PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

VALCYTE® 450 film-coated tablet

VALCYTE® 50 mg/mL powder for oral solution

Valganciclovir

Contains sugar, i.e. mannitol (5,78 g per bottle)

Contains sodium saccharin as sweetener (0,03 g per bottle)

Read all of this leaflet carefully before you start using VALCYTE

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

What is in this leaflet

1. What VALCYTE is and what it is used for

VALCYTE is a medicine which prevents the growth of viruses.

VALCYTE is indicated for:

- the treatment of cytomegalovirus (CMV) retinitis in adult patients with acquired immunodeficiency syndrome (AIDS)
- the prevention of CMV disease in adult and paediatric solid organ transplant (SOT) patients at risk.

After taking VALCYTE, the valganciclovir is quickly changed in your body to release ganciclovir, which is the active medicine. Ganciclovir prevents the growth and the increase in numbers of a virus called Cytomegalovirus (CMV).

2. What you need to know before you take VALCYTE

Please take special note of the advice regarding taking VALCYTE during pregnancy below.

Do not take VALCYTE if:

- you have ever had an allergic reaction to valganciclovir, or to ganciclovir, or to any of the other ingredients of VALCYTE.

Warnings and precautions

Talk to your doctor or pharmacist before taking VALCYTE:

- If you have ever had an allergic reaction to aciclovir or penciclovir (or their prodrugs valaciclovir or famciclovir).
- If you have (or have recently had) low numbers of white blood cells, red blood cells or platelets (small cells involved in blood clotting) in your blood. Your doctor will perform blood tests before you start taking VALCYTE and more tests will be done while you are taking VALCYTE.
- If you have problems with your kidneys. Your doctor may need to prescribe a reduced dose for you and may need to check your blood frequently during treatment.

- If you are on haemodialysis or receiving radiotherapy. VALCYTE 450 film-coated tablets are not suitable for people on haemodialysis, however, VALCYTE 50 mg/mL oral solution may be used. If your doctor decides to give you VALCYTE 50 mg/mL oral solution, your blood will need to be checked frequently.
- If you are currently taking ganciclovir capsules and your doctor wants you to switch to VALCYTE. It is important that you do not take more than the dose prescribed by your doctor or you could risk an overdose.

Safety and efficacy - studies of VALCYTE use in children are limited.

Other medicines and VALCYTE

Taking other medicines with VALCYTE:

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

Special care is needed when some other medicines are taken with VALCYTE. Make sure that you tell your doctor about ALL the medicines that you are taking before you take VALCYTE, including all medicines that have been prescribed for you and any medicines that you have bought without a prescription.

Your doctor may still advise you to take VALCYTE, but may ask to see you more often during treatment and it may be necessary to check your blood more often if you are taking the medicines listed below.

Taking VALCYTE with these medicines may increase the number and severity of any side effects.

Tell your doctor if you are already taking medicines that contain the following:

- Imipenem-cilastatin (an antibiotic). There may be an increased risk of seizures when this antibiotic is taken with VALCYTE.
- Trimethoprim with or without sulphonamides, pentamidine, flucytosine, amphotericin B and dapsone taken for the treatment of infections.

- Vincristine, vinblastine and hydroxyurea used in the treatment of cancer.
- Zidovudine, didanosine, zalcitabine, stavudine or other medicines used in the treatment of HIV infection. Your doctor may reduce the dose of didanosine that you need to take.
- Probenecid taken for the treatment of gout may increase your blood levels of ganciclovir.
- Mycophenolate mofetil, ciclosporin or tacrolimus, medicines used in patients who have received an organ transplant.
- Cidovir, foscarnet, or nucleoside analogues used against viral infections.

Taking VALCYTE with food and drink

VALCYTE should be taken with food. If you are unable to eat for any reason, you should still take your dose of VALCYTE as usual.

See also section 3 “How to take VALCYTE”.

Pregnancy and breastfeeding

Pregnancy

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

VALCYTE should not be given to pregnant women because it is possible that this could lead to the loss of the baby or to the birth of a malformed baby or to problems in the baby after birth.

If you are already pregnant before starting to take VALCYTE, or if you think you may possibly be pregnant, you **must** tell your doctor before you take VALCYTE.

Your doctor will only advise you to take VALCYTE if it is clearly needed and only after discussing the risks to the unborn baby with you. If you have any questions, ask your doctor.

It is also extremely important that both men and women of child-bearing age use effective contraception during treatment with VALCYTE.

