



Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	Atezolizumab
Condition	Atezolizumab in combination with bevacizumab and chemotherapy is used to treat a specific type of lung cancer, when it has spread to other parts of the body and after other specific treatments have failed to stop its progression
Full indication	In combination with bevacizumab, paclitaxel and carboplatin, treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) with EGFR activating or ALK positive tumour mutations after failure of appropriate targeted therapies
Company	Roche Products Limited
EAMS number	00031/0005

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/guidance/ethical_guidance/14327.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 adults with a specific type of cancer that affects the lungs, called non-small cell lung cancer with specific characteristics of tumour cells, called EGFR or ALK mutations. It is used in this cancer when it has spread to other parts of the body and after other specific treatments have failed to stop its progression.

It is used in combination with Avastin (bevacizumab), another monoclonal antibody used to treat lung cancer, and a chemotherapy combination of paclitaxel and carboplatin.



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.

All treatments will be given as an infusion into a vein every three weeks for four or six cycles: atezolizumab (1,200 mg), bevacizumab (15 mg/kg), paclitaxel and carboplatin. After these cycles, only atezolizumab and bevacizumab will be continued every three weeks until cancer progression (for bevacizumab), until there is no longer any benefit from the treatment (for atezolizumab) 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 bevacizumab and chemotherapy has enrolled 1202 patients with metastatic non-squamous non-small lung cancer, who had not received any chemotherapy. Out of these patients, 157 had tumours with EGFR or ALK mutations and had generally been treated before the study with treatments specific for these mutations.

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 benefits and risks has atezolizumab shown during the studies?

Benefits

One year after starting treatment, 42% of the patients treated with atezolizumab combined with bevacizumab and chemotherapy were alive without cancer progression compared to 21% of those treated without atezolizumab. The addition of atezolizumab also prolonged overall survival as 78% of the patients receiving atezolizumab were still alive at one year compared to 60% of the patients who received only bevacizumab and chemotherapy.

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 with bevacizumab and chemotherapy has worse tolerability than atezolizumab alone and some fatal side effects have been reported.

The most frequent side effects, affecting at least 20% of the patients treated with the combination of atezolizumab with bevacizumab and chemotherapy, were peripheral neuropathy (nerve damage), low count of various types of blood cells (white cells, red cells, platelets), fatigue (tiredness), nausea



(feeling sick), diarrhoea, constipation, decreased appetite, skin rash, arthralgia (joint pain) and asthenia (lack of energy).

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

After failure of the treatments specific to EGFR or ALK mutations, the addition of atezolizumab and bevacizumab to chemotherapy has been shown to notably slow the progression of cancer and increase patient survival despite worse tolerability of this combination compared to atezolizumab alone. Metastatic lung cancer is a fatal condition and chemotherapy currently available after failure of specific treatments for these mutations has low efficacy.

What are the uncertainties?

The number of patients studied was small and data are limited in patients over 75 years.

Are there on-going clinical studies?

There are currently no other clinical studies ongoing specifically looking at EGFR and ALK mutations in NSCLC.

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