

## Health Technology Briefing May 2024

### Epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma previously treated with at least one line of systemic therapy

Company/Developer

AbbVie

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 38344

NICE ID: Not available

UKPS ID: 670081

#### Licensing and Market Availability Plans

Currently in phase III clinical development.

#### Summary

Epcoritamab is in clinical development for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after one or more lines of therapy. DLBCL is a cancer of B cells, a type of immune cell, and the most common type of fast-growing non-Hodgkin's lymphoma - a disease in which cancer cells form in the lymph system, which forms part of the immune system. Relapsed or refractory DLBCL refers to the disease reappearing after treatment or when the lymphoma does not respond to treatment. In DLBCL, the body makes abnormal B cells which build up in lymph nodes or other body organs. The affected cells start to divide before they are fully mature and lose their infection-fighting properties, which makes the body more vulnerable to infection. A high proportion of cases of DLBCL relapse or are refractory to treatment with currently available therapies.

Epcoritamab, administered subcutaneously, 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 could offer an additional treatment option for relapsed or refractory DLBCL where patients have failed or are not eligible for standard treatment options.

## Proposed Indication

Treatment of adults with relapsed or refractory diffuse large B-Cell Lymphoma (DLBCL) previously treated with at least one line of systemic therapy.<sup>1</sup>

## Technology

### Description

Epcoritamab (DuoBody®-CD3xCD20, GEN3013) is a novel bispecific IgG1 antibody redirecting T-cells toward CD20<sup>+</sup> tumor cells.<sup>2</sup> Epcoritamab recognises and attaches to two targets simultaneously: 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 (cells in the immune system). By attaching to CD20 and CD3 proteins, epcoritamab brings the cancer cells and T cells together.<sup>3</sup> This encourages the T cells to destroy the cancer cells and helps control the disease.<sup>3</sup>

Epcoritamab is in clinical development for adults with relapsed or refractory DLBCL who have failed or are ineligible for high dose chemotherapy and autologous stem cell transplant (HDT-ASCT). In a phase III trial (NCT04628494), epcoritamab is administered in cycles of 28 days via subcutaneous (SC) injection until any of the discontinuation criteria are met.<sup>1</sup>

### Key Innovation

The current standard of treatment for relapsed or refractory DLBCL is high-dose salvage chemotherapy and consolidation with autologous stem cell transplant but there remains unmet need for patients who have failed or are ineligible for this therapy.<sup>4</sup> Several CD20-targeting monoclonal antibodies (mAbs) have been successfully applied for the treatment of B-Non-Hodgkin's Lymphoma, often in combination with chemotherapy. Nonetheless, a high incidence of disease relapse occurs after treatment with currently available CD20-targeting mAbs, urging the development of more innovative and powerful therapies targeting CD20.<sup>2</sup> For patients who relapse or don't respond to initial therapy there are currently limited second line treatment options.<sup>4</sup>

Results of a phase I/II trial suggested that SC epcoritamab showed deep and durable responses and a manageable safety profile in DLBCL patients who were relapsed or refractory to at least two prior lines of therapy.<sup>5</sup> If licensed for the treatment of adult patients with relapsed or refractory DLBCL after at least one line of systemic antineoplastic therapy, epcoritamab may offer a novel therapy for patients with relapsed or refractory DLBCL who have failed or are ineligible for HDT-ASCT.

### Regulatory & Development Status

Epcoritamab currently has Marketing Authorisation in the EU/UK as monotherapy for the treatment of adult patients with relapsed or refractory DLBCL after two or more lines of systemic therapy.<sup>3</sup>

Epcoritamab is in phase II/III clinical development for various types of lymphoma, such as follicular lymphoma and non-Hodgkin's lymphoma (NHL).<sup>6</sup>

Epcoritamab was designated as an orphan drug in the EU in February 2022 for treating DLBCL.<sup>7</sup>

## Patient Group

### Disease Area and Clinical Need

DLBCL is a cancer of the lymphatic system and a common type of fast-growing NHL.<sup>8</sup> In DLBCL, the body makes abnormal B lymphocytes, which build up in lymph nodes or other body organs.<sup>8</sup> The affected lymphocytes start to multiply in an abnormal way and lose their infection-fighting properties, which makes the patient more vulnerable to infection.<sup>9</sup> Relapsed or refractory DLBCL refers to the disease reappearing after treatment or when the lymphoma does not respond to treatment, respectively.<sup>8</sup> 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 your 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, brother or sister with DLBCL. It is also more common in men than women.<sup>10</sup> Symptoms of DLBCL include: painless swelling, usually in the neck, armpit or groin. Other symptoms can include: night sweats; fevers; unintentional weight loss; feelings of breathlessness; and persistent itching of the skin all over the body.<sup>11</sup>

Each year about 5000 people are diagnosed with DLBCL in the UK, making up about 40 out of 100 cases (40%) of NHL in adults.<sup>8,12</sup> In England, 2022-2023, there were 33,914 finished consultant episodes (FCE) for DLBCL (ICD-10 code C83.3) which resulted in 30,060 admissions, 24,352 day cases and 83,284 FCE bed days.<sup>13</sup>

### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommend salvage therapy with multi-agent immunotherapy to people with relapsed or refractory DLBCL who are fit enough to tolerate intensive therapy, and consolidation with autologous stem cell transplant to people with chemosensitive DLBCL who are fit enough for transplantation.<sup>4</sup> NICE have also recommended axicabtagene ciloleucel as well as polatuzumab vedotin with rituximab and bendamustine for people with relapsed or refractory DLBCL.<sup>14,15</sup>

