



Early Access to Medicines Scheme – Treatment protocol – Information for patients

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation or are used outside their licence) to UK patients that have a high unmet clinical need. The medicines included in the scheme after they have received a positive scientific opinion are those that are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment options. More information about the scheme can be found here:

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

The information below is intended for you, the patient, and is provided by the pharmaceutical company (called scientific opinion holder) that manufactures the EAMS medicine. This medicine, which does not yet have a drug licence or is used outside its licence, may also be used in combination with other medicines. More information about medicines licensing can be found here:

<http://www.nhs.uk/conditions/medicines-information>

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Your physician will be responsible for giving you all the information you need to make this decision and for obtaining informed consent from you prior to treatment. You will be asked to sign a form to confirm that you are providing informed consent to receiving the EAMS treatment. Information on consent can be found here:

<https://www.nhs.uk/conditions/Consent-to-treatment>

The information below is provided to help you decide with your physician on whether to use the EAMS medicine and helps explain how to use it in accordance with the pharmaceutical company's instructions for safe and proper use. 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 the medicine 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 information below may change during the time you are using the medicine if more data become available. Your physician will highlight to you any changes that you need to be aware of.

Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine continue to outweigh any potential risks. Your physician will answer all your questions during and after the treatment and will provide you with contact details that you should use in case of any events or problems.

Each patient enrolled in the scheme will continue to receive the EAMS product until the end of the treatment in line with prescribing and NHS guidance and as long as benefit is seen. In rare cases where the EAMS treatment may not be available anymore, your physician will discuss other options with you.

Information for the patient

Atezolizumab 1,200 mg concentrate for solution for infusion atezolizumab

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What atezolizumab is and what it is used for
2. What you need to know before you are given atezolizumab
3. How atezolizumab is given
4. Possible side effects
5. How to store atezolizumab
6. Contents of the pack and other information

1. What atezolizumab is and what it is used for

What atezolizumab is

Atezolizumab is an anti-cancer medicine that contains the active substance atezolizumab.

- It belongs to a group of medicines called monoclonal antibodies.
- A monoclonal antibody is a type of protein designed to recognise and attach to a specific target in the body.
- This antibody can help your immune system fight your cancer.

What atezolizumab is used for

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. Atezolizumab will be given to you in combination with bevacizumab.

How atezolizumab works

Atezolizumab works by attaching to a specific protein in your body called programmed death-ligand 1 (PD-L1). This protein suppresses the body's immune (defense) system, thereby protecting cancer cells from being attacked by the immune cells. By attaching to the protein, atezolizumab helps your immune system to fight your cancer.

2. What you need to know before you are given atezolizumab

You must not be given atezolizumab if:

- you are allergic to atezolizumab or any of the other ingredients of this medicine (listed in section 6).

If you are not sure, talk to your doctor or nurse before you are given atezolizumab.

Warnings and precautions

Talk to your doctor or nurse before you are given atezolizumab if you:

- have an auto-immune disease (a condition where the body attacks its own cells)
- have been told that your cancer has spread to your brain
- have any history of inflammation of your lungs (called pneumonitis)
- have or have had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C (HCV)
- have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS)
- have had serious side effects because of other antibody therapies that help your immune system to fight cancer
- have been given medicines to stimulate your immune system
- have been given medicines to suppress your immune system
- have been given a live, attenuated vaccine.

If any of the above applies to you (or you are not sure), talk to your doctor or nurse before you are given atezolizumab.

Atezolizumab may cause some side effects that you must tell your doctor about straight away. They may happen weeks or months after your last dose. Tell your doctor straight away if you notice any of the symptoms below:

- inflammation of the lung (pneumonitis): symptoms may include new or worsening cough, shortness of breath, and chest pain
- inflammation of the liver (hepatitis): symptoms may include yellowing of skin or eyes, nausea, vomiting, bleeding or bruising, dark urine, and stomach pain
- inflammation of the intestines (colitis): symptoms may include diarrhoea (watery, loose or soft stools), blood in stools, and stomach pain
- inflammation of the thyroid, adrenal glands and the pituitary gland (hypothyroidism, hyperthyroidism, adrenal insufficiency or hypophysitis): symptoms may include tiredness, weight loss, weight gain, change in mood, hair loss, constipation, dizziness, headaches, increased thirst, increased urination and changes in vision
- type 1 diabetes, including acid in the blood produced from diabetes (diabetic ketoacidosis): symptoms may include feeling more hungry or thirsty than usual, need to urinate more often, weight loss, and feeling tired
- inflammation of the brain (encephalitis) or inflammation of the membrane around the spinal cord and brain (meningitis): symptoms may include neck stiffness, headache, fever, chills, vomiting, eye sensitivity to light, confusion and sleepiness
- inflammation or problems of the nerves (neuropathy): symptoms may include muscle weakness and numbness, tingling in hands and feet
- inflammation of the pancreas (pancreatitis): symptoms may include abdominal pain, nausea and vomiting
- inflammation of the heart muscle (myocarditis): symptoms may include shortness of breath, decreased exercise tolerance, feeling tired, chest pain, swelling of the ankles or legs, irregular heartbeat, and fainting
- inflammation of the kidneys (nephritis); symptoms may include changes in urine output and colour, pain in pelvis, and swelling of the body and may lead to failure of the kidneys
- severe reactions associated with infusion (events occurring during the infusion or within one day of the infusion): may include fever, chills, shortness of breath and flushing.

