**Package leaflet: Information for the patient**

**Bavencio 20 mg/mL concentrate for solution for infusion**
avelumab

▼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 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**



## 1. What Bavencio is and what it is used for

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

Bavencio is used in adults to treat:
- Merkel cell carcinoma (MCC)**, a rare type of skin cancer**, when it is metastatic (has spread to other parts of the body).
- Urothelial carcinoma (UC), **a cancer that originates in the urinary tract**, when it is advanced or metastatic (has spread beyond the urinary bladder or to other parts of the body). Bavencio is used as maintenance treatment if the tumour has not grown after so called platinum-based chemotherapy as the first treatment.
- Renal cell carcinoma (RCC)**, a type of kidney cancer**, when it is advanced (has spread beyond the kidney or to other parts of the body).

For renal cell cancer, Bavencio is to be used in combination with axitinib.

It is important that you also read the package leaflet for the medicine containing axitinib. If you have any questions about axitinib, ask your doctor.

## 2. What you need to know before you use Bavencio

**Do not use Bavencio**
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 Bavencio.
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 Bavencio:
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 Bavencio **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 Bavencio,
- or stop your treatment with Bavencio altogether.

Check with your doctor or nurse before you receive Bavencio 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**
Bavencio has not been studied in children and adolescents below 18 years of age.

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

**Pregnancy**
Bavencio 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 Bavencio 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 Bavencio 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 Bavencio and for at least 1 month after your last dose.

It is unknown if Bavencio 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 Bavencio if you are not feeling well enough. Tiredness is a very common side effect of Bavencio and can affect your ability to drive or to use machines.

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

## 3. How to use Bavencio

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

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

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

**Before you receive Bavencio**
For at least the first 4 treatments, you will receive paracetamol and an antihistamine before being given Bavencio, 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 Bavencio treatments.

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

**If you stop receiving Bavencio**
**Do not** stop treatment with Bavencio 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. Some side effects may happen weeks or months after your last dose.

Bavencio 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 Bavencio.

**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 with avelumab alone:

**Very common (may affect more than 1 in 10 people)**
- 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)
- Decrease in the number of platelets in the blood
- Increases in blood pressure
- Low level of sodium
- Headache, dizziness
- Feeling cold
- Dryness in the mouth
- Increased liver enzymes in the blood
- 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)**
- Redness in the skin
- Bowel occlusion
- Red, itchy, scaly patches on the skin, dry skin
- Decreases in blood pressure
- Increased muscle enzyme in the blood
- Increase in the number of a type of white blood cells (eosinophils)
- Inflammation of the joints (rheumatoid arthritis)
- Myasthenia gravis, myasthenic syndrome, an illness that can cause muscle weakness

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

**Very common (may affect more than 1 in 10 people)**
- Loose stools, nausea, constipation, vomiting
- Increases in blood pressure
- Feeling tired or weak
- Hoarseness, cough, shortness of breath
- Feeling less hungry, weight loss
- Headache, dizziness
- Joint pain, back pain, belly pain, muscle 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, acne-like rash
- Swelling in the arms, feet or legs
- Dryness in the mouth
- Increased pancreatic enzymes in the blood
- Decreased kidney function
- Decrease in the number of red blood cells
- Decreases in blood pressure
- Increased glucose in the blood
- Flu-like illness (includes feeling of fever, muscle aches)

- Increased muscle enzyme in the blood
- Decrease in the number of platelets in the blood
- Numbness, tingling, weakness, burning sensation in arms or legs
- Redness in the skin

**Uncommon (may affect up to 1 in 100 people)**
- Decrease in the number of a type of white blood cells (lymphocytes)
- Increase in the number of a type of white blood cells (eosinophils)
- Bowel occlusion
- Myasthenia gravis, myasthenic syndrome, an illness that can cause muscle weakness

**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. You can also report side effects directly via

**United Kingdom**

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

**Ireland**

HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

## 5. How to store Bavencio

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 vial label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Store in the original package in order to protect from light.

Do not store any unused portion of the concentrate or of the diluted infusion solution for reuse.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

## 6. Contents of the pack and other information

**What Bavencio 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 “Bavencio has a low sodium content”).

**What Bavencio looks like and contents of the pack**
Bavencio is a clear, colourless to slightly yellow concentrate for solution for infusion (sterile concentrate).

The pack size is 1 glass vial per carton.

**Marketing Authorisation Holder**
Merck Europe B.V.
Gustav Mahlerplein 102
1082 MA Amsterdam
The Netherlands

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

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**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

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The following information is intended for healthcare professionals only:

**Handling instructions**

Preparation and administration
An aseptic technique for the preparation of the solution for infusion should be used.

- The vial should be visually inspected for particulate matter and discoloration. Bavencio is a clear, colourless to slightly yellow solution. If the solution is cloudy, discoloured, or contains particulate matters, the vial should be discarded.
- An infusion bag of appropriate size (preferably 250 mL) containing either sodium chloride 9 mg/mL (0.9%) solution for injection or with sodium chloride 4.5 mg/mL (0.45%) solution for injection should be used. The required volume of Bavencio should be withdrawn from the vial(s) and be transferred to the infusion bag. Any partially used or empty vials have to be discarded.
- The diluted solution should be mixed by gently inverting the bag in order to avoid foaming or excessive shearing of the solution.
- The solution should be inspected to ensure it is clear, colourless, and free of visible particles. The diluted solution should be used immediately once prepared.
- Do not co-administer other medicinal products through the same intravenous line. Administer the infusion using a sterile, non-pyrogenic, low-protein binding 0.2 micrometre in-line or add-on filter.

After administration of Bavencio, the line should be flushed with either sodium chloride 9 mg/mL (0.9%) solution for injection or with sodium chloride 4.5 mg/mL (0.45%) solution for injection.

Do not freeze or shake the diluted solution. If refrigerated, allow the diluted solution in the intravenous bags to come to room temperature prior to use.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.