

Package leaflet: Information for the user
Cymevene® 500 mg powder for concentrate for solution for infusion
ganciclovir

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, 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 Cymevene is and what it is used for
2. What you need to know before you use Cymevene
3. How to use Cymevene
4. Possible side effects
5. How to store Cymevene
6. Contents of the pack and other information

1. What Cymevene is and what it is used for

What Cymevene is

Cymevene contains the active substance ganciclovir. This belongs to a group called anti-viral medicines.

What Cymevene is used for

Cymevene is used to treat diseases caused by a virus called cytomegalovirus (CMV) in patients who have a weak immune system. It is also used to prevent CMV infection after an organ transplant or during chemotherapy.

It is used in adults and adolescents 12 years and older.

- The virus can affect any part of the body. This includes the retina at the back of the eye – this means the virus can cause problems with eye sight.
- The virus can affect anyone, but it is a particular problem in people with a weak immune system. In these people the CMV virus can lead to a serious disease. A weak immune system may be caused by other diseases (such as AIDS) or by medicines (such as chemotherapy or immunosuppressants).

2. What you need to know before you use Cymevene

Do not use Cymevene if:

- you are allergic to ganciclovir, valganciclovir or any of the other ingredients of this medicine (listed in section 6)
- you are breast-feeding (see Breast-feeding subsection).

Do not use Cymevene if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before using Cymevene.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Cymevene if:

- you are allergic to aciclovir, valaciclovir, penciclovir or famciclovir – these are other medicines used for viral infections
- you have low white blood cell, red blood cell or platelet counts – your doctor will do blood tests before you start and during your treatment
- you have had problems with your blood cell counts caused by medicines in the past
- you have kidney problems – your doctor will need to give you a lower dose and check your blood cell counts more often during treatment
- you are having radiotherapy.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before using Cymevene.

Look out for side effects

Cymevene can cause some serious side effects that you need to tell your doctor about straight away. Look out for these while you are taking Cymevene – your doctor may tell you to stop taking Cymevene and you may need urgent medical treatment:

- low white blood cell counts – with signs of infection such as sore throat, mouth ulcers or a fever
- low red blood cell counts – signs include feeling short of breath or tired, palpitations or pale skin
- low level of platelets – signs include bleeding or bruising more easily than usual, blood in urine or stools or bleeding from gums, the bleeding could be severe
- allergic reaction – the signs may include red itchy skin, swelling of the throat, face, lips or mouth, difficulty swallowing or breathing.

Tell your doctor straight away if you notice any of the serious side effects above. See Serious side effects at the top of section 4 for more information.

Tests and checks

While you are using Cymevene your doctor will do regular blood tests. This is to check the dose you are having is right for you. For the first 2 weeks these blood tests will be done often. After that the tests will be done less often.

Children and adolescents

There is limited information on how safe or effective Cymevene is in children under 12 years.

Other medicines and Cymevene

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist if you are taking any of the following medicines:

- imipenem/cilastatin – used for bacterial infections,
- pentamidine – used for parasite or lung infections,
- flucytosine, amphotericin B – used for fungal infections,
- trimethoprim, trimethoprim/sulfamethoxazole, dapsone – used for bacterial infections,
- probenecid – used for gout,
- mycophenolate mofetil – used after an organ transplant,
- vincristine, vinblastine, doxorubicin – used for cancer,
- hydroxyurea – used for a problem called polycythemia, sickle cell disease and cancer,
- didanosine, stavudine, zidovudine or any other medicines used for HIV.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before using Cymevene.

Pregnancy, breast-feeding and fertility

Pregnancy

Cymevene should not be used by pregnant women unless the benefits to the mother outweigh the possible risks to the unborn baby.

If you are pregnant or think you might be pregnant, do not use this medicine unless your doctor tells you to. This is because Cymevene may harm the unborn baby.

Contraception

You should not become pregnant while using this medicine. This is because it may affect the unborn baby.

Women

If you are a woman who could get pregnant – use contraception while you are using Cymevene.

Also do this for at least 30 days after Cymevene has been stopped.

Men

If you are a man whose female partner could get pregnant – use a barrier method of contraception (such as condoms) while you are using Cymevene. Also do this for at least 90 days after Cymevene has been stopped.

If you or your partner becomes pregnant while using Cymevene, talk to your doctor straight away.

Breast-feeding

Do not use Cymevene if you are breast-feeding. If your doctor wants you to start using Cymevene you must stop breast-feeding before you start using the medicine. This is because Cymevene may pass into breast milk.

