PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Avastin® 100; concentrate for solution for infusion

Avastin® 400; concentrate for solution for infusion

The active substance is bevacizumab

Contains sugar (α,α trehalose dihydrate)

Read all of this leaflet carefully before you start receiving Avastin

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor.

What is in this leaflet

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

1. What Avastin is and what it is used for

- the treatment of advanced cancer in the large bowel, i.e., in the colon or rectum.
- the treatment of metastatic breast cancer.
- the treatment of advanced, metastatic or recurrent adenocarcinoma of the lung, a subgroup of non-small cell lung cancer.
- treatment of advanced kidney cancer.
- treatment of glioblastoma, a form of brain cancer.

- treatment of recurrent, platinum-sensitive epithelial ovarian, fallopian tube and primary peritoneal cancer.
- the treatment of persistent, recurrent, or metastatic cancer of the cervix.

Avastin will be administered in combination with other cancer therapy medicine, as your doctor prescribes.

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

You should not have Avastin administered:

- if you are hypersensitive (allergic) to bevacizumab or any of the other ingredients of Avastin.
- if you are allergic (hypersensitive) to Chinese hamster ovary (CHO) cell products or to other recombinant human or humanised antibodies.
- if you are pregnant. You must not receive Avastin if you are pregnant. Avastin 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 Avastin and for at least 6 months after the last dose of Avastin.

  Tell your doctor if you are pregnant, become pregnant during treatment with Avastin, or plan to start a family in the near future.
- If you are breastfeeding. You must not breastfeed your baby during treatment with Avastin and for at least 6 months after the last dose of Avastin, as Avastin may interfere with the growth and development of your baby.

Warnings and precautions

Talk to your doctor or healthcare professional before being given the injection:

- if you have abdominal inflammation (e.g. diverticulitis, stomach ulcers, colitis associated with chemotherapy), as it is possible that Avastin and chemotherapy may increase the risk of perforation of (or holes in) the gut.
- if you are going to have an operation, or if you had major surgery within the last 28 days or if you still have an unhealed wound following surgery, you should not receive this medicine as Avastin can increase the risk of post-operative bleeding or of problems with wound healing.

- if you develop red and swollen tissue under the skin and severe pain, as well as fever, chills or nausea, vomiting, dizziness and weakness, you could be suffering from a disease caused by bacteria (necrotising fasciitis); it usually occurs if you have open wounds that are not yet healed or after an operation. Avastin therapy should be stopped immediately in patients who develop such symptoms.
- if you have high blood pressure which is not well controlled with hypertension medicines, as Avastin can increase the incidence of hypertension. Your doctor should make sure that your blood pressure is under control before starting Avastin treatment.
- if you have high blood pressure, as you may have a higher risk of having protein in your urine.
- if you are over 65 years old and also have had blood clots in your arteries (a type of blood vessel) in the past, as these factors can increase the risk of further blood clots.
- if you or your family tend to suffer from bleeding problems or you are taking medicines to thin the blood for the treatment of blood clots.
- if you have recently received anthracyclines (a specific type of antibiotic used for chemotherapy) or had radiotherapy to your chest, or if you have had heart disease, as Avastin can increase the risk of developing a weak heart.
- if you have pre-existing heart diseases.
- if you have headache, vision changes, confusion or seizure (fits) with or without high blood pressure, you should contact your doctor. This could be a rare side effect on the nervous system called reversible posterior leukoencephalopathy syndrome.

Please consult your doctor, even if these statements were applicable to you at any time in the past.

Before you are given Avastin, or while you are being treated with Avastin:

- 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 Avastin, in particular when you are also receiving or have received an intravenous bisphosphonate.

You may be advised to have a dental check-up before you start treatment with Avastin.

Children and adolescents:

Avastin is not for use in patients under the age of 18 years as safety and efficacy have not been established.

Other medicines and Avastin

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

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed. If you are taking medicines on a regular basis, using Avastin at the same time with another medicine may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.

Combinations of Avastin with another medicine sunitinib malate (prescribed for kidney and gastrointestinal cancer), may cause severe side effects. Discuss with your healthcare professional to make sure that you healthcare professional do not combine these medicines.

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

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

Pregnancy and Breastfeeding

You must not use Avastin if you are pregnant. Avastin 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 Avastin and for at least 6 months after the last dose of Avastin.

Avastin may also have an effect on female fertility. If you are a women who is looking to having a baby in the future, talk to your doctor or gynaecologist about fertility preservation strategies before you start treatment with Avastin.

Tell your doctor if you are pregnant, become pregnant during treatment with Avastin, or plan to become pregnant in the near future.

You must not breastfeed your baby during treatment with Avastin and for at least 6 months after the last dose of Avastin, as Avastin may interfere with the growth and development of your baby. Ask your doctor or pharmacist for advice before Avastin is administered to you.

If you are pregnant or breastfeeding your baby please consult your doctor, pharmacist or other healthcare professional for advice before taking Avastin.

Driving and using machines

Avastin may to impair your ability to drive or to operate machinery.

3. How you are given Avastin

Do not share medicines prescribed for you with any other person.

Avastin must always be administered by a doctor.

