Health Technology Briefing
November 2025

Epcoritamab with R-CHOP for newly diagnosed diffuse large B-cell lymphoma

Company/Developer	AbbVie

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 36131	NICE ID: Not available	UKPS ID: 675211

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Epcoritamab + R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) is currently in clinical development for the treatment of newly diagnosed diffuse large B-cell lymphoma (DLBCL). DLBCL is a type of blood cancer that develops when white blood cells, called lymphocytes, grow out of control. The affected lymphocytes lose their infection-fighting ability making the body more susceptible to infection. The most widely used treatment for DLBCL presently is R-CHOP, which is an immunochemotherapy (a combination of immunotherapy and chemotherapy drugs). R-CHOP is an accepted standard treatment for patients with previously untreated DLBCL; however, approximately 40% of patients are either not cured or require further treatment.

Epcoritamab, administered subcutaneously (under the skin), is an antibody (a type of protein) that recognises and attaches to two targets at the same time: CD20, a protein that is present on the surface of B cells (including the cancer cells), and CD3, a protein found on the surface of healthy T cells (another type of immune cell). By attaching to CD20 and CD3 proteins, epcoritamab brings the cancer cells and T cells together. This encourages the T cells to destroy the cancer cells and helps control the disease. If licensed, epcoritamab will offer an additional treatment option for newly diagnosed DLBCL.

Proposed Indication

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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Treatment of newly diagnosed diffuse large B-cell lymphoma (DLBCL).[1]

Technology

Description

Epcoritamab (DuoBody®-CD3xCD20, GEN3013) is a humanised IgG1-bispecific antibody that binds to a specific extracellular epitope of CD20 on B cells and to CD3 on T cells. CD20 is expressed on most human B-cell lymphomas and leukaemias and on B cells in peripheral blood, but not haematopoietic stem cells or plasma cells. The activity of epcoritamab is dependent upon simultaneous engagement of CD20-expressing cancer cells and CD3-expressing endogenous T cells by epcoritamab that induces specific T-cell activation and T-cell-mediated killing of CD20-expressing cells, as epcoritamab does not have direct immune effector mechanisms. Epcoritamab fragment crystallizable (Fc) region is silenced for direct immune effector mechanisms, such as antibody-dependent cellular cytotoxicity, complement-dependent cellular cytotoxicity, and antibody-dependent cellular phagocytosis.[2]

Epcoritamab is currently in development for the treatment of newly diagnosed DLBCL. In the phase III trial (EPCORE DLBCL-2, NCT05578976), participants will receive subcutaneous epcoritamab combined with intravenous rituximab, cyclophosphamide, doxorubixin hydrochloride, vincristine and oral prednisone (R-CHOP) followed by epcoritamab in 21-day cycles.[1]

Key Innovation

Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is an accepted standard treatment for patients with previously untreated DLBCL; however, relapse rates can reach 40%.[3] Epcoritamab is currently licensed for treatment of DLBCL in adult patients whose cancer has returned (relapsed) or stopped responding (refractory) after at least two previous treatments.[2] The design of epcoritamab allows for enhanced tumour-specific immune activation, that offers a significant advantage over conventional monoclonal antibodies, which typically rely on direct tumour cell targeting and may not fully engage the immune system.[4] As its mechanism of action and safety profile are distinct from immunochemotherapy, epcoritamab may be suited for use in combination therapy and in earlier lines of therapy.[5] Combining epcoritamab with chemotherapeutic agents may improve efficacy with a low potential for overlapping toxicities.[6]

If licensed, epcoritamab will offer an additional treatment option for newly diagnosed DLBCL.

Regulatory & Development Status

Epcoritamab is currently marketed in the EU/UK as a monotherapy for the following indications:[2]

- the treatment of adult patients with relapsed or refractory DLBCL after two or more lines of systemic therapy
- the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy

Epcoritamab is in phase III/II clinical development for:[7]

- Burkitt lymphoma
- Primary mediastinal large B-cell lymphoma
- Marginal zone lymphoma
- Chronic lymphocytic leukemia
- Richter's syndrome
- Small lymphocytic lymphoma

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Patient Group

Disease Area and Clinical Need

DLBCL, the most common non-Hodgkin lymphoma (NHL) subtype, accounts for 25% to 45% of all NHL cases worldwide.[8] DLBCL develops when the body makes abnormal B lymphocytes, so it is a type of B-cell lymphoma. The abnormal lymphocytes build up in the lymph nodes or other body organs. This type of lymphoma has abnormal B cells that are larger than normal B cells, and cancer cells in a spread-out pattern (diffuse) rather than being grouped together. The most common symptom is one or more painless swellings in the neck, armpit, and groin. These swellings are enlarged lymph nodes. Other general symptoms include heavy sweating at night, high temperatures that come and go with no obvious cause and losing a lot of weight (more than one-tenth of the total weight).[9] The exact cause of DLBCL is unknown but factors that may increase the risk of developing DLBCL include: a medical condition or treatment that weakens the immune system; autoimmune diseases such as rheumatoid arthritis; the Epstein-Barr virus; the human T-cell lymphotropic virus; a *Helicobacter pylori* infection; having received chemotherapy or radiotherapy for an earlier cancer; coeliac disease; and having a parent or sibling with DLBCL. It is also more common in men than women.[10]

