



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) to UK patients that have a high unmet clinical need. The medicines included in the scheme 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 that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation) in this indication but is already authorised in a type of skin cancer. More information about medicines licensing can be found here:

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm>

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. Informed consent should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. 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 outweigh any potential risks.

Information for the patient

Avelumab 20 mg/mL concentrate for solution for infusion

Read all of this leaflet carefully before you start using 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.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

- What avelumab is and what it is used for
- What you need to know before you use avelumab
- How to use avelumab
- Possible side effects
- How to store avelumab
- Contents of the pack and other information

- **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 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 defenses). Avelumab binds to PD-L1, and blocks this protective effect, allowing the immune system to attack the tumour cells.

Avelumab in combination with axitinib is used in adults to treat renal cell carcinoma (RCC), **a type of kidney cancer**, when it is advanced.

It is important that you also read the patient information leaflet for axitinib (Inlyta®). If you have any questions about axitinib, ask your doctor.

- **What you need to know before you use avelumab**

Do not use avelumab

- If you are allergic to avelumab or any of the other ingredients of this medicine (listed in section 6)
- If your performance status evaluated by your doctor with the ECOG scale is greater than 1
- If you have newly diagnosed brain metastases or brain metastases requiring steroids
- If you have received an experimental treatment in the last month.

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:

- reactions related to infusion of the medicine;
- problems due to inflammation of your lungs (pneumonitis);
- inflammation of your liver (hepatitis);

- 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);
- increased liver enzymes in the blood.

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 has not been studied 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.

Pregnancy

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.

You must not use avelumab if you are pregnant unless your doctor specifically recommends it.

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.

Breast-feeding

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 and using machines

Do not drive 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 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.

- **How to use avelumab**

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

How much avelumab you will receive

The recommended dose is 800 mg of avelumab every 2 weeks.

You will also receive axitinib as a tablet of 5 mg twice daily approximately 12 hours apart.

How you will receive avelumab

You will receive avelumab as an infusion (a drip) into a vein (intravenously) over a period of 1 hour. Your doctor will decide how many treatments you need.

Before you receive avelumab

For at least the first 4 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 your avelumab treatments.

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.

- **Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them. Some side effects may happen weeks or months after your last dose.

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. Some inflammatory conditions may lead to death and need specific treatment or avelumab to be stopped.

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 the hormone producing glands (the thyroid, adrenal and pituitary glands) 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 glands) and common (for adrenal and pituitary glands).
- 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 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

The following side effects of avelumab have been reported in clinical trials with avelumab in combination with axitinib:

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

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

- Loose stools, nausea, constipation, vomiting
- Increases in blood pressure
- Feeling tired or weak
- Hoarse voice
- Feeling less hungry, weight loss
- Underactive thyroid gland
- Joint pain, back pain, belly pain
- Increased liver enzymes in the blood
- Feeling cold
- Skin rash, itching
- Fever

Common (may affect up to 1 in 10 people)

- Red, itchy, scaly patches on the skin
- Swelling in the arms, feet or legs
- Dryness in the mouth
- Decrease in the number of red blood cells
- Overactive thyroid gland
- Decreases in blood pressure
- Decrease in the number of platelets in the blood
- Decreased secretion of hormones produced by adrenal glands
- Redness in the skin

Uncommon (may affect up to 1 in 100 people)

- Severe form of allergic reaction (anaphylactic reaction)
- Inflammation of the muscles
- Inflammation of the kidneys
- Inflammatory reaction of the whole body (Systemic inflammatory response syndrome)
- Type 1 diabetes
- Decrease in the number of white blood cells
- Bowel occlusion
- Inflammation of the eye
- Inflammation or reduced function of the pituitary gland (a gland in the head)
- Guillain-Barré Syndrome (an immune system disorder that causes nerve inflammation and can result in pain, numbness, muscle weakness and difficulty walking)

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.

- **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

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Middlesex

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Manufacturer

Merck Serono S.p.A.

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70026 Modugno (BA)

Italy

This leaflet was last revised in July 2019.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>.

Additional information

You will be given an **Information for Patients Brochure** and a **Patient Alert Card**.

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

Watching for side effects**It is important to be aware of symptoms**

If you notice any signs or symptoms while receiving avelumab, you should talk to your doctor right away. Be aware that side effects may still occur weeks or months after receiving the last dose of avelumab.

Certain medications, such as corticosteroids, may be used to prevent more severe complications and reduce your symptoms. Your doctor may delay or completely stop your treatment if your side effects are too severe.

What to do if symptoms occur when you are away from home

It is important that you contact your doctor whenever symptoms occur. Always carry your Alert Card with your doctor's contact information so that he or she may be reached in case of emergency. The Alert Card contains important information about symptoms that need to be reported immediately to the doctor or nurse treating you while you are away from home. It also alerts other doctors that you are being treated with avelumab.

Carry your Alert Card with you at all times.

Contact information

Contact details for Medical Information

Telephone: 0208 818 7373

Email: medinfo.uk@merckgroup.com