PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

BEVACIZUMAB 100 EQUITY, concentrate for solution for infusion

BEVACIZUMAB 400 EQUITY, concentrate for solution for infusion

Bevacizumab

Sugar free

Read all of this leaflet carefully before you are given BEVACIZUMAB EQUITY

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist or nurse.

What is in this leaflet

1. What BEVACIZUMAB EQUITY is and what it is used for

What BEVACIZUMAB EQUITY is

BEVACIZUMAB EQUITY contains the active substance bevacizumab, which is a humanised monoclonal antibody (a type of protein that is normally made by the immune system to help defend the body from infection and cancer).

What BEVACIZUMAB EQUITY is used for

BEVACIZUMAB EQUITY is used for the treatment of adult patients with:

- Advanced cancer in the large bowel, i.e., in the colon or rectum. BEVACIZUMAB EQUITY will be administered in combination with chemotherapy treatment containing a fluoropyrimidine medicine.
- Metastatic breast cancer. When used for patients with breast cancer, BEVACIZUMAB EQUITY will be administered with a chemotherapy medicine called paclitaxel.
- Advanced, metastatic and recurrent adenocarcinoma of the lung. BEVACIZUMAB EQUITY will be administered together with a chemotherapy regimen containing platinum.
- Advanced, metastatic kidney cancer. When used for patients with kidney cancer, it will be administered with another type of medicine called interferon.

2. What you need to know before you use BEVACIZUMAB EQUITY

BEVACIZUMAB EQUITY should not be administered to you if:

- you are hypersensitive (allergic) to bevacizumab or to any of the other ingredients of BEVACIZUMAB EQUITY (listed in section 6)
- you are hypersensitive (allergic) to Chinese hamster ovary (CHO) cell products or to other recombinant human or humanised antibodies

- you are pregnant or breastfeeding your baby
- you have untreated cancer that has spread from the original tumour to the central nervous system.

BEVACIZUMAB EQUITY must not be administered together with a medicine called sunitinib. It must also not be injected into the eye.

Warnings and precautions

Talk to your doctor or healthcare professional before being given BEVACIZUMAB EQUITY.

- It is possible that BEVACIZUMAB EQUITY may increase the risk of developing holes in the gut wall. If you have conditions causing inflammation inside the abdomen (e.g. diverticulitis, stomach ulcers, colitis associated with chemotherapy), please discuss this with your doctor.
- BEVACIZUMAB EQUITY may increase the risk of developing an abnormal connection or passageway between two organs or vessels. The risk of developing connections between the vagina and any parts of the gut can increase if you have persistent, recurrent or metastatic cervical cancer.
- BEVACIZUMAB EQUITY can increase the risk of bleeding or increase the risk of problems with wound healing after surgery. If you are going to have an operation, if you have had major surgery within the last 28 days or if you still have an unhealed wound following surgery, you should not receive this medicine.
- BEVACIZUMAB EQUITY may increase the risk of developing serious infections of the skin or deeper layers under the skin, especially if you had holes in the gut wall or problems with wound healing.
- BEVACIZUMAB EQUITY can increase the incidence of high blood pressure. If you have high blood pressure which is not well controlled with blood pressure medicines, please consult your doctor as it is important to make sure that your blood pressure is under control before starting BEVACIZUMAB EQUITY treatment.

- If you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.
- This medicine increases the risk of having protein in your urine especially if you already have high blood pressure.
- The risk of developing blood clots in your arteries (a type of blood vessel) can increase if you are over 65 years old, if you have diabetes, or if you have had previous blood clots in your arteries. Please talk to your doctor since blood clots can lead to heart attack and stroke.
- BEVACIZUMAB EQUITY can also increase the risk of developing blood clots in your veins (a type of blood vessel).
- This medicine may cause bleeding, especially tumour-related bleeding. Please consult your doctor if you or your family tend to suffer from bleeding problems or you are taking medicines to thin the blood for any reason.
- It is possible that BEVACIZUMAB EQUITY may cause bleeding in and around your brain. Please discuss this with your doctor if you have metastatic cancer affecting your brain.
- It is possible that BEVACIZUMAB EQUITY can increase the risk of bleeding in your lungs, including coughing or spitting blood. Please discuss with your doctor if you noticed this previously.
- BEVACIZUMAB EQUITY can increase the risk of developing a weak heart. It is important that your doctor knows if you have ever received anthracyclines (for example doxorubicin, a specific type of chemotherapy used to treat some cancers) or had radiotherapy to your chest, or if you have heart disease.
- This medicine may cause infections and a decreased number of your neutrophils (a type of blood cell important for your protection against bacteria).
- It is possible that BEVACIZUMAB EQUITY can cause hypersensitivity and/or infusion reactions (reactions related to your injection of the medicine). Please let your doctor, pharmacist or nurse know if you have previously experienced problems after injections, such as dizziness/feeling of fainting, breathlessness, swelling or skin rash.