If you need advice on contraception, ask your doctor before you start to take VALCYTE. Women of childbearing age must use effective contraception when taking VALCYTE and for at least 30 days after treatment has finished. Men should use condoms while taking VALCYTE and should continue to use condoms for 90 days after treatment has finished (see section *Possible Side Effects*).

Breastfeeding

VALCYTE must not be used if you are breastfeeding. The active ingredient, ganciclovir, may pass into the milk and may harm your baby.

Driving and using machines

If you feel dizzy, sleepy or confused while taking VALCYTE, do not drive or operate machinery. Other side effects that can occur with VALCYTE and may cause problems if you drive or operate machinery are seizures and loss of co-ordination (see *Possible Side Effects* below for details).

Important information about some of the ingredients of VALCYTE

VALCYTE 50 mg/mL contains mannitol (5.78 g per bottle) and may have a laxative effect. If you have been told that you have an intolerance to some sugars, you should not take VALCYTE 50 mg/mL.

VALCYTE 50 mg/mL contains sodium benzoate and sodium (salt). This medicine contains 100 mg of sodium benzoate in each 12 g bottle, which is equivalent to 1 mg/ml after reconstitution. Benzoate salt may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old). For patients on a sodium-controlled diet, this medicine contains a total of 0.193 mg/ml sodium, that is to say essentially 'sodium-free'.

3. How to take VALCYTE

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

Always take VALCYTE exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are not sure.

Whenever possible, VALCYTE should be taken with food. If you are unable to eat for any reason, you should still take the dose when it is due.

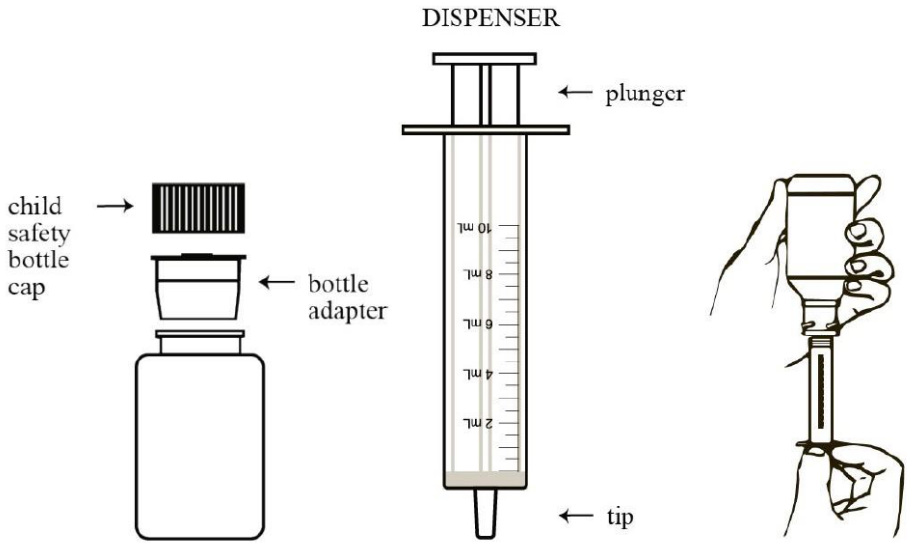
VALCYTE 450 tablets should be handled with care and should not be broken or crushed. You should swallow them whole and with food whenever possible.

VALCYTE 50 mg/mL Oral Solution should be handled with care. You should avoid getting the solution on your skin or in your eyes.

If you do accidentally get the solution on your skin, or touch damaged tablets, wash the area thoroughly with soap and water. If you accidentally get any solution or powder in your eyes, rinse your eyes thoroughly with water.

It is important that you use the syringe provided in the pack to measure your dose of VALCYTE 50 mg/mL oral solution.

Once the solution has been prepared, follow the instructions below to withdraw and take your medication.



1. Shake closed bottle well for about 5 seconds before each use.
2. Remove the child-resistant cap.
3. Before inserting the tip of the dispenser into bottle adapter, push the plunger completely down toward the tip of the dispenser. Insert tip firmly into opening of the bottle adapter.
4. Turn the entire unit (bottle and dispenser) upside down.

5. Pull the plunger out slowly until the desired amount of solution is withdrawn into the dispenser (see diagram).
6. Turn the entire unit right side up and remove the dispenser slowly from the bottle.
7. Dispense directly into mouth and swallow. Do not mix with any liquid prior to dispensing.
8. Close bottle with child-resistant cap after each use.
9. Immediately after administration:

   Disassemble the dispenser, wash with distilled or boiled water and air dry prior to next use.

