PART III: CONSUMER INFORMATION

[Pr]Aranesp®
(darbepoetin alfa)

Single-use Vials[†] and SingleJect® Prefilled Syringes

This section is part III of a three-part "Product Monograph" published when ARANESP was approved in Canada and is designed specifically for patients who will be receiving ARANESP and their caregivers. This leaflet is a summary and will not tell you everything about ARANESP. Contact your doctor or pharmacist if you have any questions about ARANESP.

[†]Single-use vials are not available in Canada.

ABOUT THIS MEDICATION

What is ARANESP used for?

ARANESP is used to treat anemia associated with chronic kidney disease (kidney failure) or anemia associated with chemotherapy administration in cancer patients.

What is Anemia?

Anemia is a condition where your blood does not contain enough red blood cells. Red blood cells are responsible for carrying oxygen to your organs and body tissues. If the number of red blood cells in your blood is decreased, the amount of oxygen delivered throughout your body is also decreased. This may cause several symptoms that are typical of anemia including fatigue, weakness and shortness of breath.

Anemia and kidney failure

In kidney failure, the kidneys do not produce enough of the natural hormone, erythropoietin, which encourages your bone marrow to produce more red blood cells.

Anemia and cancer

When chemotherapy is given to cancer patients, the body may not be able to produce enough and/or respond adequately enough to its own erythropoietin, the natural hormone that encourages bone marrow to make more red blood cells. As a result, not enough red blood cells are produced in order to overcome the effect of chemotherapy.

How does ARANESP work?

In cancer, when chemotherapy is given to cancer patients, the body may not be able to produce enough and/or respond adequately enough to its own erythropoietin, the natural hormone that encourages bone marrow to make red blood cells. If your kidneys are no longer able to produce enough erythropoietin you may benefit by receiving ARANESP. ARANESP will stimulate your bone marrow to produce more red blood cells. Like the natural hormone erythropoietin, the active ingredient of ARANESP, "darbepoetin alfa", travels through the blood and binds to specific cells in the bone marrow. This signals the bone marrow to produce more red blood cells and release them into the blood. As a result, the number of red blood cells circulating in the blood increases and they can deliver more oxygen to your organs and tissues. This helps in managing the symptoms that are associated with anemia. It takes a few weeks for this process to occur.

Your doctor will know when ARANESP is working because your blood tests will show an increase in the number of red blood cells. He/she may refer to the results of your blood tests as hemoglobin and/or hematocrit, and will check these tests while you are being treated with ARANESP. These blood tests may be done more often at the beginning of your treatment or if your dose of ARANESP changes. The increase in the number of red blood cells is not immediate; it may take several weeks. The amount of time it takes to reach the red blood cell level that is right for you, and the dose of ARANESP needed to make the red blood cell level rise, is different for each person. You may need several ARANESP dose adjustments before you reach your correct dose of ARANESP and the correct dose may change over time. Your doctor will also check your blood pressure regularly. In some cases, your doctor may recommend that you take iron supplements.

Who should not take ARANESP?

- People with uncontrolled high blood pressure should not take ARANESP.
- People who are allergic to other erythropoietins, medicines made using mammalian cells, or any of the ingredients (for example, polysorbate 80) in ARANESP should not take ARANESP.
- Patients who make antibodies (develop Pure Red Cell Aplasia) following treatment with any erythropoiesis- stimulating agent (ESA).

Talk to your doctor if you have any questions about this information.

How long will it take to feel better?

Because it will take your bone marrow some time to make more red blood cells, it may take a few weeks before you notice any effects.

I have been treated with Epoetin alfa for my renal failure; what can I expect from ARANESP?

In clinical trials, ARANESP has proved to be as efficacious in correcting and regulating anemia as Epoetin alfa, in patients with chronic kidney disease who have been switched from Epoetin alfa to ARANESP as well as in new patients. Because ARANESP has been designed to work in your body for a longer period of time, it is possible to achieve the same results with fewer injections.

What is the medicinal ingredient in ARANESP?

darbepoetin alfa

What are the nonmedicinal ingredients in ARANESP?

Polysorbate 80
Sodium Chloride
Sodium Phosphate Dibasic Anhydrous
Sodium Phosphate Monobasic Monohydrate

What dosage forms does ARANESP come in?

ARANESP is available as a liquid for injection, and comes in vials† or syringes. The needle cover on the single-use prefilled syringe contains dry natural rubber (latex), which should not be handled by persons sensitive to this substance.

†Single-use vials are not available in Canada.

