

Package leaflet: Information for the user

Cidofovir 75 mg/ml concentrate for solution for infusion

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects

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 or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness 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 Cidofovir is and what it is used for
2. What you need to know before you use Cidofovir
3. How to use Cidofovir
4. Possible side effects
5. How to store Cidofovir
6. Contents of the pack and other information

1. What Cidofovir is and what it is used for

Cidofovir is used to treat an eye infection called CMV retinitis in patients with AIDS (Acquired Immunodeficiency Syndrome). Cidofovir will not cure CMV retinitis but may improve your condition by delaying progression of the disease.

The safety and efficacy of cidofovir has not been demonstrated in diseases other than CMV retinitis in patients with AIDS.

Cidofovir must be administered by a healthcare professional (doctor or nurse) in a hospital setting.

What is CMV retinitis?

CMV retinitis is an eye infection caused by a virus named cytomegalovirus (CMV). CMV attacks the retina of the eye and may cause loss of vision, and eventually lead to blindness. Patients with AIDS are at high risk of developing CMV retinitis or other forms of CMV disease such as colitis (an inflammatory bowel disease). Treatment for CMV retinitis is necessary to reduce the potential for blindness.

Cidofovir is an antiviral medicine which blocks the replication of CMV by interfering with viral DNA production.

2. What you need to know before you use Cidofovir

Do not use cidofovir

- **If you are allergic** to cidofovir or any of the other ingredients of this medicine (listed in section 6).
- **If you have ever had kidney disease.**
- **If you cannot take the medicine probenecid** because of a serious allergy to probenecid or other sulfa-containing medicines (e.g. sulfamethoxazole).

If any of these apply to you, talk to your doctor. **You are not to be given cidofovir.**

Warnings and precautions

Talk to your doctor or pharmacist or nurse before using cidofovir.

- • **Kidney damage is the major side effect of cidofovir treatment.** Therefore, your doctor may need to monitor carefully, particularly if you already have kidney problems or are on haemodialysis.
- **If you have diabetes mellitus.** cidofovir should be used with caution in diabetic patients due to the potential increased risk of developing low pressure in the eye (*ocular hypotony*).

During treatment with cidofovir you should receive regular follow-up eye examinations for possible eye irritation, inflammation or swelling. **If you get pain, redness or itching of the eye or changes in your vision, tell your doctor promptly.**

Cidofovir caused reduced testes weight and low sperm count (*hypospermia*) in animals. Although not observed in human studies of cidofovir, such changes may occur in humans and cause infertility. **Men should practice barrier birth control methods during and for 3 months after treatment with cidofovir.**

Cidofovir is not used for the treatment of HIV infection. Cidofovir will not stop you passing HIV infection onto other people so **you should continue to take precautions to avoid infecting others.**

Children

Cidofovir has not been studied in children. Therefore, **this medicine should not be used in children.**

Other medicines and cidofovir

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription, as these may interact with cidofovir or probenecid.

It is very important to tell your doctor if you are receiving other medicines that may damage your kidneys.

These include:

- tenofovir containing medicines, used to treat HIV-1 infection and/or chronic hepatitis B infection aminoglycosides, pentamidine or vancomycin (for bacterial infections)
- amphotericin B (for fungal infection)
- foscarnet (for viral infection)
- adefovir (for HBV infection)

These medicines must be stopped **at least 7 days** before taking cidofovir.

Probenecid may interact with other medicines commonly used in the treatment of AIDS and AIDS-related illnesses, such as zidovudine (AZT). If you are taking zidovudine, you should discuss with your doctor whether to temporarily stop taking zidovudine or decrease the dose of zidovudine by 50% on days when cidofovir and probenecid are given.

The potential for interactions between cidofovir and anti-HIV protease inhibitors has not been studied.

Cidofovir with food and drink

Food should be taken before you are given cidofovir. Your doctor may instruct you to drink plenty of fluids before receiving cidofovir.

Pregnancy and breast-feeding

You should not be given cidofovir if you are pregnant. If you become pregnant while receiving this medication, you must inform your doctor immediately. Cidofovir has been shown to cause damage in unborn animals and should not be used during pregnancy unless the potential benefits justify the risks to the foetus.

Women of childbearing potential should use effective contraceptive measures while being treated with cidofovir and for six months following completion of treatment.

