweats or fever.[9,11] Sometimes, MCL is refractory meaning it does not respond to the first-line treatment. MCL can relapse (return) several times and require different treatments each time.[11]

Each year around 600 people are diagnosed with MCL in the UK. Out of all people with non-Hodgkin lymphoma in the UK, around 5 in every 100 people (around 5%) have MCL.[9] In terms of survival, more than 45% of people diagnosed with MCL survive their cancer for 5 years or more after diagnosis. Survival rates for younger people are more optimistic. For those aged between 60-79 years almost 55% will survive for 5 years after their diagnosis, and those 80 years or older only 20% will survive their diagnosis for 5 years or more.[12] In England (2024-25), there were 9,236 finished consultant episodes (FCE) and 8,664 admissions for MCL (ICD-10 code C83.1) resulting in 7,419 day cases and 11,728 FCE bed days.[13]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following treatment options for r/r MCL:[14-16]

- Ibrutinib
- Brexucabtagene autoleucel
- Zanubrutinib

Clinical Trial Information

Trial	**GLOBRYTE; NCT06084936; EudraCT 2023-503206-37-00;** A Phase III, Open-Label, Multicentre Randomised Study Evaluating Glofitamab as a Single Agent Versus Investigator's Choice in Patients With Relapsed/Refractory Mantle Cell Lymphoma **Phase III**: Recruiting **Locations:** 4 EU countries, UK, USA, Canada and other countries **Primary completion date:** August 2027
Trial Design	Randomised, parallel assignment, open label
Population	N=182 (estimated); participants with r/r MCL following at least one prior systemic therapy including a BTK inhibitor; aged 18 years and older
Intervention(s)	Glofitamab intravenous (IV) infusion with step up dosing on cycle 1 day 8 (2.5 mg), and cycle 1 day 15 (10 mg) followed by 30 mg on cycle 2 day 1 and day 1 of the remaining 12 cycles (cycle length = 21 days) after two 1000 mg pretreatments of obinutuzumab (IV) on cycle 1 day 1
Comparator(s)	• Bendamustine (IV) on days 1 and 2 every 4 weeks (Q4W) + rituximab (IV) every 28 days for up to 6 cycles (cycle length = 28 days) • Rituximab (IV) every 28 days + lenalidomide (oral) once daily on days 1-21 Q4W until disease progression

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Outcome(s)	Primary outcome measure: Progression-free survival (PFS) [Time frame: From randomisation to the first occurrence of disease progression or death from any cause (up to approximately 24 months)] See trial record for full list of all outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Glofitamab is already marketed in the UK; a 2.5mg/2.5ml concentrate vial costs £687, and 10mg/10ml concentrate vial costs £2,748.[17]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Venetoclax with ibrutinib for treating relapsed mantle cell lymphoma [ID3879] (GID-TA10774). Expected date to issue to be confirmed.
- NICE technology appraisal in development. Pirtobrutinib for treating relapsed or refractory mantle cell lymphoma [ID3975] (GID-TA10858). Expected date to issue to be confirmed.
- NICE technology appraisal in development. Sonrotoclax for treating relapsed or refractory mantle cell lymphoma after an anti-CD20 treatment and a BTK inhibitor [ID6654] (GID-TA11866). Expected date to issue to be confirmed.
- NICE technology appraisal in development. Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma after 2 or more systemic treatments (review of TA677) [ID6325] (GID-TA11545). Expected February 2026.
- NICE technology appraisal guidance. Zanubrutinib for treating relapsed or refractory mantle cell lymphoma (TA1081). July 2025.
- NICE technology appraisal guidance. Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma (TA677). February 2021.
- NICE technology guidance. Ibrutinib for treating relapsed or refractory mantle cell lymphoma (TA502). January 2018.
- NICE guideline. Non-Hodgkin's lymphoma: diagnosis and management (NG52). July 2016.
- NICE guideline. Haematological cancers: improving outcomes (NG47). May 2016.
- NICE quality standard. Haematological cancers (QS150). June 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Adult Lymphoma. 190702P. July 2019.
- NHS England. Clinical Commissioning Policy: Bendamustine with rituximab for relapsed and refractory mantle cell lymphoma (all ages). 170054P. June 2018.
- NHS England. Clinical Commissioning Policy: Bortezomib for relapsed/refractory mantle cell lymphoma (all ages). 170035P. March 2018.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a. April 2013.

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Other Guidance

- European Society for Medical Oncology (ESMO). Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. November 2025.[18]
- British Society for Haematology. Diagnosis and management of mantle cell lymphoma: A British Society for Haematology Guideline. October 2023.[19]
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