



Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	Atezolizumab
Condition	Atezolizumab in combination with chemotherapy is used to treat a specific form of lung cancer (small cell lung cancer) when it has spread beyond a single area that can be treated with radiotherapy (extensive disease) and no specific treatments have been given for this stage of the disease.
Full indication	In combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).
Company	Roche Products Limited
EAMS number	00031/0007

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 license such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here: <https://www.gmc-uk.org/guidance/28349.asp>

What is atezolizumab?

Atezolizumab is the active substance of a medicine, which is available as a concentrated solution (liquid) that is diluted for infusion (drip) into a vein.

What is atezolizumab used to treat?

Atezolizumab is used to treat a specific type of lung cancer called small cell lung cancer. It is used in this cancer when it has spread beyond a single area that can be treated with radiotherapy (extensive stage disease) and no specific treatments have been given for this stage of the disease.

It is used in combination with the chemotherapy agents carboplatin and etoposide.

How is atezolizumab used?

Treatment with atezolizumab 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.

Atezolizumab will be given as an infusion into a vein at a dose of 1,200 mg, followed by carboplatin and then etoposide as an infusion into the vein on day 1. Etoposide is also administered as an infusion into a vein on days 2 and 3. This regimen is administered every three weeks for 4 cycles.

Atezolizumab is then continued without chemotherapy at a dose of 1,200 mg administered as an infusion into a vein every three weeks. Atezolizumab will be continued until there is no longer any benefit from the treatment or the treatment is no longer tolerated.

How does atezolizumab work?

Atezolizumab is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognise and attach to a specific structure (called an antigen) that is found in certain cells in the body. Atezolizumab has been designed to attach to and block the activity of a protein called PD-L1, which is found on the surface of tumour and immune cells. By blocking PD-L1, atezolizumab restores the capacity of immune cells to fight cancer cells.

How has atezolizumab been studied?

The main study of the effects of atezolizumab in combination with carboplatin and etoposide chemotherapy has enrolled 403 patients with extensive stage small cell lung cancer and had not received other specific treatments for this stage of the disease.

The measures of effectiveness (how well the medicine worked) were 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 atezolizumab?

Benefits

The addition of atezolizumab prolonged overall survival as 52% of the patients receiving atezolizumab combined with carboplatin and etoposide chemotherapy were still alive at one year compared to 38% of the patients who received only carboplatin and etoposide. The time before cancer progression was also improved. Six months after starting treatment, 31% of patients receiving atezolizumab were alive without cancer progression compared with 22% of patients receiving chemotherapy alone.

Risks

Atezolizumab may be associated with side effects resulting from excessive activity of the immune system, including endocrine abnormalities (e.g. hypothyroidism, diabetes), diarrhoea/colitis, hepatitis, pneumonitis, and rash. Most will resolve following appropriate treatment or on stopping atezolizumab.

The combination of carboplatin and etoposide to atezolizumab led to the appearance or increased frequency of certain side-effects: anaemia (low red blood cells), thrombocytopenia (low platelet count), hypothyroidism (underactive thyroid gland) and hypophysitis (inflammation of the pituitary gland).

The most common side effects were anaemia, nausea (feeling sick), fatigue (tiredness), and decreased appetite.

Why has atezolizumab been given a positive Early Access to Medicine Scientific opinion?

In patients with extensive stage small cell lung cancer, whilst initial responses to chemotherapy are often good, most patients become resistant to chemotherapy and the prognosis is poor. The addition of atezolizumab to carboplatin and etoposide chemotherapy has been shown to slow the progression of cancer and increase patient survival.

What are the uncertainties?

The data are limited in patients over 75 years. Furthermore, the data on overall survival are still preliminary so that longer-term survival benefit cannot be determined. The company that makes atezolizumab will provide additional information when it becomes available.

Are there on-going clinical studies?

There are currently no other clinical studies ongoing specifically looking at atezolizumab in the first-line treatment of extensive stage small cell lung cancer.

What measures are in place to monitor and manage risks?

A risk management plan has been developed to ensure that atezolizumab is used as safely as possible. Based on this plan, the company that makes atezolizumab 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 the excessive activity of the immune system 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 atezolizumab through the scheme. 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 important risks with the medicine and the details of their treating oncologist. Patients should carry the card with them at all times in case they need treatment or advice from a healthcare professional that is not familiar with atezolizumab treatment.

Other information about atezolizumab – see EAMS Treatment Protocol