Receiving Avastin

Dosage and frequency of administration

The dose of Avastin needed depends on your body weight and the kind of cancer to be treated. Your doctor will prescribe a dose of Avastin that is right for you. You will be treated with Avastin 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 Avastin until it fails to stop your tumour growing. Your doctor will discuss this with you.

The administration of Avastin 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 Avastin 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, or between internal organs and skin or other tissues that are not normally connected, and are judged by your doctor to be severe,
- a blood clot in your arteries,
- a blood clot in the veins of your lungs,
- any severe bleeding.

If too much Avastin is given

- you may develop a severe migraine. If this happens you should talk to your doctor or pharmacist immediately.

Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If a dose of Avastin is missed

Do not receive a double dose to make up for forgotten individual doses.

Effects when treatment with Avastin is stopped

Do not stop your Avastin treatment without talking to your doctor first. If you have any further questions on the use of Avastin talk to your doctor or nurse.

4. Possible side effects

Avastin can have side effects which may be serious.

Not all side effects reported for Avastin are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.

Serious side effects - *Tell your doctor or nurse straight away, if you notice any of the following side effects:*

Frequent:

- high blood pressure, increase in heart rate (pulse),
- problems with wound healing after surgery,
- 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, and cells that help the blood to clot,
- lack of energy or tiredness, falling asleep or fainting,
- nausea, vomiting and diarrhoea,
- perforation of the gut,
- bleeding associated with the tumour, including bleeding in the lungs in patients with non-small cell lung cancer,
- blood clots in the veins of the lungs or the legs or difficulties in getting the blood to clot,
- blood clots in the arteries, which can lead to a stroke and a heart attack,
- loss of appetite, change in the sense of taste,
- pain, including headache and abdominal pain,
- dry mouth in combination with thirst and/or reduced or darkened urine,
- localised pus collection,
- infection, and in particular infection in the blood or bladder,
- fever,
- reduced blood supply to the brain or stroke,
- problems with the heart due to breathing difficulties,
- shortness of breath or low levels of oxygen in the blood,
- nose bleed, runny nose,
- blockage in the gut or bowel, constipation, bleeding from the lower part of the large bowel,
- inflammation of the lining of the mouth,
- abnormal urine test (protein in the urine),
- dry skin, flaking and inflammation of the skin, change in skin colour,
- inflammation of the tissue surrounding finger or toenails,

- low salt (sodium) levels in the blood, characterised by weakness, drowsiness and muscle cramps,
- low magnesium levels in the blood, which may cause spasms of hands and feet, muscular twitching, cramps, and spasmodic closure of the larynx,
- problems with the eye (tearing), changes in vision,
- voice changes, hoarseness, speech problems.
- 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.

Allergic reactions

If you have an allergic reaction, call your doctor or a member of the medical staff straight away. The signs may include: difficulty in breathing or chest pain. You could also experience redness or flushing of the skin or a rash, increased muscle tension, feeling sick (nausea) or being sick (vomiting).

Other side effects which have been reported are seizures (fits), confusion, heart failure, bleeding from the lining of the mouth or vagina, and abnormal tube-like connection between internal organs and skin or other tissues that are not normally connected and ulcers in the digestive system (the signs may include abdominal pain, feeling bloated, black tarry stools or blood in your stools (faeces) or blood in your vomit).

Some patients may experience increased formation of tears, diarrhoea, inflammation of the mouth, joint pains, muscle pains, inflammation of mucous membranes, stomach ulcer.

There have been reports of patients developing a hole in the septum of the nose – the structure, which separates the nostrils.

Some side effects are more common in elderly patients. These side effects include blood clot in the arteries which can lead to a stroke or a heart attack. In addition, elderly patients have a higher risk of a reduction in the number of white cells in the blood, and cells that help the blood clot.

Other side effects reported with a higher frequency in elderly patients were diarrhoea, sickness, headache and fatigue.

Avastin 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); decreased haemoglobin (found in red blood cells, which carry oxygen), which may be severe.

Not all side effects reported for Avastin are included in this leaflet. Should your general health worsen while taking Avastin, consult your doctor, pharmacist or other healthcare professional for advice.

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

Reporting of side effects

If you get side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Avastin.

5. How to store Avastin

Store all medicines out of reach of children.

Avastin will be stored by the healthcare professionals at the hospital or clinic, in a refrigerator between 2 °C - 8 °C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Avastin contains

Each single-use vial contains bevacizumab 25 mg/mL:

Avastin 100 contains 100 mg bevacizumab per 4 mL

Avastin 400 contains 400 mg bevacizumab per 16 mL

Excipients: α,α Trehalose dihydrate, polysorbate 20 sodium phosphate, and water for injections

What Avastin looks like and contents of the pack

Avastin 100: packs of 1 or 4 vials in an outer carton.

Avastin 400: packs of 1 or 4 vials in an outer carton.

Single-use, preservative free, clear glass vials with grey rubber stoppers, containing clear to slightly opalescent, colourless to pale brown, sterile liquid concentrate. The concentrate must be diluted before use.

Not all packs may be marketed.

Holder of Certificate of Registration

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Botswana	S2 BOT0901577A	S2 BOT0901577B
Namibia	NS2 07/26/0068	NS2 07/26/0069
Zimbabwe	2016/9.7/5262 PP	2016/9.7/5263 PP