- A neurological side effect named posterior reversible encephalopathy syndrome (PRES) has been associated with BEVACIZUMAB EQUITY treatment. If you have headache, vision changes, confusion or seizure with or without high blood pressure, please contact your doctor.

Before you are given BEVACIZUMAB EQUITY or while you are being treated with BEVACIZUMAB EQUITY:

- if you have or have had pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth tell your doctor and dentist immediately.
- if you need to undergo an invasive dental treatment or dental surgery, tell your dentist that you are being treated with BEVACIZUMAB EQUITY, in particular when you are also receiving or have received an injection of bisphosphonate into your blood.

Children and adolescents

Talk to your doctor, pharmacist or nurse before you are given BEVACIZUMAB EQUITY if you, or your child, are under 18 years of age. The safety and efficacy of BEVACIZUMAB EQUITY have not been established in children less than 18 years old.

Other medicines and BEVACIZUMAB EQUITY

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Combinations of BEVACIZUMAB EQUITY with another medicine called sunitinib malate

(prescribed for renal and gastrointestinal cancer) may cause severe side effects. Discuss with your doctor to make sure that you do not combine these medicines.

Tell your doctor if you are using platinum- or taxane-based therapies for lung or metastatic breast cancer. These therapies in combination with BEVACIZUMAB EQUITY may increase the risk of severe side effects.

Please tell your doctor if you have recently received, or are receiving, radiotherapy.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please tell your doctor, pharmacist or other healthcare provider straightaway before receiving BEVACIZUMAB EQUITY.

You must not use this medicine if you are pregnant. BEVACIZUMAB EQUITY may cause damage to your unborn baby as it may stop the formation of new blood vessels. Your doctor should advise you about using contraception during treatment with BEVACIZUMAB EQUITY and for at least 6 months after the last dose of BEVACIZUMAB EQUITY.

You must not breastfeed your baby during treatment with BEVACIZUMAB EQUITY and for at least 6 months after the last dose of BEVACIZUMAB EQUITY, as this medicine may interfere with the growth and development of your baby.

BEVACIZUMAB EQUITY may impair female fertility. Please consult your doctor for more information.

Driving and using machines

BEVACIZUMAB EQUITY has not been shown to reduce your ability to drive or to use any tools or machines. However, sleepiness and fainting have been reported with BEVACIZUMAB EQUITY use. If you experience symptoms that affect your vision or concentration, or your ability to react, do not drive and use machines until symptoms disappear.

It is not always possible to predict to what extent BEVACIZUMAB EQUITY may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which BEVACIZUMAB EQUITY affects you.

3. How to use BEVACIZUMAB EQUITY

You will not be expected to give yourself BEVACIZUMAB EQUITY. It will be given to you by a person who is qualified to do so. They will watch you closely while you are being given BEVACIZUMAB EQUITY. This is in case you get any side effects.

Dosage and frequency of administration

The dose of BEVACIZUMAB EQUITY needed depends on your body weight and the kind of cancer to be treated. The recommended dose is 5 mg, 7,5 mg, 10 mg or 15 mg per kilogram of your body weight. Your doctor will prescribe a dose of BEVACIZUMAB EQUITY that is right for you. You will be treated with BEVACIZUMAB EQUITY once every 2 or 3 weeks. The number of infusions

that you receive will depend on how you are responding to treatment; you should continue to receive BEVACIZUMAB EQUITY until it fails to stop your tumour growing. Your doctor will discuss this with you.

Method and route of administration

BEVACIZUMAB EQUITY is a concentrate for solution for infusion. Depending on the dose prescribed for you, some or all of the contents of the BEVACIZUMAB EQUITY vial will be diluted with sodium chloride solution before use. A doctor or nurse will give you this diluted BEVACIZUMAB EQUITY solution by intravenous infusion (a drip into your vein). The first infusion will be given to you over 90 minutes. If this is well-tolerated the second infusion may be given over 60 minutes. Later infusions may be given to you over 30 minutes.

The administration of BEVACIZUMAB EQUITY should be temporarily discontinued

- if you develop severe high blood pressure requiring treatment with blood pressure medicines,
- if you have problems with wound healing following surgery,
- if you undergo surgery.