If you notice any of the symptoms above, tell your doctor straight away.

Do not try to treat yourself with other medicines. Your doctor may:

- Give you other medicines to prevent complications and reduce symptoms.
- Delay giving your next dose of atezolizumab.
- Stop your treatment with atezolizumab.

Tests and checks

Before your treatment, your doctor will check your general health. You will also have blood tests during your treatment.

Children and adolescents

This medicine should not be given to children or adolescents below 18 years of age. This is because the effects of atezolizumab in this age group are not known.

Other medicines and atezolizumab

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

Pregnancy and contraception

- Tell your doctor if you are pregnant, think you might be pregnant or are planning to become pregnant.
- You will not be given atezolizumab if you are pregnant unless your doctor considers it necessary. This is because the effect of atezolizumab in pregnant women is not known - it is possible that it could harm your unborn baby.
- If you could become pregnant, you must use effective contraception;
 - while you are being treated with atezolizumab and
 - for 5 months after the last dose.
- If you become pregnant while you are being treated with atezolizumab tell your doctor.

Breast-feeding

It is not known if atezolizumab gets into breast milk. Ask your doctor if you should stop breast-feeding or if you should stop treatment with atezolizumab.

Driving and using machines

Atezolizumab has minor influence on your ability to drive and use machines. If you feel tired, do not drive or use machines until you feel better.

3. How atezolizumab and bevacizumab are given

You will be given atezolizumab and bevacizumab by a doctor experienced in cancer treatment in a hospital or clinic.

How much atezolizumab and bevacizumab are given

The recommended dose is 1,200 milligrams (mg) atezolizumab, every three weeks.

The recommended dose of bevacizumab is 15 mg per kilogram of your body weight, every three weeks. Your doctor will prescribe a dose of bevacizumab that is right for you.

How atezolizumab and bevacizumab are given

Atezolizumab is given as a drip into a vein (an intravenous infusion).

Your first infusion will be given over 60 minutes.

- Your doctor will monitor you carefully during the first infusion.
- If you do not have an infusion reaction during the first infusion, the next infusions will be given to you over a period of 30 minutes.

Bevacizumab is given as a drip into a vein (an intravenous infusion).

Your first infusion will be given over 90 minutes.

- Your doctor will monitor you carefully during the first infusion.
- If this is well tolerated, the next infusions may be given to you over a period of 60 minutes.
- Later infusions may be given to you over 30 minutes

How long treatment lasts

Your doctor will keep giving you atezolizumab until you no longer benefit from it. However, it may be stopped if the side effects become too much of a problem.

If you miss a dose of atezolizumab or bevacizumab

If you miss an appointment, make another one straight away. For the treatment to be fully effective, it is very important to keep having the infusions.

If you stop receiving atezolizumab or bevacizumab

Do not stop treatment unless you have discussed this with your doctor. This is because stopping treatment may stop the effect of the medicine.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

For a full overview of the possible side effects of bevacizumab, please refer to the patient leaflet of Avastin®.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you notice any of the side effects below or if they get worse. They may happen weeks or months after your last dose. Do not try to treat yourself with other medicines.

Atezolizumab used alone

The following side effects have been reported in clinical trials with atezolizumab used alone:

Very common: may affect more than 1 in 10 people

- fever
- nausea

- vomiting
- feeling very tired with no energy (fatigue)
- lack of energy
- itching of the skin
- diarrhoea
- joint pain
- rash
- loss of appetite
- shortness of breath
- urinary tract infection
- back pain
- cough
- pain in the muscles and bones.

Common: may affect up to 1 in 10 people

- inflammation of the lungs (pneumonitis)
- low oxygen levels, which may cause shortness of breath as a consequence of inflamed lungs (hypoxia)
- stomach pain
- inflammation of the liver
- elevated liver enzymes (shown in tests), which may be a sign of an inflamed liver
- difficulty swallowing
- blood tests showing low levels of potassium (hypokalaemia) or sodium (hyponatremia)
- low blood pressure (hypotension)
- underactive thyroid gland (hypothyroidism)
- allergic reaction (infusion-related reaction, hypersensitivity or anaphylaxis)
- flu-like illness
- chills
- inflammation of the intestines
- low platelet count, which may make you more likely to bruise or bleed
- blocked nose (nasal congestion)
- high blood sugar
- common cold
- mouth and throat pain.