Men should use effective contraceptive measures and not father a child while being treated with cidofovir and for three months following completion of treatment.

You should not be given cidofovir if you are breast-feeding. It is not known whether cidofovir is passed on to the baby in human milk. Because many medicines are passed through to human milk, nursing mothers should stop cidofovir or stop breast-feeding if they continue to receive cidofovir.

In general, women with HIV should not breast-feed in order to avoid passing HIV to their infant through the milk.

Driving and using machines

Cidofovir may cause short-term side effects such as fatigue or weakness. If you drive or operate machinery, discuss this with your doctor to get advice about stopping these activities based upon your disease and your tolerance of the medicine.

Cidofovir 75 mg/ml concentrate for solution for infusion contains sodium

This medicine contains 2.5 mmol (or 57 mg) sodium per vial which should be taken into consideration if you are on a controlled sodium diet.

3. How to use Cidofovir

Cidofovir 75 mg/ml concentrate for solution for infusion **is given by intravenous infusion (a drip into a vein)**. It must **not** be administered by other methods including intraocular injection (direct injection into the eye) or topically (on the skin). Cidofovir must be given by a doctor or nurse with appropriate experience in treating people with AIDS.

The doctor or nurse will transfer the appropriate dose of cidofovir from the vial to an infusion bag containing 100 ml 0.9% (normal) saline solution. The entire volume of the bag will be infused into your vein at a constant rate over a period of 1 hour using a standard infusion pump. The recommended dose, frequency of use, or rate of infusion must not be exceeded. At the end of this leaflet, there is further information for healthcare professionals on how to administer cidofovir.

To lower the risk of kidney damage, probenecid tablets and intravenous fluids (saline solution) must be given on the day of each cidofovir (See sub-sections “How to take probenecid with cidofovir” and “How IV fluids are given before cidofovir” below.)

Dose in adults

The dose you will need is calculated based on your body weight.

Starting (induction) treatment

The recommended dose of cidofovir in patients with normal kidney function is 5 mg per kg of body weight given once weekly for two consecutive weeks.

Maintenance treatment

Beginning two weeks after completion of induction treatment, the recommended maintenance dose of cidofovir in patients with normal kidney function is 5 mg per kg of body weight given once every two weeks.

Dose adjustment

If you have kidney problems, cidofovir may not be appropriate treatment for you. Samples of your urine and/or blood will be taken before each infusion of cidofovir and used for testing kidney function. For patients with evidence of decreased kidney function, your cidofovir dose may be interrupted or stopped depending on your individual case.

If you use more cidofovir than you should

If you have accidentally been given more cidofovir than prescribed for you, tell your doctor immediately.

How to take probenecid with cidofovir

Probenecid tablets are given to lower the risk of kidney damage. You must take 3 doses of probenecid tablets orally on the same day as cidofovir as shown in the following table:

Time	Dose
3 hours before start of cidofovir	2 g probenecid

2 hours after end of cidofovir	1 g probenecid
8 hours after end of cidofovir	1 g probenecid
Total	4 g probenecid

Probenecid is only taken on the same day that cidofovir is given.

How IV fluids are given before cidofovir

Normal saline is given to lower the risk of kidney damage. You should receive a total of one litre of 0.9% (normal) saline solution intravenously (as a drip into a vein) before each cidofovir dose. The saline solution should be infused over a 1 hour period immediately before the cidofovir. If you can tolerate the additional fluid load, your doctor may administer a second litre of fluid. If administered, the second litre of saline should be given either at the start of the cidofovir or immediately afterwards, and infused over a 1 to 3 hour period. Your doctor may also tell you to drink plenty of fluids.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

These side effects usually disappear when treatment with cidofovir is stopped. **If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist immediately.**

The most common side effect observed with cidofovir is damage to the kidneys.

Very common side effects

(These can affect more than 1 user in 10)

low white blood cell counts, headache, nausea, vomiting, protein in the urine, increase in blood creatinine (a measure of kidney function), hair loss, rash, weakness/fatigue and fever.

Common side effects

(These can affect 1 to 10 users in 100)

inflammation of the eye, reduced pressure in the eyes, difficult or laboured breathing, shortness of breath, diarrhoea and chills.

