ARANESP®

Solution of injection
Response to BMU recommendation dated 25 July 2020;
Response to PV safety directive dated 30 July 2020;
SmPC reformat;
Updates v44, 75, 79, 82, 86, 87, 87, 92, 108, 130, 141, 143, 150 & CDSv21 & 27-28

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ARANESP® 10 µg solution for injection in a pre-filled syringe

ARANESP® 15 µg solution for injection in a pre-filled syringe

ARANESP® 20 µg solution for injection in a pre-filled syringe

ARANESP® 30 µg solution for injection in a pre-filled syringe

ARANESP® 40 µg solution for injection in a pre-filled syringe

ARANESP® 50 µg solution for injection in a pre-filled syringe

ARANESP® 60 µg solution for injection in a pre-filled syringe

ARANESP® 80 µg solution for injection in a pre-filled syringe

ARANESP® 100 µg solution for injection in a pre-filled syringe

ARANESP® 130 µg solution for injection in a pre-filled syringe

ARANESP® 150 µg solution for injection in a pre-filled syringe

ARANESP® 300 µg solution for injection in a pre-filled syringe

ARANESP® 500 µg solution for injection in a pre-filled syringe

Darbepoetin alfa

Read all of this leaflet carefully before you start using ARANESP® because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- ARANESP® has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ARANESP® is and what it is used for

Your doctor has given you **ARANESP®** (an anti-anaemic) to treat your anaemia. Anaemia is when your blood does not contain enough red blood cells and the symptoms may be fatigue, weakness and shortness of breath.

ARANESP® works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. The active substance of **ARANESP®** is darbepoetin alfa produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

If you have chronic renal failure

ARANESP® is used to treat symptomatic anaemia that is associated with chronic renal failure (kidney failure) in adults and children. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause anaemia.

Because it will take your body some time to make more red blood cells, it will be about four weeks before you notice any effect. Your normal dialysis routine will not affect the ability of **ARANESP®** to treat your anaemia.

If you are receiving chemotherapy

ARANESP® is used to treat symptomatic anaemia in adult cancer patients with non-bone marrow cancers (non-myeloid malignancies) who are receiving chemotherapy.

One of the main side effects of chemotherapy is that it stops the bone marrow producing enough blood cells. Towards the end of your chemotherapy course, particularly if you have had a lot of chemotherapy, your red blood cell count may fall making you anaemic.

2. What you need to know before you use ARANESP®

You should not use ARANESP®:

- if you are allergic to darbepoetin alfa or any of the other ingredients of **ARANESP®** (listed in section 6).
- if you have been diagnosed with high blood pressure which is not being controlled with other medicines prescribed by your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Aranesp.

Please tell your doctor if you are **suffering** or **have suffered** from:

- high blood pressure which is being controlled with medicines prescribed by your doctor;
- sickle cell anaemia;
- epileptic fits (seizures);
- convulsions (fits or seizures);
- liver disease;
- significant lack of response to medicines used to treat anaemia;
- an allergy to latex (the needle cap on the pre-filled syringe contains a derivative of latex); or
- hepatitis C.

Special warnings

- If you have symptoms which include unusual tiredness and a lack of energy this could mean you have pure red cell aplasia (PRCA), which has been reported in patients. PRCA means that the body has stopped or reduced the production of red blood cells which causes severe anaemia. If you experience these symptoms you should contact your doctor who will determine the best course of action to treat your anaemia.
- Take special care with other products that stimulate red blood cell production: **ARANESP®** is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional should always record the exact product you are using.
- If you are a patient with chronic renal failure, ARANESP® places you at a higher risk fordeath, problems of the heart (myocardial infarction) or blood vessels, stroke, blood clots (thrombosis) and tumour progression or recurrence. Particularly if you do not respond properly to **ARANESP®** your doctor will check your dose of **ARANESP®** repeatedly increasing your dose of **ARANESP®** if you are not responding to treatment.
- Your doctor should try to keep your haemoglobin between 10 and 12 g/dl. Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin concentrations could put you at risk of

having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- If you have symptoms which include severe headache, drowsiness, confusion, problems with your eyesight, nausea, vomiting or fits (seizures), it could mean that you have very high blood pressure. If you experience these symptoms you should contact your doctor.
- If you are a **ARANESP®** acts as a blood cell growth factor and increases the risk of tumour progression or recurrence. You should not use **ARANESP®** ® if you are receiving chemotherapy that suppresses you bone marrow's production of blood cells and platelets. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.
- Misuse by healthy people can cause life-threatening problems with the heart or blood vessels.
- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.