Fertility

Cymevene may affect fertility. Cymevene may temporarily or permanently stop men from producing sperm. If you are planning to have a baby, talk to your doctor or pharmacist before using Cymevene.

Driving and using machines

You may feel sleepy, dizzy, confused or shaky, or you may lose your balance or have fits while using Cymevene. If this happens, do not drive or use any tools or machines.

Cymevene contains sodium

Cymevene contains 43 mg of sodium in each 500 mg dose. This should be taken into consideration by patients on a controlled sodium diet.

3. How to use Cymevene

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

Using this medicine

Cymevene will be given to you by a doctor or nurse. It will be given through a tube into your vein. This is called an intravenous infusion and it will usually take one hour.

The dose of Cymevene varies from one patient to another. Your doctor will work out how much you need. It will depend on:

- your weight
- your age
- how well your kidneys are working
- your blood counts
- what you are using the medicine for.

How often you will have Cymevene and how long you keep using it will also vary.

- You will usually start by having one or two infusions every day.
- If you have two infusions a day, this will continue for up to 21 days.
- After that the doctor may prescribe the infusion once a day.

People with kidney or blood problems

If you have any kidney or blood problems your doctor might suggest a smaller dose of Cymevene and check your blood cell counts more often during treatment.

If you use more Cymevene than you should

If you think you have been given too much Cymevene talk to your doctor or go to hospital straight away. You may get the following symptoms if you have too much:

- stomach pain, diarrhoea or being sick
- shaking or fits
- blood in your urine
- kidney or liver problems
- changes in blood cell counts.

If you stop using Cymevene

Do not stop using Cymevene without talking to your doctor.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Serious side effects

Tell your doctor straight away if you notice any of the following serious side effects – your doctor may tell you to stop taking Cymevene and you may need urgent medical treatment:

Very common: may affect more than 1 in 10 people

- low white blood cell counts – with signs of infection such as sore throat, mouth ulcers or a fever
- low red blood cell counts – signs include feeling short of breath or tired, palpitations or pale skin.

Common: may affect up to 1 in 10 people

- low level of platelets – signs include bleeding or bruising more easily than usual, blood in urine or stools or bleeding from gums, the bleeding could be severe.

Uncommon: may affect up to 1 in 100 people

- allergic reaction – the signs may include, red itchy skin, swelling of the throat, face, lips or mouth, difficulty swallowing or breathing.

Tell your doctor straight away if you notice any of the side effects above.

Other side effects

Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people

- diarrhoea
- feeling short of breath.

Common: may affect up to 1 in 10 people

- headache
- trouble sleeping
- fever, chills or night sweats
- feeling tired, dizzy, weak or generally unwell
- feeling depressed, anxious, confused or having abnormal thoughts
- pain
- ear pain
- hands or feet feeling weak or numb, which may affect your balance
- muscle pain or spasms
- back, chest or joint pain
- sight problems or eye pain
- eczema, skin problems, itching
- changes to your sense of touch, tingling, tickling, pricking or burning feeling
- fits
- cough
- feeling or being sick
- problems swallowing
- changes to the way things taste
- loss of appetite, anorexia or weight loss
- stomach pain, constipation, wind, indigestion
- urine infection – signs include fever, passing urine more often, pain when passing urine
- thrush and oral thrush
- bacterial skin infection – signs include red, painful or swollen skin
- blood poisoning (sepsis)
- changes in blood cell counts
- liver and kidney problems shown in tests
- a skin reaction where the medicine was injected – such as inflammation, pain and swelling.

Uncommon: may affect up to 1 in 100 people

- hair loss
- deafness
- mouth ulcers
- hives, dry skin

- feeling agitated or nervous
- eye infection (conjunctivitis)
- abnormal thoughts or feelings, losing contact with reality
- blood in urine
- tremor, shaking
- swollen stomach
- uneven heartbeat
- low blood pressure, which may make you feel dizzy or faint
- serious kidney problems shown in tests
- low red blood cell counts shown in tests
- infertility in men – see ‘Fertility’ section
- pancreatitis – signs are severe stomach pain which spreads into your back.

Rare: may affect up to 1 in 1,000 people

- rash
- hallucinations – hearing or seeing things that are not real.

Side effects in children and adolescents

The following side effects are more likely in children:

- fever
- stomach pain
- low white blood cell counts.

