

PACKAGE LEAFLET: INFORMATION FOR THE USER

Mannitol Intravenous Infusion EP 20% w/v
Active substance: mannitol

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 or pharmacist
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

Throughout this leaflet Mannitol Intravenous Infusion EP 20% w/v will be called Mannitol 20% Infusion.

What is in this leaflet:

1. What Mannitol 20% Infusion is and what it is used for
2. What you need to know before you are given Mannitol 20% Infusion
3. How you will be given Mannitol 20% Infusion
4. Possible side effects
5. How Mannitol 20% Infusion is stored
6. Contents of the pack and other information

1. What Mannitol 20% Infusion is and what it is used for

Mannitol 20% Infusion is a solution of mannitol in water. Mannitol is an osmotic diuretic. Osmotic diuretics act in the kidney to make it produce more urine. This will reduce the amount of water in your body. Mannitol 20% Infusion is given by infusion into a vein.

Mannitol 20% Infusion is used to:

- produce an increase in your urine production (diuresis) when your kidneys are not working properly (acute kidney failure). This can help prevent your kidney disease becoming more serious.
- reduce the pressure within the skull caused by an accumulation of liquid within the brain (oedema). This is sometimes necessary following an injury to the head or before brain surgery, when the natural protective barrier between the blood vessels in your head and your brain is intact.
- reduce pressure in the eye (intraocular pressure). This may be necessary during eye surgery, or during attacks of glaucoma (a disease that causes eye pressure to rise).
- treat certain types of poisoning or drug overdose. Mannitol helps the kidney to remove these substances from the blood. They are then eliminated from the body in the urine.

2. What you need to know before you are given Mannitol 20% Infusion

You must NOT receive Mannitol 20% Infusion if you are suffering from any of the following conditions:

- if you are allergic (hypersensitive) to mannitol or any of the other ingredients of Mannitol 20% Infusion. See Section 6.
- if you have a high concentration of salts in your blood (hyperosmolarity). This is due to an excessive loss of water from the blood and can be caused by problems such as:
 - prolonged, profuse sweating
 - excess treatment with certain medicines such as water tablets
 - kidney disease

In this situation, Mannitol can cause the osmolarity of the blood to increase even more.

- if you are severely dehydrated (a loss of water from the body, e.g. due to vomiting or diarrhoea). Severe dehydration gives you a dry mouth and makes you very thirsty.
- if it is known that your kidneys cannot produce urine (anuria)

- if you have severe heart disease that is difficult to control with medicines (heart failure)
- if you have a build up of fluid in the lungs (pulmonary oedema) associated with heart failure
- if you have bleeding inside the skull (active intracranial bleeding), except during an operation on the skull (craniotomy)
- if the natural protective barrier between the blood vessels in your head and your brain is damaged. This could occur, for example, after severe injury to the head (e.g. an injury causing a fracture of the skull)
- if you failed to respond to test dosing that your doctor or nurse will do in case it is suspected that kidneys do not work properly (failure to respond to test dosing)
- if your kidney progressively lost its function (progressive renal damage or dysfunction) and you experienced a low output of urine (oliguria) and abnormally high levels of nitrogen containing substances in the blood (azotemia)

Warnings and precautions

Please tell your doctor if you have or have had any of the following medical conditions:

- kidney disease or poor kidney function
- if you are receiving medicines which may be harmful to your kidneys (for example, certain antibiotics or anticancer medicines). Your doctor will know if any of the medicines you are taking could affect your kidneys.

a medical condition where there is inadequate supply of blood to the tissues (shock). In this case your doctor will have to restore your levels of fluids and electrolytes before to continue the administration.

- heart failure
- a low level of sodium (salt) in your blood (hyponatremia)
- not enough water in your body (dehydration)
- a low volume of blood in your blood vessels (hypovolaemia)
- hypersensitivity to mannitol (as mannitol is found in the nature and is used in other medical products you may have developed sensitivity to this substance without having received intravenous treatment with mannitol)

if you have nervous disorders related to preexisting deficiency of the natural protective barrier that separates the circulation of your blood from your brain particularly in case of impaired renal function

When you are given this infusion, your doctor will regularly monitor:

- how well your heart, lungs and kidneys are working
- the amount of liquid you are receiving
- the amount of urine you are producing
- the blood pressure in the veins returning blood to your heart (central venous pressure)
- the amount of chemicals such as sodium and potassium in your blood and urine (electrolytes)
- the acidity of your blood and urine (your acid-base balance)

Your doctor will take into account if you are receiving parenteral nutrition (nutrition given by infusion into a vein). During long term treatment with Mannitol 150 mg/ml Infusion you may need to be given extra nutrition.