  If you develop a serious rash or another of these skin symptoms, stop taking **ARANESP®** and contact your doctor or seek medical attention immediately.
- If you are undergoing surgery, blot clotting prevention is recommended as **ARANESP®** places you at higher risk of developing blood clots (deep vein thrombosis).

Other medicines and ARANESP®

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Ciclosporin and tacrolimus (medicines which suppress the immune system) may be affected by the number of red cells in your blood. It is important to tell your doctor if you are taking either of these medicines.

Using ARANESP® with food and drink

Food and drink do not affect **ARANESP®.**

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or other healthcare professional for advice before taking this medicine.

ARANESP® has not been tested in pregnant women. It is important to tell your doctor if you:

- are pregnant;
- think you may be pregnant; or
- plan to get pregnant.

It is not known whether darbepoetin alfa is excreted in human milk. You must stop breast-feeding if you use **ARANESP®**.

Driving and using machines

ARANESP® should not affect your ability to drive or use machinery.

ARANESP® contains sodium

ARANESP® contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

2. How to use ARANESP®

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Following blood tests, your doctor has decided you need **ARANESP®** as your haemoglobin level is 10 g/dl or less. Your doctor will tell you how much and how often you must take **ARANESP®** in order to maintain a haemoglobin level between 10 and 12 g/dl. This may vary depending on whether you are an adult or a child.

Injecting ARANESP® yourself

Your doctor may decide that it is best for you or a carer to inject **ARANESP®**. Your doctor, nurse or pharmacist will show you how to inject yourself with a pre-filled syringe. Do not try to inject yourself if you have not been trained.

Never inject ARANESP® into a vein yourself.

If you have chronic renal failure

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, **ARANESP®** is given as a single injection, either under your skin (subcutaneous) or into a vein (intravenous).

In order to correct your anaemia, your initial dose of **ARANESP®** per kilogram of your body weight will be either:

- 0,75 micrograms once every two weeks, or
- 0,45 micrograms once weekly

For adult patients not on dialysis, 1,5 micrograms/kg once monthly may also be used as the initial dose.

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, once your anaemia is corrected you will continue to receive **ARANESP®** given as a single injection, either once a week or once every two weeks. For all adults and paediatric patients ≥ 11 years of age not on dialysis, **ARANESP®** could also be given as an injection once monthly.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose once every four weeks as necessary in order to maintain long-term control of your anaemia.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to **ARANESP®**, your doctor will check your dose and will inform you if you need to change doses of **ARANESP®**.

Your blood pressure will also be checked regularly, particularly at the beginning of your treatment.

In some cases, your doctor may recommend that you take iron supplements.

Your doctor may decide to change the way that your injection is given (either under the skin or into a vein). If this changes you will start on the same dose as you have been receiving and your doctor will take blood samples to make sure that your anaemia is still being managed correctly.

If your doctor has decided to change your treatment from r-HuEPO (erythropoietin produced by gene-technology) to **ARANESP®**, they will choose whether you should receive your **ARANESP®** injection once weekly or once every two weeks. The route of injection is the same as with r-HuEPO but your doctor will tell you how much you should take, and when, and may adjust your dose if necessary.

If you are receiving chemotherapy

ARANESP® is given as a single injection, either once a week or once every three weeks, under your skin.

In order to correct your anaemia, your initial dose will be

- 500 micrograms once every three weeks (6,75 micrograms of **ARANESP®** per kilogram of your body weight), or
- 2, 25 micrograms (once weekly) of **ARANESP®** per kilogram of your body weight.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose as necessary. Your treatment will continue until approximately four weeks after the end of your chemotherapy. Your doctor will tell you exactly when to stop taking **ARANESP®**.

In some cases, your doctor may recommend that you take iron supplements.

If you use more ARANESP® than you should

You could have serious problems if you use more **ARANESP®** than you need, such as very high blood pressure. You should contact your doctor, nurse or pharmacist if this does happen. If you feel unwell in any way you should contact your doctor, nurse or pharmacist immediately.

