(GSK logo)

Package leaflet: Information for the user

Zovirax® IV for Infusion 250 mg
Powder for solution for infusion
aciclovir

Read all of this leaflet carefully before you start having 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.

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 Zovirax is and what it is used for

Zovirax IV for Infusion 250 mg Powder for solution for infusion (called 'Zovirax' in this leaflet) contains a medicine called aciclovir. This belongs to a group of medicines called antivirals. It works by stopping the growth of viruses.

Zovirax IV can be used to:
- treat recurring chicken-pox and shingles in people whose immune system works well
- treat severe first cases of genital herpes in people whose immune system works well
- treat primary and recurring chickenpox and shingles in people whose immune systems work less well, which means their bodies are less able to fight infections
- treat and stop cold sores and genital herpes in people whose immune systems work less well, which means their bodies are less able to fight infections
- prevent herpes simplex infections in people whose immune systems work less well, which means their bodies are less able to fight infections
- treat inflammation of the brain. This can rarely be caused by the virus responsible for cold sore infection and genital herpes.

2 What you need to know before you have Zovirax

Do not have Zovirax if:
- you are allergic (hypersensitive) to aciclovir or valaciclovir or any of the other ingredients (listed in Section 6).

Do not have Zovirax if the above applies to you. If you are not sure, check with your doctor or pharmacist before having Zovirax.

Warnings and precautions
Check with your doctor, pharmacist or nurse before having Zovirax if:
- you have kidney problems
- you are over 65 years of age.
- your immune system is weak

If you are not sure if the above apply to you, check with your doctor, pharmacist or nurse before having Zovirax.

Check with your doctor or pharmacist before your child has Zovirax if they are newborn or under 3 months of age.

Other medicines and Zovirax
Tell your doctor, pharmacist or nurse if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

In particular tell your doctor, pharmacist or nurse if you are taking any of the following medicines:
- probenecid, used to treat gout

- cimetidine, used to treat stomach ulcers
- tacrolimus, cyclosporin or mycophenolate mofetil, used to stop your body rejecting transplanted organs.

Zovirax with food and drink

Food and drink should not affect the absorption of your medicine.

Pregnancy, breast-feeding and fertility

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

The ingredients in Zovirax can pass into breast milk. If you are breast-feeding, you must check with your doctor before you take Zovirax.

Driving and using machines
Some side effects such as feeling drowsy or sleepy may impair your ability to concentrate and react. Make sure you are not affected before you drive or operate machinery

Zovirax Contains
This medicine contains 28.03 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.4% of the recommended maximum daily dietary intake of sodium for an adult. To be taken into consideration for patients on a controlled sodium diet.

3 How to take Zovirax

How your medicine is given
You will never be expected to give yourself this medicine. It will always be given to you by a person who is trained to do so.

Before the medicine is given to you it will be diluted.

Zovirax will be given to you as a continuous infusion into your vein. This is where the drug is slowly given to you over a period of time.

The dose you will be given, the frequency and the duration of the dose will depend on:
- the type of infection you have
- your weight and body size
- your age.

Your doctor may adjust the dose of Zovirax if:
- you have kidney problems.

People over 65 years of age or with kidney problems:
It is very important while you are taking Zovirax that you drink water regularly during the day. This will help to reduce side effects that can affect the kidney or nervous system. Your doctor will closely monitor you for signs of these. Nervous system side effects might include feeling confused or agitated, or feeling unusually sleepy or drowsy.

Talk to your doctor before having Zovirax if any of the above apply.

If you are given more Zovirax than you should
If you think you have been given too much Zovirax, talk to your doctor or nurse straight away.

If you have been given more Zovirax than you should you may:
- feel confused or agitated
- have hallucinations (seeing or hearing things that aren't there)
- have fits
- become unconscious (coma).

