Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Atezolizumab**
EAMS indication	**Atezolizumab, in combination with bevacizumab, is indicated for the treatment of adult patients with a cancer that affects the liver called hepatocellular carcinoma (HCC), which cannot be treated by removing the affected portion of the liver and when no other specific medicines have been given for this cancer.**
Company	**Roche Products Limited**
EAMS number	**00031/0012**
EAMS Scientific Opinion date	**18 June 2020**

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS 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 assessment of the information supplied to the MHRA on the benefits and risks of the 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, nor should it be regarded as an authorisation to sell or supply such a medicine. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS the risk and legal responsibility for prescribing a 'special' remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product.

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 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 cancer that affects the liver, called hepatocellular carcinoma (HCC), which cannot be treated by removing the affected portion of the liver and when no other specific medicines have been given for this cancer.

It is used in combination with another anti-cancer medicine bevacizumab.

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 bevacizumab as an infusion into the vein at a dose of 15mg/kg. This regimen is administered every three weeks 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 compared treatment with atezolizumab in combination with bevacizumab to standard anticancer treatment with sorafenib (a multikinase blocking agent) in patients with HCC that had advanced locally or spread to another part of the body and who had not previously received any other specific medicines for their cancer. A total of 501 patients were entered into the study.

The main 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 combination of atezolizumab and bevacizumab prolonged the time that patients lived without their cancer getting worse. After 6 months, the proportion of patients without progression of disease was 54.5% in the group of patients treated with atezolizumab and bevacizumab compared to 37.2% in those treated with sorafenib.

The combination of atezolizumab and bevacizumab also prolonged overall survival as 84.8% patients were still alive at 6 months compared with 72.3% in patients treated with sorafenib.

Risks
Atezolizumab may be associated with side effects resulting from excessive activity of the immune system, including thyroid disorders (inflammation of the thyroid), colitis (inflammation of the intestine), hepatitis (inflammation of the liver), reaction to the infusion (e.g. fever, chills), rash and diabetes. Most will resolve following appropriate treatment or on stopping atezolizumab.

The side effects of the combination of atezolizumab and bevacizumab were generally consistent with those seen with the individual treatments and/or underlying disease. One new side effect, peripheral

oedema (swelling in the arms or legs), was observed with the combination. Thyroid disorders and infusion-related reactions were more common with the combination than with atezolizumab treatment alone.

The most frequent side effects, affecting at least 20% of the patients treated with the combination of atezolizumab and bevacizumab, were hypertension (high blood pressure), proteinuria (protein in the urine), fatigue (tiredness) and decreased appetite. The most frequent serious side effects were, pyrexia (high temperature) which affected 3% of patients, oesophageal varices haemorrhage (bleeding of swollen veins in the gullet) and gastrointestinal haemorrhage (bleeding in the gut) both of which affected 2% of patients.

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

There are a limited number of medicines available for patients that have advanced HCC that cannot be treated by removing the affected portion of the liver. Most patients also have significant liver damage which can further limit their treatment options. The combination of atezolizumab and bevacizumab has been shown to notably slow the progression of cancer and prolong patient survival compared to standard current treatment with sorafenib. The risks associated with atezolizumab in combination with bevacizumab can be managed and do not outweigh the benefits.

What are the uncertainties

The data on overall survival are still preliminary so the longer-term survival benefit cannot be determined. Data is only available in patients with less severe chronic liver disease (Child Pugh class A). Minimal data is available in patients with more severe chronic liver disease (Child-Pugh class B and C).

The company that makes atezolizumab will provide any additional information when it becomes available.

Are there on-going clinical studies?

The main study previously described is ongoing. A separate study is also ongoing evaluating the combination of atezolizumab and bevacizumab compared with active surveillance in patients whose hepatocellular carcinoma has been completely removed but are at high risk of their cancer returning.

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 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 also receive an alert card from their doctor summarising the important risks with the medicine and the details of their treating dermatologist.

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 atezolizumab treatment.

Other information about Atezolizumab – see EAMS Treatment Protocol