Do not use the solution after the expiry date which is 49 days from the day of preparation.

The usual dose is:

Standard dosage

Prevention of CMV disease in transplant patients

Adult patients

You should start to take VALCYTE within 10 days of your transplant. The usual dose is 900 mg VALCYTE (two 450 mg tablets) taken ONCE daily. You should continue with this dose for up to 100 days following your transplant. If you have received a kidney transplant, your doctor may advise you to take the dose for 200 days.

Paediatric patients

Children should start to take this medicine within 10 days of their transplant. The dose given will vary depending on the size of the child and should be taken ONCE daily. Your doctor will decide the most appropriate dose based on your child's height, weight and renal function. You should continue with this dose for up to 100 days. If your child has received a kidney transplant, your doctor may advise you to take the dose for 200 days.

Treatment of very active CMV retinitis in AIDS patients (called induction treatment)

The usual dose is 900 mg (450 mg x 2 tablets/amounts) (2 full syringes) taken TWICE a day for 21 days (three weeks) with food. That is, two 450 mg tablets/amounts (i.e. 2 full syringes) of the VALCYTE in the morning and two 450 mg tablets/ amounts (i.e. 2 full syringes) in the evening.

Do not continue with this dose for more than 21 days unless your doctor tells you to as this may increase your risk of possible side effects.

Longer term treatment to prevent recurrence of active inflammation in AIDS patients with CMV retinitis (called maintenance treatment)

The usual dose is 900 mg (450 mg x 2 tablets/amounts) (2 full syringes) VALCYTE taken ONCE a day with food. You should try to take VALCYTE at the same time each day. Your doctor will advise you how long you should continue to take VALCYTE. If your retinitis worsens while you are on this dose, your doctor may tell you to repeat the induction treatment (as above) or may decide to give you a different medicine to treat the CMV infection.

Patients with kidney disorders:

f your kidneys are not working properly, your doctor may instruct you to take a lower dose of the VALCYTE each day or may ask you to take VALCYTE only on some days of the week.

It is VERY IMPORTANT that you follow these special dose instructions from your doctor.

Your doctor will tell you how long your treatment with VALCYTE will last.

Do not stop treatment early. If you have the impression that the effect of VALCYTE is too strong or weak, tell your doctor or pharmacist.

If you take more VALCYTE than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Contact your doctor or hospital immediately if you have taken, or think you have taken more VALCYTE than you should. Taking too much VALCYTE can cause serious side effects, particularly affecting your blood or kidneys. You may need hospital treatment.

If you forget to take/missed a dose of VALCYTE

Contact your doctor or pharmacist as soon as possible. Do not take a double dose to make up for forgotten individual doses.

If you stop taking VALCYTE

You must not stop taking VALCYTE unless your doctor tells you to. If you have any further questions on the use of VALCYTE, ask your doctor or pharmacist.

4. Possible side-effects

VALCYTE can have side effects.

Although VALCYTE can help fight CMV infection, it can have some serious side effects. Your doctor may advise stopping your treatment either temporarily or permanently depending on your condition.

Allergic reactions

Infrequently, people may have a sudden and severe allergic reaction to VALCYTE (anaphylactic shock). STOP taking VALCYTE and go to the nearest hospital emergency room if you experience any of the following:

- A raised, itchy skin (hives)
- Sudden swelling of the throat, face, lips and mouth which may cause difficulty swallowing or breathing
- Sudden swelling of the hands, feet or ankles

Frequent side effects:

- Effects on the blood: a reduction in the number of white blood cells in the blood (neutropenia) - which will make you more likely to get infections, a reduction in the pigment in the blood that carries oxygen (anaemia) - which can cause tiredness and breathlessness when you exercise
- Effects on breathing: feeling short of breath or having trouble breathing (dyspnoea)
- Effects on the stomach and digestive system: diarrhoea
- Effects on the blood: a reduction in the number of leucocytes (blood cells that fight infection) in the blood (leukopenia) a reduction in the number of platelets in the blood (thrombocytopenia) - which can cause bruising and bleeding, a reduction in several types of blood cells at the same time (pancytopenia)