Any pain, redness or itching of the eye or changes in your vision should be promptly reported to your doctor so that your treatment can be reviewed.

Additional reactions reported from post-marketing experience include kidney failure, damage to kidney tubule cells, inflammation of the pancreas and hearing impairment.

Possible side effects of taking probenecid

Very common side effects possibly related to probenecid

(These can affect more than 1 user in 10)

nausea, vomiting, rash and fever.

Common side effects possibly related to probenecid

(These can affect 1 to 10 users in 100)

headache, weakness/fatigue, chills and allergic reactions.

To reduce the risk of nausea and/or vomiting associated with taking probenecid, you should eat food before each dose. Your doctor might instruct you to take other medicines such as anti-emetics (anti sickness medicines), antihistamines and/or paracetamol to decrease the side effects of probenecid.

Probenecid may also cause other side effects including loss of appetite, sore gums, flushing, hair loss, dizziness, reduced red blood cell count and increased frequency of passing water (urinating). Allergic reactions, with skin inflammation, itching, hives and, rarely, severe allergic reactions, and serious skin

reaction have occurred. There have been reports of reduced white blood counts, liver toxicity, kidney toxicity and destruction of red blood cells. Reductions in blood cell and platelet counts have also occurred.

Therefore before giving you probenecid your doctor should consult the current prescribing information regarding the safety of probenecid. **You should also read the probenecid package leaflet.**

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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 to store Cidofovir

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label.

Do not store above 25°C. Do not refrigerate or freeze.

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

6. Contents of the pack and other information

What Cidofovir 75 mg/ml concentrate for solution for infusion contains

The active substance is cidofovir. Each ml contains 75 mg cidofovir anhydrous. Each vial contains 375 mg/5 ml cidofovir anhydrous.

The other ingredients are sodium hydroxide, hydrochloric acid, water for injections

What Cidofovir looks like and contents of the pack

Cidofovir is supplied as a sterile concentrate for solution for infusion in clear, glass vials containing 375 mg of the active ingredient, anhydrous cidofovir, formulated in 5 ml water for injections at a concentration of 75 mg/ml. The formulation is pH-adjusted with sodium hydroxide (and hydrochloric acid if needed) and contains no preservatives.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Tillomed Laboratories Limited

220 Butterfield

Great Marlings

Luton, LU2 8DL

United Kingdom

Manufacturer¹:

MIAS Pharma Limited

Suite 2, Stafford House,

Strand Road, Portmarnock,

Co. Dublin

Ireland

Emcure Pharma UK Limited

Basepoint Business Centre

110 Butterfield

Great Marlings Luton
LU2 8DL
United Kingdom

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

Cidofovir vials should be inspected visually prior to use. If visible particles or discolouration are observed, the vial should not be used.

Adequate precautions including the use of appropriate safety equipment are recommended for the preparation, administration and disposal of cidofovir. The preparation of cidofovir diluted solution should be done in a laminar flow biological safety cabinet. Personnel preparing the solution should wear surgical gloves, safety glasses and a closed front surgical-type gown with knit cuffs. If cidofovir contacts the skin, wash membranes and flush thoroughly with water.

The appropriate dose of cidofovir should be transferred from the vial to an infusion bag containing 100 ml 0.9% (normal) saline solution. The entire volume of the bag should be infused into the patient's vein at a constant rate over a period of 1 hour using a standard infusion pump. The recommended dose, frequency of use, or rate of infusion must not be exceeded.

The chemical stability of cidofovir mixed in saline solution has been demonstrated in glass bottles, in infusion bags composed of either polyvinyl chloride (PVC) composition or ethylene/propylene copolymer, and in PVC based vented IV administration sets. Other types of IV set tubing and infusion bags have not been studied.

Compatibility of cidofovir with Ringer's Solution, Lactated Ringer's Solution or bacteriostatic infusion fluids has not been evaluated.

From a microbiological point of view, the product must be used immediately.

Chemical and physical in-use stability has been demonstrated for up to 24 hours at 2 - 8°C when dilution is performed under controlled and validated aseptic conditions. Storage beyond 24 hours or freezing is not recommended. Refrigerated infusion bags should be allowed to warm to room temperature prior to use.

Cidofovir is supplied in single-use vials. Partially used vials must be discarded

¹Only the actual manufacturer is listed on the leaflet