The infusion of solution through a needle in your vein could create irritation and inflammation at the point the needle enters your vein.

This solution should not be given through the same needle as blood transfusion. This can damage the red blood cells or cause them to clump together.

Taking other medicines

Please tell your doctor or pharmacist if you are taking, have recently taken or might use any other medicines, including medicines obtained without a prescription.

Some medicines can affect or be affected by Mannitol 20% Infusion. If you are taking any of these medicines, it may be necessary to change the dose.

The following medicines are known to affect or be affected by Mannitol 20% Infusion. Please tell your doctor if you are taking any of these medicines:

- diuretics (water tablets, to increase the amount of urine you produce)
- ciclosporin (used to prevent rejection of a transplant)
- lithium (used for mental disorders)
- aminoglycosides (a type of antibiotic)
- depolarising neuromuscular blocking drugs (used during anaesthesia to cause muscle paralysis). These will be controlled by your anaesthetist.
- oral anticoagulants (medicines to thin the blood, for example warfarin)
- digoxin (a heart medicine)

Using Mannitol 20% Infusion with food, drink and alcohol

You should ask your doctor about what you can eat or drink.

Pregnancy and breast-feeding

If you are pregnant or breast –feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine.

It is not known whether mannitol could affect your unborn baby or your pregnancy. It is also not known whether mannitol could reach your baby through your breast milk. Your doctor will therefore only give you Mannitol 20% Infusion during pregnancy or breast-feeding if it is clearly needed.

Driving and using machines

Ask your doctor or nurse for advice before driving or using machines.

3. How you will be given Mannitol 20% Infusion

Mannitol 20% Infusion will be given to you by a doctor or nurse. Your doctor will decide on how much you need and when it is to be given. This will depend on your age, weight, condition and the reason for treatment. The amount you are given may also be affected by other treatments you are receiving.

You should NOT be given Mannitol 20% Infusion if there are particles in the solution or if the pack is damaged in any way.

Crystals may form in the solution when exposed to low temperatures. Your doctor or nurse will ensure these crystals have been resorbed before the administration of the solution.

Mannitol 20% Infusion will usually be given to you through a plastic tube attached to a needle in a vein. Usually a vein in your arm is used to give you the infusion. However, your doctor may use another method to give you the medicine. Due to its concentration the mannitol solution can create pain and damage your vein at the point where the solution is infused.

The choice of the specific mannitol concentration, dosage and rate of administration depend on the age, weight and clinical condition of the patient and concomitant therapy.

The normal speed of infusion is 30 to 50 ml per hour. This means that the infusion of a half-litre bag would take at least 10 hours.

If your kidneys are not working properly, your doctor may give you a test dose of the infusion. The amount of urine you produce will then be measured. If your kidneys do not respond well enough, you will be given a different treatment.

Mannitol 20% Infusion can also be used in children and in the elderly (over 65 years of age). Your doctor will adjust the dose as necessary.

If you receive more Mannitol 20% Infusion than you should

If you are given too much Mannitol 20% Infusion (over-infusion) or it is given too fast, this may lead to the following symptoms:

- too much blood in the blood vessels (hypervolaemia). The symptoms of hypervolemia include fluid buildup in the abdomen (ascites) swelling in the arms and legs (peripheral oedema), swelling in the lungs causing difficulty breathing (dyspnea) or waking you up at night short of breath (paroxysmal nocturnal dyspnea).
- imbalances of chemicals in your body (electrolytes imbalance)
- your blood may become too acid (acidosis). The symptoms of acidosis include drowsiness, feeling and being sick and acetone smelling breath
- headache
- feeling sick (nausea)
- shivering, but without fever.
- symptoms of Central nervous system problems:
 - o confusion
 - o tiredness
 - o fits
 - o reduced consciousness (stupor) and unconsciousness (coma).
- severe impairment of your kidney function (acute renal failure)

If you develop any of these symptoms, you must inform your doctor immediately. Your infusion will be stopped and you will be given treatment depending on the symptoms.

If a medication has been added to Mannitol 20% Infusion before over-infusion occurs, that medicine may also cause symptoms. You should read the Patient Information Leaflet of the added medicine for a list of possible symptoms.

Stopping your Mannitol 20% Infusion

Your doctor will decide when to stop giving you this infusion.

If you have any further questions on the use of this product, ask your doctor.

4. Possible Side Effects

Like all medicines, Mannitol 20% Infusion can cause side effects, although not everybody gets them.