The administration of BEVACIZUMAB EQUITY should be permanently discontinued if you develop

- severe high blood pressure which cannot be controlled by blood pressure medicines; or a sudden severe rise in blood pressure,
- presence of protein in your urine accompanied by swelling of your body,
- a hole in your gut wall,

- an abnormal tube-like connection or passage between the windpipe and the gullet, between internal organs and skin, between the vagina and any parts of the gut or between other tissues that are not normally connected (fistula), and are judged by your doctor to be severe,
- serious infections of the skin or deeper layers under the skin,
- a blood clot in your arteries,
- a blood clot in the blood vessels of your lungs,
- any severe bleeding.

If you take more BEVACIZUMAB EQUITY than you should

Since a healthcare provider will administer BEVACIZUMAB EQUITY, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

You may develop a severe migraine if too much BEVACIZUMAB EQUITY is given. If this happens you should talk to your healthcare provider immediately.

If you forget to use BEVACIZUMAB EQUITY

Since a healthcare provider will administer BEVACIZUMAB EQUITY, it is unlikely that the dose will be missed.

4. Possible side effects

BEVACIZUMAB EQUITY can have side effects.

Not all side effects reported for BEVACIZUMAB EQUITY are included in this leaflet. Should your general health worsen or if you experience any untoward effects while being treated with BEVACIZUMAB EQUITY, please consult healthcare provider for advice.

The side effects listed below were seen when BEVACIZUMAB EQUITY was given together with chemotherapy. This does not necessarily mean that these side effects were strictly caused by BEVACIZUMAB EQUITY.

If any of the following happens, stop using BEVACIZUMAB EQUITY and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,
- chills or shivering,
- feeling sick (nausea) or being sick (vomiting).

These are all very serious side effects. If you have them, you may have had a serious reaction to BEVACIZUMAB EQUITY. You may need urgent medical attention or hospitalisation.

You should seek help immediately if you suffer from any of the below mentioned side effects.

Severe side effects, which may be **frequent**, include:

- high blood pressure,
- feeling of numbness or tingling in hands or feet,
- decreased number of cells in the blood, including white cells that help to fight against infections (this may be accompanied by fever), and cells that help the blood to clot,
- feeling weak and having no energy,
- tiredness,

- diarrhoea, nausea, vomiting and abdominal pain,
- perforation of the gut,
- bleeding, including bleeding in the lungs in patients with non-small cell lung cancer,
- blocking of the arteries by a blood clot,
- blocking of the veins by a blood clot,
- blocking of the blood vessels of the lungs by a blood clot,
- blocking of the veins of the legs by a blood clot,
- heart failure,
- problems with wound healing after surgery,
- redness, peeling, tenderness, pain, or blistering on the fingers or feet,
- decreased number of red cells in the blood,
- lack of energy,
- stomach and intestinal disorder,
- muscle and joint pain, muscular weakness,
- dry mouth in combination with thirst and/or reduced or darkened urine,
- inflammation of the moist lining of mouth and gut, lungs and air passages, reproductive, and urinary tracts,
- sores in the mouth and the tube from the mouth to the stomach, which may be painful and cause difficulty swallowing,
- pain, including headache, back pain and pain in the pelvis and anal regions,
- localised pus collection,
- infection, and in particular infection in the blood or bladder,
- reduced blood supply to the brain or stroke,
- sleepiness,
- nose bleed,
- increase in heart rate (pulse),

- blockage in the gut or bowel,
- abnormal urine test (protein in the urine),
- shortness of breath or low levels of oxygen in the blood,
- infections of the skin or deeper layers under the skin,
- fistula: abnormal tube-like connection between internal organs and skin or other tissues that are not normally connected, including connections between vagina and the gut in patients with cervical cancer.

Severe side effects of **unknown** frequency, include:

- serious infections of the skin or deeper layers under the skin, especially if you had holes in the gut wall or problems with wound healing,
- allergic reactions (the signs may include difficulty breathing, facial redness, rash, low blood pressure or high blood pressure, low oxygen in your blood, chest pain, or nausea/vomiting),
- a negative effect on a woman's ability to have children (see the paragraphs below the list of side effects for further recommendations),
- a brain condition with symptoms including seizures (fits), headache, confusion, and changes invision (Posterior Reversible Encephalopathy Syndrome or PRES),
- symptoms that suggest changes in normal brain function (headaches, vision changes, confusion, or seizures), and high blood pressure,
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections),
- clogging of a very small blood vessel(s) in the kidney,
- abnormally high blood pressure in the blood vessels of the lungs which makes the right side of the heart work harder than normal,
- a hole in the cartilage wall separating the nostrils of the nose,

- a hole in the stomach or intestines,
- an open sore or hole in the lining of the stomach or small intestine (the signs may include abdominal pain, feeling bloated, black tarry stools or blood in your stools (faeces) or blood in your vomit),
- bleeding from the lower part of the large bowel,
- lesions in the gums with an exposed jaw bone that does not heal and may be associated with pain and inflammation of the surrounding tissue (see the paragraphs below the list of side effects for further recommendations),
- hole in the gall bladder (symptoms and signs may include abdominal pain, fever, and nausea/vomiting).