Each year, about 5,000 people are diagnosed with DLBCL in the UK. This makes up more than 40 out of 100 cases (40%) of NHL in adults.[9] The five-year survival rates, are as follows: 79.2% for Stage 1, where cancer is found in just one location; 75.5% for Stage 2, where cancer cells are in at least two lymph nodes on the same side of the body, either in the upper or lower half; 67.4% for Stage 3, where cancer is located on both the upper and lower halves of the body; and 55.2% for Stage 4, where cancer has spread to organs like the liver, lungs, or bone marrow.[11] In England in 2024-25, there were 37,839 finished consultant episodes (FCE) and 33,197 hospital admissions for DLBCL (ICD-10 code C83.3), resulting in 85,375 FCE bed days and 27,368 day cases.[12]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommend chemotherapy with rituximab for first-line treatment for DLBCL in adults.[13]

Standard treatment for untreated DLBCL in adults is R-CHOP. For patients with an International Prognostic Index (IPI) score of 2 to 5, polatuxumab vedotin with R-CHP (rituximab, cyclophosphamide, doxorubicin and prednisolone) is recommended.[14]

Clinical Trial Information

Trial	**EPCORE DLBCL-2**, NCT05578976, EudraCT 2021-000168-31; A phase 3, randomized, open-label study to evaluate safety and efficacy of epcoritamab in combination with R-CHOP compared to R-CHOP in subjects with newly diagnosed diffuse large B-cell lymphoma (DLBCL) **Phase III**: Active, not recruiting **Locations**: Sixteen EU countries, UK, USA, Canada and other countries **Primary completion date**: June 2027
Trial Design	Randomised, parallel assignment, open label
Population	N (estimated)=900; subjects with newly diagnosed DLBCL; aged 18 to 79 years old

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Intervention(s)	• Participants will receive subcutaneous (SC) epcoritamab combined with intravenous (IV) R-CHOP followed by epcoritamab in 21-day cycles • Participants will receive IV R-CHOP followed by IV rituximab in 21-day cycles
Comparator(s)	-
Outcome(s)	Primary outcome measure: Number of participants with progression-free survival with an IPI of 3-5 [Time frame: up to approximately 46 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**EPCORE™ NHL-2, NCT04663347, Eudra CT-2020-000845-15**; A phase 1b/2, open-label trial to assess the safety and preliminary efficacy of epcoritamab (GEN3013; DuoBody®-CD3xCD20) in combination with other agents in subjects with B-cell non-hodgkin lymphoma (B-NHL) **Phase Ib/II**: Active, not recruiting **Locations**: Ten EU countries, UK, USA and Australia **Primary completion date**: September 2028
Trial Design	Non-randomised, parallel assignment, open label
Population	N (actual)=543; subjects with B-NHL; 18 years and older
Intervention(s)	Experimental arms 1-10: • Epcoritamab + R-CHOP • Epcoritamab + R2 • Epcoritamab + BR • Epcoritamab + R-DHAX/C • Epcoritamab + Gem0x • Epcoritamab + R2 • Epcoritamab maintenance • Epcoritamab + R mini-CHOP • Epcoritamab + lenalidomide • Epcoritamab + R-ICE
Comparator(s)	-
Outcome(s)	Primary outcome measures: • Part 1: number of participants with dose limiting toxicities [Time frame: during the first cycle (28 days) in each cohort] • Part 1 and 2: number of participants with adverse events [Time frame: from first dose of drug until either 60 days after last dose, date participant withdraws consent, date participant starts a new systemic anticancer therapy, or date participant dies, whichever occurs first (up to approximately 3 years)]

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	• Part 2: overall response rate [Time frame: up to 3 years] See trial record for full list of other outcomes
Results (efficacy)	Arm 1: Rates of overall response and complete metabolic response were high, and no relapses were reported as of the data cutoff date.[5] Long term results: Fixed-duration epcoritamab + R-CHOP induced deep, durable complete responses (CRs) (24-month estimated duration of CR, 83%) and high rates of minimal residual disease negativity (91% of evaluable patients), leading to long-term remissions (24-month estimated overall survival, 87%) beyond 2 years in patients with 1L DLBCL, including those with high-risk features, such as double-hit/triple-hit disease.[3]
Results (safety)	Arm 1: The results show that epcoritamab + R-CHOP has a manageable safety profile. Cytokine release syndrome events were observed to be mostly of low grade and were not associated with treatment discontinuation.[5] Long term results: The safety profile was manageable, with no new safety signals detected.[3]

Estimated Cost

The list price for epcoritamab is £6,568 per 48 mg vial and £547.33 per 4 mg vial (excluding VAT).[15]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma (TA874). March 2023.
- NICE clinical guideline. Non-Hodgkin's lymphoma: diagnosis and management (NG52). July 2016.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Teenagers & Young Adults. B17/S/a.

Other Guidance

- Fox C, Chaganti S, McIlroy G, Barrington S, Burton C, Cwynarski K, et al. The management of newly diagnosed large B- cell lymphoma: A British Society for Haematology Guideline. 2024.[16]
- National Comprehensive Cancer Network. NCCN Guidelines Insights: B-Cell Lymphomas, Version 3.2019. 2019.[17]
- Chaganti S, Illidge T, Barrington S, Mckay P, Linton K, Cwynarski K, et al. Guidelines for the management of diffuse large B-cell lymphoma. 2016.[18]

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- European Society for Medical Oncology. Diffuse large B-cell lymphoma (DLBCL): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2015.[19]

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