If you have any of the following symptoms you should tell your doctor or nurse immediately. These may be signs of a very severe or even fatal hypersensitivity (allergic) reaction called anaphylactic shock:

- swelling of the skin of the face and throat
- difficulty breathing
- a low blood pressure (hypotension)
- skin rash
- hives (urticaria)

You will be given treatment depending on the symptoms.

The side effects can include

- too much or too little liquid in the body (fluid imbalance). Too much liquid causes swelling (oedema). Too little liquid in the body causes the symptoms of dehydration
- imbalance in the concentrations of chemicals in the blood (electrolyte imbalance).
- a low blood pressure (hypotension)
- allergic (hypersensitivity) reaction

- not enough water in the body (dehydration). Causing thirst, loss of appetite, dry skin, skin flushing, dark colored urine, dry mouth, tiredness (fatigue), weakness, chills, dizziness, faintness or light-headedness.
- fluid collecting under the skin, usually around the ankles (oedema)
- headache
- convulsions (seizures)
- dizziness
- an increase in pressure within the skull (raised intracranial pressure), causing headaches, feeling sick (nausea), being sick (vomiting), back pain, blurred vision and other changes to your sight, such as difficulty moving your eyes (ocular palsy).
- blurred vision
- an irregular heartbeat (cardiac arrhythmia)
- a high blood pressure (hypertension)
- fluid on the lung (pulmonary oedema), causing shortness of breath, especially when lying down, with the same symptoms as pulmonary congestion (above).
- runny/itchy nose (rhinitis)
- dryness of the mouth
- death of an area of skin (skin necrosis)
- thirst
- feeling sick (nausea)
- vomiting
- hives (urticaria)
- cramps
- production of a large volume of urine (excessive diuresis)
- blood in the urine
- damage to the kidney (osmotic nephrosis), causing difficulty with passing water (urinating) or less water being passed, swelling of ankles, fingers or face due to build up of fluid in the body.
- an inability to pass water (urinary retention)
- chills
- chest pain (oppressive pain in the middle of the chest)
- fever
- heart failure associated with fluid on the lungs and swelling of the ankles (congestive heart failure)
- abnormal heartbeat
- sudden onset of kidney failure, with a marked decrease in urine production (acute renal failure)
- your body produces too much acid or your kidneys are not removing enough acid from your body (metabolic acidosis)
- coma
- confusion
- tiredness (lethargy)
- abnormally high levels of nitrogen containing substances in the blood (azotemia)
- your kidneys cannot produce urine (anuria)
- your kidney produce low urine output (oliguria)
- your kidney produce high urine output (polyuria)
- decreased muscle strength (asthenia)
- fatigue (malaise)
- infusion site reactions including
 - infusion site inflammation of the vein with redness, swelling and pain along the path of the vein (infusion site thrombophlebitis)
 - infusion site swelling (inflammation)
 - infusion site pain
 - infusion site rash
 - infusion site redness
 - infusion site itching
- escape of the infusion solution into the tissues around the vein (extravasation) and swelling at the injection site. This may result in decreased blood flow and severe injury to the surrounding area.

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.

Ireland:

You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

United Kingdom:

Via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard

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

5. How Mannitol 20% Infusion is stored

VIAFLEX containers should be stored within their overpouch at a temperature between 20°C - 30°C

Keep out of the reach and sight of children.

Do not remove Mannitol 20% Infusion from the outer plastic bag until it is to be used.

Mannitol 20% Infusion should NOT be given to you after the expiry date shown on the bag after EXP. The expiry date refers to the last day of that month.

After opening, with or without additives:

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user

You should not be given Mannitol 20% Infusion if there are particles in the solution or if the unit is damaged in any way.

6. Contents of the pack and other information

What Mannitol 20% Infusion contains

The active substance is mannitol.

The other ingredients are:

- water for injections.
- sodium hydroxide.

Each 1000 ml of solution contains 200 grammes of mannitol.

What Mannitol 20% Infusion looks like and contents of the pack

- The solution is supplied in a plastic VIAFLEX infusion bag made from PVC. The bag contains either 200ml, 250ml, 500ml or 1000ml and is sealed in a protective plastic overpouch.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers

Marketing Authorisation Holder :
Baxter Healthcare Ltd.

Caxton Way
Thetford
Norfolk – IP24 3SE
United Kingdom

Send all enquiries to this address.

Mannitol 20% Infusion can be made at any of these addresses:

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Thetford
Norfolk – IP24 3SE
United Kingdom

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For information about Mannitol 20% Infusion or to request this leaflet in formats such as audio or large print please contact the Marketing Authorisation Holder: Tel: +44 (0)1635 206345.