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 directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

5. How to store Cymevene

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

Powder: Does not require any special storage conditions. It should not be used after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

After reconstitution:

Chemical and physical in-use stability has been demonstrated for the reconstituted product for 12 hours at 25°C after dissolving with water for injections. Do not refrigerate or freeze.

From a microbiological point of view, the reconstituted solution should be used immediately.

If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

After dilution in infusion solutions (sodium chloride 0.9%, dextrose 5%, Ringer's or lactated Ringer's solution for injection) :

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 – 8°C (do not freeze).

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

6. Contents of the pack and other information

What Cymevene contains

- The active substance is ganciclovir. Each glass vial contains 500 mg ganciclovir as ganciclovir sodium. Following reconstitution of the powder, 1ml solution contains 50 mg ganciclovir.
- The other ingredients are sodium hydroxide and hydrochloric acid.

What Cymevene looks like and contents of the pack

Cymevene is a white to off white powder for concentrate for solution for infusion, supplied in a single-dose glass vial, with a rubber stopper and aluminium closure with flip-off cap. Reconstituted solutions of Cymevene range in colour from colourless to light yellow.

Vials of Cymevene are supplied in packs of 1 or 5. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Roche Products Limited
6 Falcon Way
Shire Park
Welwyn Garden City, AL7 1TW
United Kingdom.

Manufacturer

Roche Pharma AG
Emil-Barell-Str. 1
D-79639 Grenzach-Wyhlen
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Cymevene: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Lithuania, Luxembourg, The Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Spain, Sweden, United Kingdom.

Cymeven i.v.: Germany

Cymevan: France

Citovirax: Italy

This leaflet was last revised in July 2016.

Other sources of information

Detailed information on this medicinal product is available on the Health Products Regulatory Agency (HPRA) website : <http://www.hpra.ie>

The following information is intended for healthcare professionals only:

INSTRUCTIONS FOR USE AND HANDLING

Please refer to the Summary of Product Characteristics for full prescribing information.

Method of administration

Caution:

Ganciclovir must be administered by intravenous infusion over 1 hour at a concentration not exceeding 10 mg/mL. Do not administer by rapid or bolus intravenous injection because the resulting excessive plasma levels may increase the toxicity of ganciclovir.

Do not administer by intramuscular or subcutaneous injection because this may result in severe tissue irritation due to the high pH (~11) of ganciclovir solutions.

The recommended dosage, frequency and infusion rates should not be exceeded.

Cymevene is a powder for solution for infusion. After reconstitution Cymevene is a colourless to slightly yellowish solution, practically free from visible particles.

The infusion should be given into a vein with adequate blood flow, preferably via a plastic cannula.

Caution should be exercised in the handling of Cymevene.

Since Cymevene is considered a potential teratogen and carcinogen in humans, caution should be observed in its handling. Avoid inhalation or direct contact of the powder contained in the vials or direct contact of the reconstituted solution with the skin or mucous membranes. Cymevene solutions are alkaline (pH ~11). If such contact occurs, wash thoroughly with soap and water, rinse eyes thoroughly with plain water.

Preparation of the reconstituted concentrate

Aseptic technique should be used throughout to reconstitute lyophilised Cymevene.

1. The flip-off cap should be removed to expose the central portions of the rubber stopper. Draw 10 mL of water for injection into a syringe, then slowly inject through the centre of the rubber stopper into the vial pointing the needle towards the wall of the vial. **Do not use bacteriostatic water for injection containing parabens (para-hydroxybenzoates), since these are incompatible with Cymevene.**

2. The vial should be gently swirled in order to ensure complete wetting of the product.

3. The vial should be gently rotated/ swirled for some minutes to obtain a clear reconstituted solution.
4. The reconstituted solution should be checked carefully to ensure that the product is in solution and practically free from visible particles prior to dilution with compatible solvent. Reconstituted solutions of Cymevene range in colour from colourless to light yellow.

Preparation of final diluted solution for infusion

Based on patient weight the appropriate volume should be removed with a syringe from the vial and further diluted into an appropriate infusion solution. Add a volume of 100 mL of diluent to the reconstituted solution. Infusion concentrations greater than 10mg/mL are not recommended. Sodium chloride, dextrose 5%, Ringer's or lactated Ringer's solutions are determined chemically or physically compatible with Cymevene.

Cymevene should not be mixed with other intravenous products.

The diluted solution should then be infused intravenously over 1 hour as directed in section 4.2. Do not administer by intramuscular or subcutaneous injection because this may result in severe tissue irritation due to the high pH (~11) of ganciclovir solution.

Disposal

For single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.