WARNINGS AND PRECAUTIONS

All Patients

- To minimize the risks for death and serious cardiovascular (heart and blood vessel-related) side effects, your doctor will follow the recommended dosage for each indication.
- Patients with uncontrolled high blood pressure should not be treated with ARANESP; blood pressure should be adequately controlled before receiving ARANESP.
- ARANESP should be used with caution in patients with a history of seizures.
- Antibody-mediated Pure Red Cell Aplasia (PRCA) has been reported after months to years of treatment with erythropoiesis-stimulating agents (ESAs). If you develop PRCA, you may suddenly become severely anemic and this could result in a dependency on blood transfusions.

Chronic Kidney Disease Patients

- If your hemoglobin is kept too high, you have an increased chance of heart attack, stroke, heart failure, blood clots, and death. Your doctor will try to keep your hemoglobin between 100 and 115 g/L, not to exceed 120 g/L.

Cancer Patients

- If you are a cancer patient and your hemoglobin is kept too high (over 120 g/L),
  - your tumour may grow faster,
  - you have an increased chance of heart attack, stroke, blood clots and death.
- Your doctor should use the lowest dose of ARANESP needed to avoid red blood cell (RBC) transfusions.
- In some instances, red blood cell transfusion should be the preferred treatment option.
- Once you have finished your chemotherapy course, ARANESP should be discontinued.

Do not take ARANESP if you are allergic to other erythropoietic agents, ARANESP or to any of the other ingredients in ARANESP.

Too much ARANESP may cause your body to produce too many red blood cells too fast (lead to a hemoglobin that is too high). Producing too many red blood cells, or producing them too fast may cause serious problems. It is important that your blood pressure be monitored often and to report any changes outside of the guidelines that your doctor has given you, especially if you have heart disease. Certain laboratory tests, such as hemoglobin, hematocrit, or iron level measurements, may also need to be done more often and be reported to your doctor or dialysis center.

It is important to keep all appointments for blood tests to allow your doctor to adjust the dosage of ARANESP as needed.

Over time, many patients also need to take iron. Your doctor will know when or if you need an iron supplement from your laboratory test results. Do not change the dose of ARANESP.

Be sure to change the site for each injection to avoid soreness at any one site. Occasionally a problem may develop at the injection site. If there is a lump, swelling, or bruising at the injection site that does not go away, talk to your doctor.

If you have a hemodialysis vascular access, continue to check the access to make sure it is working. Call your doctor or dialysis center right away if you have any problems or questions. Always call your doctor if you do not feel well while using ARANESP.

Pure Red Cell Aplasia (PRCA), in association with antibodies, has been observed in patients treated with ESAs. PRCA is a condition in which severe and sudden anemia (characterized by symptoms such as severe tiredness/fatigue, and shortness of breath on mild exertion) develops due to failure of the bone marrow to produce red blood cells. PRCA could result in a dependency on blood transfusions. Should you be diagnosed with PRCA, your doctor will stop your ARANESP therapy and may initiate treatment with blood transfusions to help increase your red blood cell count. PRCA has been reported predominantly in patients with chronic kidney disease. PRCA has been reported in a very rare number of patients exposed to ARANESP subcutaneously (under your skin).

If you are a cancer patient you should be aware that ARANESP is a red blood cell growth factor and in some circumstances your cancer may grow faster. You should discuss treatment options for your anemia with your doctor.

Special Warnings:

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

- High blood pressure
- Heart disease (e.g., angina)
- Epileptic fits (seizures)

It is important to tell your doctor if you:

- Are pregnant
- Think you may be pregnant
- Plan to get pregnant, or
- Are breast-feeding

INTERACTIONS WITH THIS MEDICATION

As with all medicines, you must tell your doctor what other medications you are taking.

PROPER USE OF THIS MEDICATION

Usual dose:

ARANESP is given to patients as an injection. The method of injection depends on your clinical condition as indicated below.

For patients with chronic kidney disease, one of the following methods will be used:

- under your skin (subcutaneous); or
- into the venous line connecting the hemodialysis machine to your vein (intravenous), if you are on hemodialysis

You and your doctor will determine which is best for you. Your doctor will determine how much you must take and how often you need to take it. ARANESP is given once a week or in some cases, once every two weeks. Your doctor will try to keep your hemoglobin between 100 and 115 g/L, not to exceed 120 g/L.

For cancer patients, there is only one method for injection as follows:

- under your skin (subcutaneous)

Your doctor will determine how much you must take and how often you need to take it. ARANESP is typically given once a week or in some cases, once every two or three weeks. Your doctor should use the lowest dose of ARANESP needed to help you avoid RBC transfusions. Once you have finished your chemotherapy course, ARANESP should be discontinued.

Overdose:

If self-administering this medication, be sure to adhere to the prescribed dose.