### Clinical Trial Information

<p>Trial</p>	<p><b>EPCORE DLBCL-1, <a href="#">NCT04628494</a>, <a href="#">EudraCT 2020-003016-27</a></b>; A Randomized, Open-Label, Phase 3 Trial of Epcoritamab vs Investigator's Choice Chemotherapy in Relapsed/Refractory Diffuse Large B-cell Lymphoma (R/R DLBCL)  <b>Phase III:</b> Active, not recruiting  <b>Location(s):</b> 12 EU countries, UK, USA, Canada and other countries  <b>Primary completion date:</b> December 2024</p>
<p>Trial Design</p>	<p>Randomised. parallel assignment, active-controlled, open-label</p>
<p>Population</p>	<p>N=552 (estimated); adults aged 18 and over with relapsed/refractory diffuse large B-cell lymphoma previously treated with at least one line of systemic antineoplastic therapy</p>
<p>Intervention(s)</p>	<p>Subcutaneous epcoritamab intravenous (IV) therapy administered in cycles of 28 days</p>
<p>Comparator(s)</p>	<p>Investigator's choice of chemotherapy:</p> <ul style="list-style-type: none"> <li>• R-GemOx administered by IV in cycles of 28 days until maximum cycles of completion or any discontinuation criteria are met; or</li> <li>• BR administered by IV in cycles of 21 days until maximum cycles of completion or any discontinuation criteria are met</li> </ul>
<p>Outcome(s)</p>	<p>Primary outcome:</p>

	<ul style="list-style-type: none"> <li>Overall survival [Time Frame: throughout the study and up to 5 years following the last patient first dose]</li> </ul> <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

### Estimated Cost

The list price for epcoritamab is £6,568 per 48 mg vial and £547.33 per 4 mg vial (excluding VAT).<sup>16</sup>

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal in development. Zamtocabtagene autoleucler for treating relapsed or refractory diffuse large B-cell lymphoma when high-dose chemotherapy and autologous stem cell transplant are unsuitable (GID-TA11271). Expected publication date TBC.
- NICE technology appraisal in development. Glofitamab with gemcitabine and oxaliplatin for treating relapsed or refractory diffuse B-cell lymphoma (GID-TA11164). Expected publication date TBC.
- NICE technology appraisal in development. Lisocabtagene maraleucler for treating relapsed or refractory diffuse large B-cell lymphoma, high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma or follicular lymphoma grade 3B after first-line chemotherapy (GID-TA10778). Expected publication date December 2024.
- NICE technology appraisal. Axicabtagene ciloleucler for treating relapsed or refractory diffuse large B-cell lymphoma after first-line chemoimmunotherapy (TA895). June 2023.
- NICE technology appraisal. Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma (TA883). May 2023.
- NICE technology appraisal. Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma (TA649). September 2020.
- 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 Haematopoietic Stem Cell Transplantation (Adult). B04/S/a.
- NHS England. Axicabtagene Ciloleucler Chimeric Antigen Receptor T Cell (CAR T) Therapy for the Treatment of Adult Patients with Relapsed or Refractory Large B-cell Lymphoma. 2018.
- NHS England. Interim Clinical Commissioning Policy Statement: Use of Plerixafor for Stem Cell Mobilisation. B04/PS/a. September 2013.
- NHS Commissioning Board. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. NHSCB/B04/P/a. April 2013.

#### Other Guidance

- Fox C, Chaganti S, McIlroy G et al. The management of newly diagnosed large B- cell lymphoma: A British Society for Haematology Guideline. 2024.<sup>17</sup>

- National Comprehensive Cancer Network. NCCN Guidelines Insights: B-Cell Lymphomas, Version 3.2019. 2019.<sup>18</sup>
- Chaganti S, Illidge T, Barrington S et al. Guidelines for the management of diffuse large B-cell lymphoma. 2016.<sup>19</sup>
- European Society for Medical Oncology. Diffuse large B-cell lymphoma (DLBCL): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2015.<sup>20</sup>
- National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Non-Hodgkin's Lymphomas. 2010.<sup>21</sup>

## Additional Information

## References

- 1 ClinicalTrials.gov. *A Phase 3 Trial of Epcoritamab vs Investigator's Choice Chemotherapy in R/R DLBCL (EPCORE DLBCL-1)*. Trial ID: NCT04628494. 2020. Status: Active, not recruiting. Available from: <https://clinicaltrials.gov/study/NCT04628494> [Accessed 04 March 2024].
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- 3 European Medicines Agency (EMA). *Tepkinly : EPAR - Product information*. 2023. Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/tepinkly#ema-inpage-item-product-info> [Accessed February 2024].
- 4 National Institute for Health and Care Excellence (NICE). *Non-Hodgkin's lymphoma: diagnosis and management (NG52)*. Available from: <https://www.nice.org.uk/guidance/ng52/chapter/Recommendations#management-of-diffuse-large-bcell-lymphoma> [Accessed 06 March 2024].
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- 6 Clinicaltrials.gov. *5 Studies found for: Epcoritamab | Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | Interventional Studies | AbbVie [Lead] | Phase 2, 3*. Available from: <https://classic.clinicaltrials.gov/ct2/results?cond=&term=Epcoritamab&type=Intr&rslt=&recr s=b&recrs=a&recrs=f&recrs=d&age v=&gndr=&intr=&titles=&outc=&spons=&lead=AbbVie &id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd s=&strd e=&prcd s=&prcd e=&sfpd s=&sfpd e=&rfpd s=&rfpd e=&lupd s=&lupd e=&sort=> [Accessed 28 February 2024].
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