Uncommon: may affect up to 1 in 100 people

- inflammation of the pancreas
- numbness or paralysis, which may be signs of Guillain-Barré syndrome
- inflammation of the membrane around the spinal cord and brain
- low levels of adrenal hormones
- overactive thyroid gland (hyperthyroidism)
- type 1 diabetes
- inflammation of muscles (myositis).

Rare: may affect up to 1 in 1,000 people

- inflammation of the heart muscle
- myasthenia gravis, an illness that can cause muscle weakness
- inflammation of the pituitary gland situated at the base of the brain
- inflammation of the kidneys.

Atezolizumab used in combination with bevacizumab

The following side effects occur more frequently when atezolizumab is given in combination with bevacizumab, compared to atezolizumab alone:

- overactive thyroid gland (hyperthyroidism)
- underactive thyroid gland (hypothyroidism)
- infusion-related reaction

The following are the most common side effects that have been reported in clinical trials when atezolizumab is given in combination with bevacizumab in patients with HCC:

Very common: may affect more than 1 in 10 people

- low platelet count, which may make you more likely to bruise or bleed
- loss of appetite
- elevated liver enzymes (shown in tests), which may be a sign of an inflamed liver
- diarrhoea
- abdominal pain
- constipation
- nausea
- itching of the skin
- rash
- joint pain
- feeling very tired (fatigue)
- fever
- cough
- nose bleed
- swelling in arms or legs
- protein in urine (proteinuria)
- high blood pressure

If you notice any of the side effects above or if they get worse, tell your doctor straight away.

5. How to store atezolizumab

Atezolizumab will be stored by the healthcare professionals at the hospital or clinic. The storage details are as follows:

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and the vial label after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 °C - 8 °C). Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- The diluted solution should not be kept more than 24 hours at 2 °C to 8 °C or 8 hours at ambient temperature (≤ 25 °C), unless dilution has taken place in controlled and validated aseptic conditions.
- Do not use if this medicine is cloudy, discoloured or contains particles

Do not throw away any medicines via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help to protect the environment.

6. Contents of the pack and other information

What atezolizumab contains

- The active substance is atezolizumab. Each mL contains 60 mg of atezolizumab. Each vial contains 1,200 mg of atezolizumab (in 20 mL).
- The other ingredients are L-histidine, glacial acetic acid, sucrose, polysorbate 20 and water for injections.

What atezolizumab looks like and contents of the pack

Atezolizumab is a concentrate for solution for infusion. It is a clear, colourless to slightly yellowish liquid.

Atezolizumab is available in a pack containing 1 glass vial.

Scientific Opinion Holder and manufacturer

Roche Products Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

Manufacturer

Roche Pharma AG
Emil Barell Strasse 1
D 79639
Grenzach Wyhlen
Germany

This protocol was revised in June 2020

Additional information:

Informed Consent Form

All patients will have the Early Access to Medicines Scheme explained to them using the informed consent form. The patient will be asked to sign this form and a copy will be given to them to keep.

Patient Alert Card

Each patient must be given a Patient Alert Card before they start treatment with atezolizumab. The patient must keep this alert card with them at all times during the treatment and for at 1 month after completing their treatment with atezolizumab. The card summarises that they are currently receiving atezolizumab, the important side effects for which patients need to seek assistance should they occur, details of the patients treating haematologist/oncologist managing their treatment, out of hours contact details and the company contact details.

Patient data to be collected

Patient data collected during the scheme are mostly used for safety surveillance and cannot replace a proper clinical trial to support a marketing authorisation. These data are required by the MHRA to help verify that the patient's condition complies with the EAMS indication and help interpret the side effects and other events occurring during and after the EAMS treatment. These data include:

- Patient initials
- Age/year of birth
- Gender

- Fitness status
- Diagnosis (including stage of cancer)
- Date of Diagnosis (DD/MM/YYYY)
- Whether your cancer can be removed by surgery (unresectable HCC Y/N)
- Condition which the product is being used for (including tumour type and location)
- Any medication taken during treatment with atezolizumab
- Classification of liver function (Child-Pugh class status)
- Prior “direct-to-liver” (locoregional) therapy received
- Duration of prior “direct-to-liver” (locoregional) therapy
- All side effects

Contact information

Contact details for reporting Adverse Events/Special Situations/Pregnancies:

SAE Email Address: welwyn.uk_dsc@roche.com

SAE Facsimile Transmission: +44 1707 367582

SAE TELEPHONE CONTACT: +44 1707 367554

Name: UK Drug Safety Centre

Contact email for the EAMS programme (excluding AE reporting):

welwyn.hcceams@roche.com

Contact Details for Medical Information

Roche Medical Information on 0800 328 1629 or email medinfo.uk@roche.com