If you forget to use ARANESP®

Do not use a double dose to make up for a forgotten dose.

If you have forgotten a dose of **ARANESP®**, you should contact your doctor to discuss when you should inject the next dose

If you stop using ARANESP®

If you want to stop using **ARANESP®** you should discuss it with your doctor first**.**

4. Possible side effects

Like all medicines, **ARANESP®** can cause side effects, although not everybody gets them.

The following side effects have been experienced by some patients taking ARANESP®:

Chronic renal failure patients

Very Common: may affect more than 1 in 10 people

- High blood pressure (hypertension)
- Allergic reactions

Common: may affect up to 1 in 10 people

- Stroke
- Pain around the area injected
- Rash and/or redness of the skin

Uncommon: may affect up to 1 in 100 people

- Blood clots (thrombosis)
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection
- Blood clots in a dialysis access

Not known: frequency cannot be estimated from available data

- pure red cell aplasia (PRCA) – (anaemia, unusual tiredness, lack of energy)

Cancer patients

Very common: may affect more than 1 in 10 people

- ~~A~~llergic reactions

Common: may affect up to 1 in 10 people

- High blood pressure (hypertension)
- Blood clots (thrombosis)
- Pain around the area injected
- Rash and/or redness of the skin
- Fluid retention (oedema)

Uncommon: may affect up to 1 in 100 people

- Convulsions (fits and seizures).
- Bruising and bleeding at the site of injection

All patients

Not known: frequency cannot be estimated from available data

Serious allergic reactions which may include:

- Sudden life-threatening allergic reactions (anaphylaxis)
- Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
- Shortness of breath (allergic bronchospasm)
- Skin rash
- Hives (urticaria)

- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms.
- Stop using **ARANESP®** if you develop these symptoms and contact your doctor or seek medical attention immediately. See also section 2.

Reporting of side effects

If you get any 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 "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 **ARANESP®**

Alternatively, suspected adverse events can be reported to:

Amgen South Africa (Pty) Ltd.

Tel: +27 (0)11 100 5300,

Email: safety-south-africa@amgen.com

5. How to store ARANESP®

Store all medicines out of reach and sight of children.

Store in a refrigerator (between 2 °C and 8 °C). Do not freeze. Do not use **ARANESP®** if you think it has been frozen.

Keep the pre-filled syringe in the outer carton in order to protect from light.

When your syringe has been removed from the refrigerator and left at room temperature for approximately 30 minutes before injection it must either be used within 7 days or disposed of.

Do not use this medicine if you notice the pre-filled syringe contents are cloudy or there are particles in it.

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 protect the environment.

Return all unused medicine to your pharmacist.

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

6. Contents of the pack and other information

What ARANESP® contains

- The active substance is darbepoetin alfa, r-HuEPO (erythropoietin produced by gene-technology). The pre-filled syringe contains either 10, 15, 20, 30, 40, 50, 60, 80, 100, 150, 300 or 500 micrograms of darbepoetin alfa.
- The other ingredients are sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 and water for injections.

What ARANESP® looks like and contents of the pack

ARANESP® is a clear, colourless or slightly pearly liquid solution for injection in a pre-filled syringe.

Aranesp® is available in packs of 1 or 4 pre-filled syringes. The syringes are provided either with (1- and 4-pack) or without (1-pack) a blister-wrapping. Not all pack sizes may be marketed.

Holder of Certificate of Registration

Amgen South Africa (Pty) Ltd. Building D, Ballyoaks Office Park

35 Ballyclare Drive

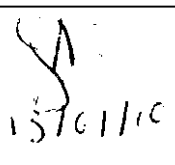
Bryanston Ext 7

2021

South Africa

This leaflet was last revised in

13 July 2020

Date of Registration:	***09 October 2009***	***Date of SAHPRA Approval:***	
Date of Amendment:	***13 July 2020***	**Initialled by: A. Jayaram (BPharm)**	

Registration numbers

ARANESP® 10 µg: 41/8.3/0884

ARANESP® 15 µg: 41/8.3/0885

ARANESP® 20 µg: 41/8.3/0886

ARANESP® 30 µg: 41/8.3/0887

ARANESP® 40 µg: 41/8.3/0888

ARANESP® 50 µg: 41/8.3/0889

ARANESP® 60 µg: 41/8.3/0890

ARANESP® 80 µg: 41/8.3/0891

ARANESP® 100 µg: 41/8.3/0892

ARANESP® 150 µg: 41/8.3/0893

ARANESP® 300 µg: 41/8.3/0894

ARANESP® 500 µg: 41/8.3/0895

7. Instructions for injecting with the ARANESP® pre-filled syringe

This section contains information on how to give yourself an injection of **ARANESP®** It is important that you do not try to give yourself the injection unless you have received training from your doctor, nurse or pharmacist. If you have questions about how to inject, please ask your doctor, nurse or pharmacist for assistance.