Severe hypertension (including hypertensive crisis and malignant hypertension) has been observed following overdose with ARANESP. If there is a significant increase in your blood pressure seek immediate medical attention.

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

You should ask your doctor what to do if you miss a dose of ARANESP.

Administration:

IMPORTANT: TO HELP AVOID CONTAMINATION AND POSSIBLE INFECTION DUE TO INJECTION, PLEASE READ AND FOLLOW THESE INSTRUCTIONS CAREFULLY.

The following section contains step-by-step instructions on self-administering ARANESP by subcutaneous (under-the-skin) injection. Part A of these instructions describes the process of setting up for your injection. Part B of these instructions contains specific instructions for patients who have been prescribed ARANESP vials†. If you have been prescribed ARANESP prefilled syringes, you can ignore Part B. Part C provides directions on selecting and preparing the injection site and the process of self-injection. Part D provides instructions on the activation of the needle guard on used prefilled syringes. Part E provides instructions on the safe disposal of used needles.

It is important that you do not try to give yourself the injection until you have received special training from your doctor or nurse. It is also important that you dispose of the used needles in a puncture-proof container. Do not use ARANESP in a prefilled syringe if the grey cover on the needle is off, or the needle guard (yellow sleeve on the syringe) has been activated (pulled to extend over the needle).

Always follow the instructions provided by your doctor, nurse or pharmacist concerning the dosage and administration of ARANESP. Do not change the dose or method of administration of ARANESP, without consulting your doctor. If you are not sure about giving the injection or you have any questions, please ask your doctor, nurse or pharmacist for help.

†Single-use vials are not available in Canada.

Part A - Setting up for the injection

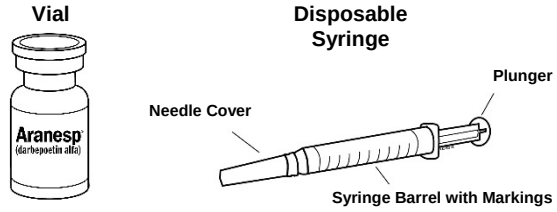
1. Find a comfortable, clean, well-lit working place with a flat surface such as a table.

2. Remove the ARANESP vial† or prefilled syringe from the refrigerator and place it on your flat working surface. Allow it to reach room temperature. This should take about 30 minutes. Do not leave the vial† or prefilled syringe in direct sunlight and do not use it if it has been frozen.

3. Inspect the vial† or prefilled syringe. Check that the strength on the vial† or syringe is the strength that your doctor prescribed for you. Check the date on the label to be sure that the product has not expired. ARANESP should be a clear, colourless solution. If the solution has particles or is discoloured, do not use it, and check with a doctor, nurse, or pharmacist. DO NOT SHAKE THE VIAL† OR PREFILLED SYRINGE. Shaking may damage the ARANESP. If the product has been shaken vigorously, the solution may appear foamy and it should not be used.

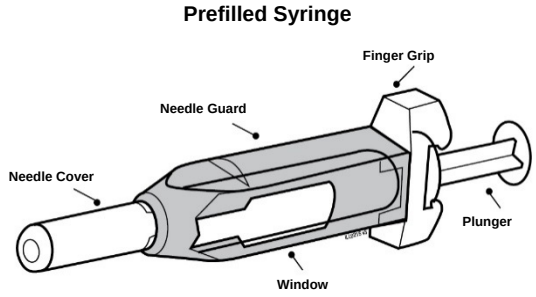
4. Assemble the supplies you will need for an injection:

   ARANESP vial† and the correct disposable syringe and needle



   OR

   ARANESP prefilled syringe with a transparent (clear) yellow plastic needle guard attached



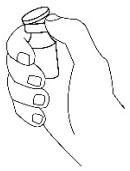
5. In addition to your medication, you will need alcohol swabs, a cotton ball or piece of gauze, and a puncture-proof container for disposal of used needles. When you have all these materials assembled, and are ready to begin, wash your hands well with soap and warm water.

†Single-use vials are not available in Canada.

Part B - ARANESP vials†

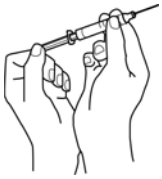
If you are using ARANESP vials†, the doctor or nurse will give you instructions on how to measure your dose of ARANESP and draw it from the vial into the syringe. Only use the syringe that your doctor prescribes. This dose will be measured in millilitres. You should only use a syringe that is marked in tenths of millilitres or mL (for example, 0.2 mL). The doctor or nurse may refer to an "mL" as a "cc" (1 mL = 1 cc). Using an unmarked syringe can lead to a mistake in the dose. If you do not use the correct syringe, you could inject too much or too little ARANESP. Each ARANESP vial is designed to be used only once. Do not put the needle through the rubber stopper more than once. Use only disposable syringes and needles. Use the syringes and needles only once and dispose of them as instructed by your doctor or nurse (see Part D below).