- Effects on the nervous system: headache, difficulty sleeping (insomnia), strange tastes (dysgeusia), becoming less sensitive to touch (hypoaesthesia), prickly or tingling skin (paraesthesia), loss of feeling in the hands or feet (peripheral neuropathy), dizziness, seizures.
- Effects in the eye: eye pain, swelling within the eye (oedema), separation of the back of the eye (detached retina), seeing floaters
- Effects in the ear: earache
- Effects on breathing: coughing
- Effects on the stomach and digestion: feeling and being sick, stomach ache, constipation, wind, indigestion (dyspepsia), difficulty swallowing (dysphagia)
- Effects on the skin: inflamed skin (dermatitis), itching (pruritus), sweating at night
- Effects on the muscles, joints or bones: back pain, pain in the muscles (myalgia) or joints (arthralgia), stiff muscles (rigor), muscle cramps
- Infections: fungal infection in the mouth (oral candidiasis), infections caused by bacteria or viruses in the blood, inflammation of cellular tissue (cellulitis), inflammation or infection of the kidneys or bladder
- Effects in the liver: a rise in some liver enzymes, which will only be seen during blood tests
- Effects in the kidney: changes to the normal working of the kidneys
- Effects on eating: loss of appetite (anorexia), weight loss
- General effects: tiredness, fever, pain, chest pain, loss of energy (asthenia), generally feeling unwell (malaise)
- Effects on mood or behaviour: depression, feeling anxious, confused, having unusual thoughts

Less frequent side effects:

- Effects in the heart: changes to the normal heartbeat (dysrhythmia)
- Effects on circulation: low blood pressure (hypotension), which can cause you to feel light headed or faint
- Effects on the blood: a decrease in the production of blood cells in the bone marrow
- Effects in the nerves: shaking or trembling (tremor)

- Effects in the eyes: red, swollen eyes (conjunctivitis), abnormal vision
- Effects in the ears: deafness
- Effects on the stomach or digestion: swollen stomach, mouth ulcers, inflammation of the pancreas (pancreatitis) where you may notice severe pain in the stomach and back
- Effects on the skin: hair loss (alopecia), itchy rash or swellings (urticaria), dry skin
- Effects in the kidneys: blood in the urine (haematuria), kidney failure
- Effects in the liver: a rise in the liver enzyme called alanine aminotransferase (which will only be seen during blood tests)
- Effects on fertility: infertility in men
- Effects on mood or behaviour: having unusual changes in mood and behaviour, losing contact with reality such as hearing voices or seeing things that are not there, feeling agitated
- Effects on the blood: failure of the production of all types of blood cells (red blood cells, white blood cells and platelets) in the bone marrow

Not all side effects reported for this medicine 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.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or other healthcare professional. 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 VALCYTE.

5. How to store VALCYTE

Store all medicines out of reach of children.

VALCYTE 450 film-coated tablets:

Store at or below 25 °C.

Do not use after the expiry date stated on the pack.

Do not break or crush the tablets. Avoid contact of broken or crushed tablets with skin or mucous membranes.

VALCYTE 50 mg/mL powder for oral solution:

Store at or below 30 °C.

Reconstituted solution: Store in the refrigerator at 2 °C to 8 °C.

Store in the original bottle. Keep the bottle tightly closed. Any remaining solution should be discarded after 49 days. Return any unused solution in the original container to your pharmacist for safe disposal.

6. Contents of the pack and other information

What VALCYTE contains

The active substance is valganciclovir.

The other ingredients are:

VALCYTE 450 film-coated tablet:

Crospovidone, microcrystalline cellulose, povidone K-30, stearic acid powder (1 % w/w), Opadry Pink which consists of: hypromellose, macrogol, polysorbate 80, red iron oxide (E172), titanium dioxide (E171).

VALCYTE 50 mg/mL powder for oral solution:

Fumaric acid, mannitol *(5,78 g per bottle), povidone K30, saccharin sodium (0,03 g per bottle), tutti frutti flavour. **Quantity may vary*

What VALCYTE looks like and contents of the pack

VALCYTE 450 film-coated tablets: The tablets are pink, oval film-coated tablets marked “VGC” on one side and “450” on the other side. 60 film-coated tablets in a white plastic bottle with a child-resistant screw closure.

VALCYTE 50 mg/mL oral solution: The reconstituted powder is a colourless to brownish-yellow clear solution. Carton containing an amber glass bottle with child-resistant white opaque plastic screw-cap, a bottle adapter and a blister pack containing 2 oral dispensers. The oral dosing dispensers have 0.5 mL graduations (25 mg) to 10 mL (500 mg).

Holder of Certificate of Registration

Pharmaco Distribution (Pty) Ltd.

3 Sandown Valley Crescent,

South Tower, 1st Floor,

Sandton 2196,

South Africa.

Ethical assistance Line: +27 (0) 11 784 00 77

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VALCYTE 50 mg/mL oral solution: 43/20.2.8/0433