Medicines & Healthcare products Regulatory Agency

MHRA

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

The following information is provided:

- Part 1: Patient Information leaflet (PIL) on the use of avelumab monotherapy to treat urothelial carcinoma, a type of bladder cancer, when it is advanced or metastatic and has not progressed with first line platinum-based induction chemotherapy.
- Part 2: Additional information including contact information and additional risk minimisation information containing key information on immune-mediated side effects with avelumab

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Part 1: PIL

Avelumab 20 mg/mL concentrate for solution for infusion

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 avelumab is and what it is used for

Avelumab contains the active substance avelumab, a monoclonal antibody (a type of protein) that attaches to a specific target in the body called programmed death-ligand 1 (PD-L1).

PD-L1 is found on the surface of certain tumour cells and helps protect them from the immune system (the body's natural defences). Avelumab binds to PD-L1, and blocks this protective effect, allowing the immune system to attack the tumour cells.

Avelumab monotherapy is used in adults to treat urothelial carcinoma, a type of bladder cancer, when it is advanced or metastatic and has not progressed with first line platinum-based chemotherapy.

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

You must not be given avelumab
If you are allergic to avelumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Blood tests and weight checks:

Your doctor will check your general health before and during treatment with avelumab.
You will have blood tests during your treatment and your doctor will monitor your weight before and during treatment.

Talk to your doctor before receiving avelumab:
It may cause side effects (see section 4). Please note that in some cases symptoms may be delayed and may develop after your last dose. If you suffer from any of these you should **seek urgent medical attention:**

- infusion-related reactions;
- problems due to inflammation of your lungs (pneumonitis);
- inflammation of your liver (hepatitis) or other liver problems;
- inflammation of your intestines (colitis), diarrhoea (watery, loose or soft stools) or more bowel movements than usual;
- inflammation of your pancreas (pancreatitis);
- inflammation of your heart (myocarditis);
- problems with your hormone producing glands (the thyroid, adrenal and pituitary glands) that may affect how these glands work;
- Type 1 diabetes, including acid in the blood produced from diabetes (diabetic ketoacidosis);
- problems with your kidneys;
- inflammation of your muscles (myositis).

If you experience any of these symptoms when taking avelumab, **do not** try to treat them on your own with other medicines. Your doctor may

- give you other medicines in order to prevent complications and reduce your symptoms,
- withhold the next dose of avelumab,
- or stop your treatment with avelumab altogether.

Check with your doctor or nurse before you receive avelumab if:

- you have an autoimmune disease (a condition where the body attacks its own cells);
- you have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS);
- you have ever had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C (HCV);
- you receive medicines to suppress your immune system;
- you have had an organ transplant.

Children and adolescents
Avelumab is not recommended in children and adolescents below 18 years of age.

Other medicines and avelumab
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Contraception, pregnancy and breast-feeding
You must not use avelumab if you are pregnant unless your doctor specifically recommends it.

Avelumab can cause harm to your unborn baby. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

If you are a woman who could become pregnant, you must use effective contraceptives while you are being treated with avelumab and for at least 1 month after your last dose.

If you are breast-feeding, tell your doctor.

Do not breast-feed while receiving avelumab and for at least 1 month after your last dose.

It is unknown if avelumab passes into your breast milk. A risk to the breast-fed child cannot be excluded.

Driving, cycling and using machines
Do not drive, cycle or use machines after you have received avelumab if you are not feeling well enough. Tiredness is a very common side effect of avelumab and can affect your ability to drive, cycle or to use machines.

Avelumab has a low sodium content
Avelumab contains less than 1 mmol sodium (23 mg) in each dose and therefore is essentially sodium-free.

3. How avelumab is given

You will receive avelumab as an infusion (a drip) into a vein (intravenously) over a period of 1 hour. Avelumab will be added to an infusion bag containing a sodium chloride solution before use.

You will receive avelumab in a hospital or clinic, under the supervision of an experienced doctor.

For at least the first four treatments, you will receive paracetamol and an antihistamine before being given avelumab, to help to prevent possible side effects related to the infusion. Depending on how your body responds to treatment, your doctor may decide to continue giving you these medicines before all of your avelumab treatments.

How much avelumab is given
The recommended dose of avelumab is 800 mg every 2 weeks. Your doctor will decide how many treatments you need.

If you miss a dose of avelumab
It is very important for you to keep all your appointments to receive avelumab. If you miss an appointment, ask your doctor when to schedule your next dose.

If you stop receiving avelumab
Do not stop treatment with avelumab unless you have discussed this with your doctor. Stopping your treatment may stop the effect of the medicine.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects have been reported with this medicine:

Serious side effects
Avelumab acts on your immune system and may cause inflammation in parts of your body (see section 2). Inflammation may cause serious damage to your body and some inflammatory conditions may lead to death and need treatment or withdrawal of avelumab.

Seek urgent medical attention if you experience inflammation in any part of your body or if you have any of the following signs or symptoms, or if they get worse.

- Signs of infusion-related reactions such as **shortness of breath or wheezing**, **chills or shaking**, **bumpy rash or skin wheals**, **flushing**, **low blood pressure** (dizziness, fatigue, nausea) **fever**, **back pain**, and **abdominal pain**. This is very common.

- Signs of inflammation of hormone producing glands (which may affect how the glands work) may include **extreme tiredness**, **rapid heartbeat**, **increased sweating**, **changes in mood or behaviour** such as irritability or forgetfulness, **feeling cold**, **very low blood pressure** (fainting, dizziness, fatigue, nausea), **weight change** or **headache**. This is very common for thyroid gland, common for adrenal glands, and uncommon for pituitary gland.