1. Take the yellow color cap off the vial. Clean the rubber stopper with one alcohol swab.



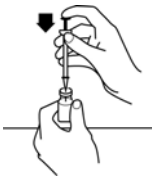
2. Check the package containing the syringe. If the package has been opened or damaged, do not use that syringe. You should dispose of that syringe in the puncture-proof disposal container (see Part D below). If the syringe package is undamaged, open the package and remove the syringe.

3. Pull the needle cover straight off the syringe. Then, pull back on the plunger to draw air into the syringe. The amount of air drawn into the syringe should be the same amount (mL or cc) as the dose of ARANESP that your doctor prescribed.



4. Keep the vial on your flat working surface and insert the needle straight down through the rubber stopper.

5. Push the plunger of the syringe down to inject the air from the syringe into the vial of ARANESP.



6. Keeping the needle inside the vial, turn the vial upside down. Make sure that the tip of the needle is in the ARANESP liquid.

7. Keeping the vial upside down, slowly pull back on the plunger to fill the syringe with ARANESP liquid to the number (mL or cc) that matches the dose your doctor prescribed.

8. Keeping the needle in the vial, check for air bubbles in the syringe. If there are air bubbles, gently tap the syringe with your fingers until the air bubbles rise to the top of the syringe. Then slowly push the plunger up to force the air bubbles out of the syringe. Keep the tip of the needle in the liquid and once again pull the plunger back to the number on the syringe that matches your dose. Check again for air bubbles. The air in the syringe will not hurt you, but too large an air bubble can reduce your dose of ARANESP. If there are still air bubbles, repeat the steps above to remove them.

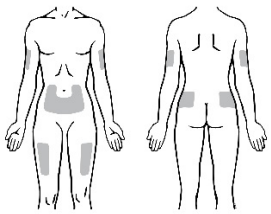
9. Check again to make sure that you have the correct dose in the syringe. It is important that you use the exact dose prescribed by your doctor.

[†] Single-use vials are not available in Canada.

Part C - Preparing Injection Site and Self-Injecting ARANESP

1. Choose an injection site. Four recommended injection sites for ARANESP include:

   - The outer area of your upper arms
   - The abdomen (except for the two inch area around your navel)
   - The front of your middle thighs
   - The upper outer areas of your buttocks

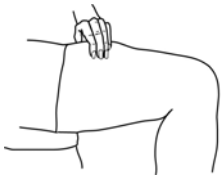


Choose a new site each time you inject ARANESP. Choosing a new site can help avoid soreness at any one site. Do not inject ARANESP into an area that is tender, red, bruised, or hard or that has scars or stretch marks.

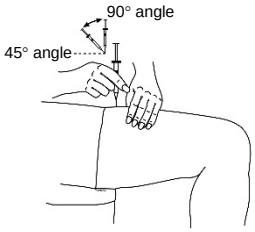
2. Clean the injection site with a new alcohol swab.

3. Hold the syringe in the hand that you will use to inject ARANESP. Use the other hand to pinch a fold of skin at the cleaned injection site.

   NOTE: If using a prefilled syringe with a needle guard, pull the needle cover straight off the needle and hold the syringe barrel through the two needle guard windows when giving the injection.



4. Holding the syringe like a pencil, use a quick "dart like" motion to insert the needle either straight up and down (90 degree angle) or at a slight angle (45 degrees) into the skin.



5. After the needle is inserted, let go of the skin. Inject the prescribed dose subcutaneously as directed by your doctor, nurse or pharmacist.

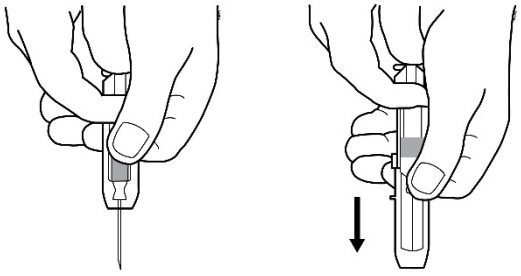
6. When the syringe is empty, pull the needle out of the skin and place a cotton ball or gauze over the injection site and press for several seconds.

You should ONLY use a syringe and vial† once. You should discard the vial† with any remaining ARANESP.

† Single-use vials are not available in Canada.

