



Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	Polatuzumab vedotin
Condition	Diffuse large B-cell lymphoma (DLBCL) is a common type of non-Hodgkin lymphoma that develops when the body makes abnormal B-cells (a type of white blood cells). It may not respond to therapy (refractory) or come back after initial disappearance (relapse).
Full indication	Polatuzumab vedotin in combination with bendamustine and rituximab is indicated for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) in adult patients who are not eligible for hematopoietic stem cell transplant.
Company	Roche Products Limited
EAMS number	00031/0010

## Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to doctors who may wish to prescribe the unlicensed medicine under their own responsibility. More information about the scheme can be found here:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The scientific opinion is based on the information supplied to the MHRA on the benefits and risks of a promising new medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to licence such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here:

<https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare#prescribing>

## What is polatuzumab vedotin?

Polatuzumab vedotin is the active substance of a medicine, which is available as a powder that is made up into a solution for infusion (drip) into a vein.

## What is polatuzumab vedotin used to treat?

Polatuzumab vedotin is used to treat adults with diffuse large B-cell lymphoma (DLBCL), a tumour that develops when the body makes abnormal B-cells (a type of white blood cells). If it does not respond to therapy (refractory) or comes back after initial disappearance (relapse), intensive treatment with high-dose chemotherapy followed by stem cell transplant (to help blood cells that are destroyed by chemotherapy to recover) may be applied. However, when this treatment option is not suitable, polatuzumab vedotin may be used in combination with bendamustine (chemotherapy) and rituximab (therapy targeting B-cells).

### **How is polatuzumab vedotin used?**

Treatment with polatuzumab vedotin should be started and supervised by a specialist doctor experienced in treating cancer. The doctor will carry out blood tests to check the patient's functions before and during treatment.

Polatuzumab vedotin will be given as an infusion into a vein at a dose of 1.8 mg for each kilogram of body weight. The treatment will last for 6 cycles of 21 days, with one infusion per cycle in combination with infusions of bendamustine and rituximab.

### **How does polatuzumab vedotin work?**

Polatuzumab vedotin is a monoclonal antibody linked to a substance intended to kill cancer cells (antibody drug conjugate). This substance enters cancer cells by the monoclonal antibody, which is designed to recognise and attach to cancer cells with a certain protein that is found on the surface of B-lymphocytes.

### **How has polatuzumab vedotin been studied?**

The main study of the effects of polatuzumab vedotin in combination with bendamustine and rituximab has enrolled 80 patients with relapsed/refractory DLBCL. The combination was compared to treatment with only bendamustine and rituximab.

The measures of effectiveness (how well the medicine worked) were the complete response to treatment by assessing the growth of the tumour, overall survival (how long the patients lived) and progression-free survival (how long the patients lived without their cancer getting worse).

### **What are the benefits and risks of polatuzumab vedotin?**

#### *Benefits*

When polatuzumab vedotin was added to bendamustine/rituximab, the tumour disappeared in 40% of the patients by the end of treatment compared to 17.5% of the patients treated only with bendamustine and rituximab. After 9 months, the proportion of patients without progression of disease was 47% in the group of patients treated with polatuzumab vedotin compared to 17% in those treated only with bendamustine and rituximab. The addition of polatuzumab vedotin also prolonged overall survival as 52% of the patients were still alive at one year compared to 24% of the patients who had only received bendamustine and rituximab.

#### *Risks*

The addition of polatuzumab vedotin to bendamustine/rituximab increases their toxicity on blood cells and may lead to peripheral neuropathy (nerve damage) with problems in sensitivity or weakness in the body's extremities (hands, feet and arms).

The most frequent side-effects, affecting at least 30% of the patients treated with the combination of polatuzumab vedotin with bendamustine/rituximab, were low counts of various types of blood cells (red cells, platelets, white cells), fatigue (tiredness), diarrhoea, nausea (feeling sick), fever and peripheral neuropathy (nerve damage).

### **Why has polatuzumab vedotin been given a positive Early Access to Medicine Scientific opinion?**

DLBCL is an aggressive form of lymphoma with limited treatment options when it is refractory to or relapses after standard therapy. In patients who cannot undergo high-dose chemotherapy and stem cell transplantation, the addition of polatuzumab vedotin to bendamustine and rituximab has been shown to notably slow the progression of cancer and prolong patient survival despite some increase in side effects.

**What are the uncertainties?**

The number of patients studied was very small, which makes it difficult to evaluate precisely the importance of the benefits and side effects. Furthermore, data on overall survival are still preliminary. The company that makes polatuzumab vedotin will provide additional information when it becomes available.

**Are there on-going clinical studies?**

The number of patients enrolled in the main trial has been expanded and other studies with different treatment combinations are on-going.

**What measures are in place to monitor and manage risks?**

A risk management plan has been developed to ensure that polatuzumab vedotin is used as safely as possible. Based on this plan, the company that makes polatuzumab vedotin must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including the side effects related to nerve and blood cells damage and recommendations for minimising these side effects.

Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the company to report adverse effects experienced by patients receiving polatuzumab vedotin in combination with bendamustine and rituximab through the scheme, as well as medication errors, overdose, and pregnancies. They will receive a physician pack and comprehensive training on adverse events prior to commencement of patient treatment. These safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Patients in the Early Access to Medicines Scheme will receive an alert card from their doctor summarising the serious side effects of the medicine and the details of their treating oncologist/haematologist. Patients should carry the card with them at all times in case they need treatment or advice from a healthcare professional who is not familiar with polatuzumab vedotin treatment.

**Other information about polatuzumab vedotin – see EAMS Treatment Protocol**