- Signs of inflammation of the lungs (pneumonitis) may be **breathing difficulties** or **cough**. This is common.

- Signs of inflammation of the intestines (colitis) may include **diarrhoea** (loose stools) or **more bowel movements than usual**, **blood in your stools or dark, tarry, sticky stools**, or **severe stomach** (abdomen) **pain** or **tenderness**. This is common.

- Signs of liver problems, including inflammation of the liver (hepatitis) may include **yellowing of your skin** (jaundice) or the **whites of your eyes**, **severe nausea or vomiting**, **pain on the right side of your stomach area** (abdomen), **drowsiness**, **dark urine** (tea coloured), **bleeding or bruising more easily than normal**, **feeling less hungry than usual**, **tiredness** or **abnormal liver function tests**. This is common.

- Signs of inflammation of the pancreas (pancreatitis) may include **abdominal pain**, **nausea** and **vomiting**. This is uncommon.

- Signs of inflammation of the heart (myocarditis) may include **trouble breathing**, **dizziness** or **fainting**, **fever**, **chest pain** and **chest tightness** or **flu-like symptoms**. This is uncommon.

- Signs of Type 1 diabetes may include **feeling more hungry** or **thirsty than usual**, **needing to urinate more often**, **weight loss**, and **feeling tired**. This is uncommon.

- Signs of inflammation of the kidney may include **abnormal kidney function tests**, **urinating less than usual**, **blood in your urine**, or **swelling in your ankles**. This is uncommon.

- Signs of inflammation of the muscles (myositis) may include **muscle pain** or **weakness**. This is uncommon.

Do not try to treat yourself with other medicines.

Other side effects
Some side effects may not have symptoms and may only be discovered through blood tests.

The following side effects have been reported in clinical trials:

Very common (may affect more than 1 in 10 people)

- Infection of the bladder
- Decrease in the number of red blood cells
- Nausea, loose stools, constipation, vomiting
- Belly pain, back pain, joint pain
- Cough, shortness of breath
- Feeling tired or weak
- Fever
- Swelling in the arms, feet or legs
- Weight loss, feeling less hungry

Common (may affect up to 1 in 10 people)

- Decrease in the number of a type of white blood cells (lymphocytes)
- Increases or decreases in blood pressure
- Headache, dizziness
- Feeling cold
- Dryness in the mouth
- Increased pancreatic enzymes in the blood
- Skin rash, itching
- Muscle pain
- Flu-like illness (includes feeling of fever, muscle aches)
- Numbness, tingling, weakness, burning sensation in arms or legs

Uncommon (may affect up to 1 in 100 people)

- Decrease in the number of platelets in the blood

- Redness in the skin
- Bowel occlusion
- Red, itchy, scaly patches on the skin
- Inflammatory reaction of the whole body (systemic inflammatory response syndrome)
- Inflammation of the eye
- Increased liver enzymes in the blood
- Increase in the number of a type of white blood cells (eosinophils)
- Increased muscle enzyme in the blood
- Guillain-Barré Syndrome (an immune system disorder that causes nerve inflammation and can result in pain, numbness, muscle weakness and difficulty walking)
- Skin colour change in patches (vitiligo)
- Inflammation of the anus and the rectal wall (marked by bloody stools and a frequent urge to defecate (proctitis))
- Inflammation of the joints (including pain and swelling)

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store avelumab

You will receive avelumab in a hospital or clinic, under the supervision of an experienced doctor. You will not need to store avelumab yourself.

6. Contents of the pack and other information

What avelumab contains

The active substance is avelumab.

One vial of 10 mL contains 200 mg of avelumab. Each mL of concentrate contains 20 mg of avelumab.

The other ingredients are mannitol, glacial acetic acid, polysorbate 20, sodium hydroxide, water for injections (see section 2 ‘Avelumab has a low sodium content’).

What avelumab looks like and contents of the pack

Avelumab is a clear, colourless to slightly yellow concentrate for solution for infusion (sterile concentrate).

The pack size is 1 glass vial per carton.

Scientific Opinion Holder

Merck Serono Limited
5 New Square
Bedfont Lakes Business Park
Feltham
Middlesex
TW14 8HA

Manufacturer

Merck Serono S.p.A.
Via Delle Magnolie 15 (loc. frazione Zona Industriale)
70026 Modugno (BA)
Italy

This protocol was revised in August 2020

Part 2: Additional information

You will also be provided with the following items:

- Patient Information brochure
- Informed consent form
- Patient Alert Card, a wallet size card to be completed and given to each patient and carried with them at all times

These items contain key information on immune-mediated side effects with avelumab and will help you identify and ensure that adverse reactions are adequately and appropriately reported and managed.

Informed Consent Form

All patients will have the EAMS explained to them using the informed consent form. You will be asked to sign this form and a copy will be given to you to keep.

Patient Alert Card

You will be given a Patient Alert Card before starting treatment with avelumab. You must keep this alert card with you at all times during the treatment and for at least 3 months after completing your treatment. The card summarises that you are currently receiving avelumab, the important side effects for which you need to seek assistance should they occur, details of your treating doctor, 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's initials, date of birth, age, gender, information on patient diagnosis, ability of the patient to tolerate the EAMS treatment, previous chemotherapy treatments, duration of time between chemotherapy treatment and starting EAMS treatment, contraception/pregnancy check, confirmation that the patient has met all eligibility criteria for the EAMS scheme, patient consent form and all side effects.

Contact information

Contact Details for Medical Information
Telephone: 0208 818 7373
Email: medinfo.uk@merckgroup.com