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The following information is intended for medical or healthcare professionals only:

Handling and Preparation

The solution for infusion should be visually inspected prior to use.

Use only if the solution is clear, without visible particles and if the container is undamaged.

Administer immediately following the insertion of infusion set.

Do not remove unit from overwrap until ready for use.

The inner bag maintains the sterility of the product.

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

Additives may be introduced before infusion or during infusion through the re-sealable medication port.

When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

Mannitol solutions may crystallize when exposed to low temperature. At higher concentrations, the solutions have a greater tendency to crystallize. Inspect for crystals prior to administration. If crystals are visible, re-dissolve by warming the solution up to 70°C, with agitation. Solutions should not be

heated in water or in a microwave oven due to the potential for product contamination or damage. Allow the solution to cool to room or body temperature before re-inspection for crystals and use.

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bags.

Preparation for Administration

The VIAFLEX container has an outlet port designed for an administration set with a short single connector. If an administration set with a combined air inlet/fluid path connector has to be used, ensure the air inlet tube is always clamped off.

1. Opening

- a. Remove the protective overpouch by tearing down from notch and remove container.
- b. Carefully straighten hanger and ports, if necessary.
- c. Squeeze container and inspect for minute leaks and examine solution for visible particles or cloudiness by viewing along seam.
- d. Discard unit if leaks, particles or cloudiness are evident.

2. Preparation for administration

Use sterile material for preparation and administration.

- a. Suspend container from base eyelet support.
- b. Use an aseptic technique to prepare the administration set.
- c. Remove blue protector from outlet port and insert set connector well into port.
- d. Prime set and regulate administration as required.
- e. If administration set becomes blocked do not pump contents back into container but replace equipment.
- f. Discard any unused portion and equipment after use. Do not store or reconnect partly used containers.

3. Techniques for injection of additive medications

The VIAFLEX container has a second port with a self-sealing rubber medication port designed for the addition of medication using a syringe. This is the only port for adding medication.

Warning: Additives may be incompatible.

To add medication before administration

- a. Swab the medication port with the appropriate anti-bacterial fluid in line with current recommended practice and procedure.
- b. Using a syringe with a 20-22 gauge needle, puncture re-sealable medication port and inject. Do not leave the syringe and needle in the port once the medication has been injected.
- c. Shake and squeeze the VIAFLEX container so that the solution and medication are thoroughly mixed. For high density medications such as potassium chloride, squeeze both ports while upright and invert the container several times while shaking and squeezing to ensure thorough mixing.

Caution: Do not store bags containing added medications.

To add medication during administration

- a. Close clamp on the set.

- b. Disinfect medication port.
- c. Using a syringe with a 20-22 gauge needle, puncture re-sealable medication port and inject.
- d. Remove container from IV pole and/or turn to an upright position.
- e. Evacuate both ports by tapping gently while the container is in an upright position.
- f. Mix solution and medication thoroughly.
- g. Return container to in use position, re-open the clamp and continue administration.

Cautions

- a. Do not vent.
- b. Do not administer unless the solution is clear and container undamaged.
- c. Do not use in series connections as this could result in air embolism due to residual air being drawn from the primary container before administration of fluid from the secondary container is completed.
- d. Discontinue infusion if adverse reaction occurs.
- e. Rapid infusion may be harmful.
- f. It is recommended that the intravenous administration set be replaced at least once every 24 hours. Details of the use of the set can be recorded - record labels are available from Baxter Healthcare Ltd.

4. In-use shelf-life

Chemical and physical stability of any additive at the pH of the Mannitol 20% Infusion in the VIAFLEX container should be established prior to use.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user, and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

5. Incompatibilities of additive medications

Additives may be incompatible with Mannitol 20% w/v Solution for infusion.

Incompatibility of the medicinal product to be added with the solution in the Viaflex container must be assessed before addition.

Before adding a medicinal product, verify it is soluble and stable in water at the pH of the mannitol solution (4.5 to 7.0). Mannitol Intravenous Infusion EP 20% w/v should not be administered simultaneously with, before, or after administration of blood through the same infusion equipment, due to risk of pseudoagglutination. See section 4.4.

Check additive compatibility before use.

The instructions for use of the medicinal product to be added must be consulted.

As an example, cefepime, imipenem, cilastin and filgrastim are incompatible with mannitol solutions, but this list is not exhaustive. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products

The addition of potassium and sodium chloride to mannitol may lead to precipitation of mannitol.