Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Atezolizumab**
Condition **Full indication**	**Atezolizumab in combination with chemotherapy is used to treat a specific form of breast cancer, when it has spread locally to become inoperable or has spread to other parts of the body and other specific treatments have not been given for this stage of the disease.** **In combination with nab-paclitaxel, for the treatment of adult patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for their metastatic disease.**
Company	**Roche Products Limited**
EAMS number	**00031/0006**

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 this promising new medicine used in combination. 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/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 adults with a specific type of breast cancer with specific characteristics of tumour cells known as "tripe-negative" since they lack expression of receptors for progesterone and oestrogen hormones, and lack increased expression of the HER-2 receptor seen in other forms of breast cancer. It is used in this cancer when it has reached an advanced stage where it has spread to other parts of the body or has spread locally to become inoperable.

It is used in combination with the chemotherapy agent nab-paclitaxel.

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 twice (at a dose of 840 mg) and nab-paclitaxel (100 mg/m^2) three times in cycles of four 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 nab-paclitaxel chemotherapy has enrolled 902 patients with triple-negative breast cancer which is metastatic or locally inoperable and has not previously been treated with chemotherapy for this stage of the disease. Out of these patients, 366 had tumours expressing the protein PD-L1 (PD-L1 group).

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 benefits of treatment are seen only in patients with tumours expressing the protein PD-L1 (PD-L1 group). One year after starting treatment, 29% of the patients treated with atezolizumab combined with nab-paclitaxel chemotherapy were alive without cancer progression compared to 16% of those treated with chemotherapy alone. The addition of atezolizumab also prolonged overall survival as 75% of patients receiving atezolizumab were still alive at one year compared to 64% of patients who received only 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 nab-paclitaxel chemotherapy has worse tolerability than atezolizumab alone. The most frequent side-effects, affecting at least 20% of the patients treated with the combination of atezolizumab with nab-paclitaxel chemotherapy, were peripheral neuropathy (nerve damage), low counts of various types of blood cells (white cells, red cells, platelets), alopecia (hair loss), fatigue (tiredness), nausea (feeling sick), diarrhoea, constipation, decreased appetite, altered sense of taste, skin rash, headache, dizzyness, arthralgia (joint pain), muscle pains (myalgia), asthenia (lack of energy), difficulty in sleeping (insomnia), swelling of the ankles (oedema), sore throat.

Why has atezolizumab been given a positive Early Access to Medicine Scientific opinion?
In patients with triple-negative breast cancer that has progressed to advanced stage disease, where it is locally inoperable or has spread to other parts of the body, the cancer is usually poorly responsive to chemotherapy and patient survival is a matter of months. The addition of atezolizumab to nab-paclitaxel

chemotherapy has been shown to notably slow the progression of cancer and increase patient survival despite worse tolerability than chemotherapy alone.

What are the uncertainties?
The number of patients studied was small and the data are limited in patients over 75 years. Furthermore, data on overall survival are still preliminary.

Are there on-going clinical studies?
A similar clinical study is currently recruiting patients with triple negative breast cancer at an advanced stage of the disease where the background chemotherapy is paclitaxel (rather than nab-paclitaxel) given with placebo or atezolizumab (IMpassion131 study).

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, 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 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