How do you or the person injecting you, use the ARANESP® ® pre-filled syringe?

Your doctor has prescribed an **ARANESP®** pre-filled syringe for injection into the tissue just under the skin.

Your doctor, nurse or pharmacist will tell you how much **ARANESP®** you need and how frequently it should be injected.

Equipment:

To give yourself an injection you will need:

- a new **ARANESP®** pre-filled syringe; and
- alcohol wipes or similar.

What should I do before I give myself a subcutaneous injection of ARANESP®

1. Remove the pre-filled syringe from the refrigerator. Leave the pre-filled syringe at room temperature for approximately 30 minutes. This will make the injection more comfortable. Do not warm **ARANESP®** in any other way (for example, do not warm it in a microwave or in hot water). Additionally, do not leave the syringe exposed to direct sunlight.
2. Do not shake the pre-filled syringe.
3. Do not remove the cap from the syringe until you are ready to inject.
4. Check that it is the correct dose that your doctor has prescribed.
5. Check the expiry date on the pre-filled syringe label (EXP:). Do not use it if the date has passed the last day of the month shown.
6. Check the appearance of **ARANESP®** It must be a clear, colourless or slightly pearly liquid. If it is cloudy or there are particles in it, you must not use it.

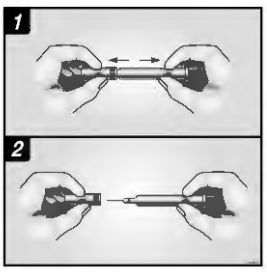
7**. Wash your hands thoroughly**.

8. Find a comfortable, well-lit, clean surface and put all the equipment you need within reach.

How do I prepare my ARANESP® injection?

Before you inject **ARANESP®** you must do the following:

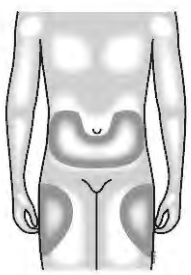
1. To avoid bending the needle, gently pull the cap from the needle without twisting as shown in pictures 1 and 2.



2. Do not touch the needle or push the plunger.
3. You may notice a small air bubble in the pre-filled syringe. You do not have to remove the air bubble before injecting. Injecting the solution with the air bubble is harmless.
4. You can now use the pre-filled syringe.

Where should I give my injection?

The best places to inject yourself are the top of your thighs and the abdomen. If someone else is injecting for you, they can also use the back of your arms.



You may change the injection site if you notice the area is red or sore.

How do I give my injection?

1. Disinfect your skin by using an alcohol wipe and pinch (without squeezing) the skin between your thumb and forefinger.

2. Insert the needle fully into the skin as shown by your doctor, nurse or pharmacist.
3. Inject the prescribed dose subcutaneously as directed by your doctor, nurse or pharmacist.
4. Push the plunger with a slow constant pressure, always keeping your skin pinched, until the syringe is empty.
5. Remove the needle and let go of your skin.
6. If you notice a spot of blood you may gently dab it away with a cotton ball or tissue. Do not rub the injection site. If needed, you may cover the injection site with a plaster.
7. Only use each syringe for one injection. Do not use any **ARANESP®** that is left in the syringe.

Remember:

If you have any problems, please do not be afraid to ask your doctor or nurse for help and advice.

Disposing of used syringes

- Do not put the cap back on used needles, as you may accidentally prick yourself.
- Keep **ARANESP®** out of the sight and reach of children.
- The used pre-filled syringe should be disposed of in accordance with local requirements. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment. Take the used syringe to your nearest pharmacist who will dispose of it.

REFERENCES:

Reference 19	Proposed Annotated Patient Information Leaflet (Pre-Filled Syringe)