Part D – Activation of the needle guard on used prefilled syringes

1. After injecting ARANESP from the prefilled syringe, do not recap the needle. Keep your hands behind the needle at all times. To activate the needle guard, hold the finger grip of the syringe with one hand and grasp the needle guard with your free hand, sliding it completely over the needle until the needle guard clicks into place. **NOTE: If an audible click is not heard, the needle guard may not be completely activated.**



Part E - Disposing of syringes and needles

Dispose of the syringe and needle or the syringe with activated needle guard as instructed by your doctor, nurse, or pharmacist, or by following these steps:

- Do NOT throw the needle or syringe in the household trash or recycle.
- Do NOT put the needle cover (the cap) back on the needle. Place all used needles and syringes in a hard plastic container, or a metal container with a plastic lid. Do not use glass or clear plastic containers, or any container that will be recycled or returned to a store.
- Properly label the container to indicate its contents. If a metal container such as a coffee can with a plastic lid is used, cut a small hole in the plastic lid and tape the lid onto the metal container. When the container is full, cover the hole and dispose of the container according to your doctor's, nurse's, or pharmacist's instructions.
- If an opaque (do not use clear plastic), hard plastic container with a screw-on cap is used, always screw the cap on tightly after each use. When the container is full, tape around the cap or lid and dispose of the container according to the instructions provided by your doctor, nurse, or pharmacist. There may be special local laws that they will discuss with you.
- Always store the container out of the reach of children.
- You should always first check with your doctor, nurse, or pharmacist for instructions on how to properly dispose of a filled container. There may be local laws for disposal of used needles and syringes. Do not throw the container in household trash. Do not recycle.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you get headaches, particularly sudden stabbing migraine-like headaches or you start to feel confused or have seizures you should tell your doctor immediately. These may be the warning signs of a sudden rise in blood pressure and may need urgent treatment.

For hemodialysis patients there may be a chance of blood clots (thrombosis) forming in your vascular access (a channel that bypasses normal blood circulation).

Patients with cancer may have an increased risk of blood clots in veins (thrombophlebitis) or the lungs (pulmonary embolus). Call your doctor if you experience pain and/or swelling in the legs or worsening in shortness of breath.

You may notice stinging around the area that you were injected. This stinging will only last for a short period of time and may be more common at the start of your treatment. Some people have also had infections, fevers, headaches, muscle aches or soreness, nausea, and chest pain. If you experience any of these symptoms, you should call your doctor. If any of these symptoms persist or you notice any side effects that are not

mentioned in this leaflet, please tell your doctor, nurse or pharmacist.

Other signs that may appear at the site of injection are redness, swelling, or itching. This may indicate an allergy to the components of ARANESP, or it may indicate a local reaction. If you have a local reaction, consult your doctor.

Serious allergic reactions have been observed, including sudden life-threatening allergic reactions with drop in blood pressure, fast pulse, difficulty breathing and sweating (anaphylaxis), swelling of the face, lips, mouth, tongue or throat (angioedema), shortness of breath (allergic bronchospasm), skin rash/rash over the whole body, hives. If you think you are having a serious allergic reaction, stop taking ARANESP and notify your doctor or emergency medical personnel immediately.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Increase in blood pressure (symptoms may include headaches, confusion, seizures)		√	
	Diarrhea		√	
	Infections		√	
	Fever		√	
	Muscle aches		√	
	Nausea		√	
	Chest Pain		√	
Uncommon	Blood clots		√	
	Stroke		√	
	Allergic reaction		√	√
Unknown	Severe Cutaneous Reactions (symptoms may include a rash, which may be severe, may cover your whole body and can also include blisters or areas of skin coming off)		√	√

This is not a complete list of side effects. For any unexpected effects while taking ARANESP, contact your doctor or pharmacist.

HOW TO STORE IT

You should store ARANESP in the refrigerator (between 2°C and 8°C), but not in the freezer. Do not let ARANESP freeze and do not use ARANESP if you think that it has been frozen. You can take ARANESP out of the refrigerator and let it warm to room temperature (approximately 30 minutes) before injecting it. ARANESP does not contain any preservatives so you should not use it if you have it at room temperature (up to 25°C) for longer than 24 hours.

Always keep the ARANESP vials[ǂ] or syringes in the original pack and do not leave them in direct sunlight.

The expiry date for ARANESP is stamped on the pack and on the vial[ǂ] or syringe label. Do not use ARANESP after the last day of the month and year shown.

As with all medicines, you should keep ARANESP out of the reach and sight of children.

[ǂ] Single-use vials are not available in Canada.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to:

    Canada Vigilance Program
    Health Canada
    Postal Locator 1908C
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: *Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.*

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Amgen Canada Inc., at: 1-866-502-6436

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