You should seek help as soon as possible if you suffer from any of the below mentioned side effects.

Frequent side effects, which were not severe, include:

- constipation,
- loss of appetite,
- fever,
- problems with the eyes (including increased production of tears),
- changes in speech,
- change in the sense of taste,
- runny nose,
- dry skin, flaking and inflammation of the skin, change in skin colour,
- loss of body weight,
- nose bleeds.
- voice changes and hoarseness.

Patients older than 65 years have an increased risk of experiencing the following side effects:

- blood clot in the arteries which can lead to a stroke or a heart attack,
- reduction in the number of white cells in the blood, and cells that help the blood clot,
- diarrhoea,
- sickness,
- headache,
- fatigue,
- high blood pressure.

BEVACIZUMAB EQUITY may also cause changes in laboratory tests carried out by your doctor. These include a decreased number of white cells in the blood, in particular neutrophils (one type of white blood cell which helps protect against infections) in the blood; presence of protein in the urine; decreased blood potassium, sodium or phosphorous (a mineral); increased blood sugar; increased blood alkaline phosphatase (an enzyme); increased serum creatinine (a protein measured by a blood test to see how well your kidneys are working); decreased haemoglobin (found in red blood cells, which carry oxygen), which may be severe.

Pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs and symptoms of bone damage in the jaw (osteonecrosis). Tell your doctor and dentist immediately if you experience any of them.

Pre-menopausal women (women who have a menstrual cycle) may notice that their periods become irregular or are missed and may experience impaired fertility. If you are considering having children you should discuss this with your doctor before your treatment starts.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store BEVACIZUMAB EQUITY

- Store all medicines out of reach of children.
- Store in a refrigerator (2 °C – 8 °C).
- Do not freeze.
- Keep the container in the outer carton in order to protect from light.
- Infusion solutions should be used immediately after dilution. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless the infusion solutions have been prepared in a sterile environment. When dilution has taken place in a sterile environment, BEVACIZUMAB EQUITY is stable for 48 hours at 2 °C to 30 °C.
- Do not use BEVACIZUMAB EQUITY if you notice any particulate matter or discolouration prior to administration.
- Do not use this medicine after the expiry date which is stated on the carton and the vial after “EXP”. The expiry date refers to the last day of that month.
- Return all unused medicine to your pharmacist.

- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Content of the pack and other information

What BEVACIZUMAB EQUITY contains

The active substance is bevacizumab. Each mL of concentrate contains 25 mg of bevacizumab, corresponding to 1,4 to 16,5 mg/mL when diluted as recommended.

Each 4 mL vial contains 100 mg of bevacizumab, corresponding to 1,4 mg/mL when diluted as recommended.

Each 16 mL vial contains 400 mg of bevacizumab, corresponding to 16,5 mg/mL when diluted as recommended.

The other ingredients are α, α-trehalose dihydrate, sodium dihydrogen phosphate monohydrate, disodium phosphate anhydrous, polysorbate 20, water for injections.

What BEVACIZUMAB EQUITY looks like and contents of the pack

BEVACIZUMAB EQUITY is a concentrate for solution for infusion. The concentrate is a clear or slightly opalescent from colourless to light brown liquid and is free of visible particulate matter.

BEVACIZUMAB 100 EQUITY is filled into clear, colourless vial (Type I glass) with a grey stopper (butyl rubber) and aluminium seal with white plastic flip-off cap. Each vial contains 100 mg bevacizumab in 4 mL of solution.

BEVACIZUMAB 400 EQUITY is filled into clear, colourless vial (Type I glass) with a grey stopper (butyl rubber) and aluminium seal with white plastic flip-off cap. Each vial contains 400 mg bevacizumab in 16 mL of solution.

Each pack of BEVACIZUMAB EQUITY contains one vial.

Holder of Certificate of Registration

Equity Pharmaceuticals (Pty) Ltd

100 Sovereign Drive

Route 21, Nellmapius drive

Irene, 0157

Pretoria, South Africa

Tel. nr: +27 (0)12 345 1747

This leaflet was last revised in

04 February 2025

REGISTRATION NUMBER

56/26/0466/7

Access to the corresponding translated Patient Information Leaflet:

An electronic copy of the translated Patient Information Leaflet (PIL) is available on the Equity website:

http://www.equitypharmaceuticals.co.za