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:

Allergic reactions (may affect up to 1 in 10,000 people)
If you have an allergic reaction, **stop taking Zovirax and see a doctor straight away**. The signs may include:
- bumpy rash, itching or hives on your skin
- swelling of your face, lips, tongue or other parts of your body (angioedema)
- shortness of breath, wheezing or trouble breathing
- unexplained fever (high temperature) and feeling faint, especially when standing up

Other side effects include:

Common (may affect up to 1 in 10 people)
- feeling or being sick
- itchy, bumpy, hive-like rash
- skin reaction after exposure to light (photosensitivity)
- itching
- swelling, redness and tenderness at the site of infusion
- increases in liver related enzymes which may be detected through a blood test
- increases in blood urea and creatinine which may be detected through a blood test

Uncommon (may affect up to 1 in 100 people)
- nosebleeds and bruising more easily than usual as a result of a decrease in blood platelets.
- fatigue, decreased energy, weakness, shortness of breath, light-headedness, palpitations, looking pale (anaemia)
- a decrease in the number of white blood cells found in blood (leukopaenia). This may leave a patient more prone to infection

Very rare (may affect up to 1 in 10,000 people)
- headache and feeling dizzy
- diarrhoea or stomach pains
- feeling tired
- fever
- inflammation at the injection site
- feeling agitated or confused
- shaking or tremors
- hallucinations (seeing or hearing things that aren't there)
- fits (seizures)
- feeling unusually sleepy or drowsy
- unsteadiness when walking and lack of coordination (ataxia)
- difficulty speaking or hoarseness (dysarthria)
- inability to think or judge clearly or concentrate
- unconsciousness (coma)
- difficulty breathing
- disturbances of behaviour and speech and bodily movements
- inflammation of the liver (hepatitis)
- yellowing of your skin and whites of your eyes (jaundice)
- kidney problems where you pass little or no urine
- pain in your lower back, the kidney area of your back or just above your hip (renal pain).
- swelling of your face, lips, tongue or other parts of your body
- damage or malfunction of the brain (encephalopathy) which is evident by an altered mental state

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance website www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Zovirax

- Keep out of the sight and reach of children.
- Do not store above 25°C.
- Do not use Zovirax after the expiry date which is stated on the carton. The expiry date (EXP:) refers to the last day of that month.
- Prepare immediately before use.
- Do not throw away any medicines. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. This will help protect the environment.

6 Contents of the pack and other information

What Zovirax IV for Infusion 250 mg Powder for solution for infusion contains

- The active substance is aciclovir. Each vial contains 250 mg of aciclovir as the sodium salt, which is dissolved in sterile water or sterile sodium chloride solution to make the injection.
- The other ingredient is sodium hydroxide (28.03 mg of sodium in each vial).

What Zovirax looks like and contents of the pack

Zovirax IV for Infusion 250 mg Powder for solution for infusion is supplied in glass vials, containing a white to off-white powder and comes in a box containing 5 vials.

Marketing authorisation holder and manufacturer

Marketing authorisation holder

GlaxoSmithKline (Ireland) Ltd., 12 Riverwalk, Citywest Business Campus, Dublin 24, Ireland

Manufacturer

GlaxoSmithKline Manufacturing S.p.A., Strada Provinciale Asolana 90, 43056 San Polo di Torrile, Parma, Italy

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GSK (logo)

Zovirax® IV for Infusion 250 mg, Powder for solution for infusion
aciclovir

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

DOSAGE AND ADMINISTRATION INFORMATION ONLY
Please refer to the Summary of Product Characteristics (SPC) for complete prescribing information.

Qualitative and Quantitative Composition

Each vial contains 250 mg aciclovir (as the sodium salt).
The quantity after reconstitution is 25 mg aciclovir per mL.
Each vial contains 28.03 mg of sodium.
The quantity of sodium after reconstitution in 10 mL of water for injection is approximately 2.789 mg/mL.
The quantity of sodium after reconstitution in 10 mL of NaCl (0.9 % w/v) is approximately 6.403 mg/mL.

For a full list of excipients see section 6.1.

Pharmaceutical Form

Powder for solution for infusion.
A white to off white freeze-dried sterile powder.

Therapeutic indications

Zovirax IV is indicated for:

Immunocompetent Patients	Immunocompromised Patients
Severe initial genital herpes	Herpes simplex infection
Recurrent varicella zoster virus infection	Primary and recurrent varicella zoster infection
	Prophylaxis of herpes simplex infection
Herpes simplex encephalitis	Herpes simplex encephalitis

Posology and method of administration

The required dose of Zovirax IV should be administered by slow intravenous infusion over 1 hour.

A course of treatment with Zovirax IV usually lasts 5 days, but this may be adjusted according to the patient's condition and response to therapy. Treatment for herpes encephalitis usually lasts 10 days. Treatment for neonatal herpes usually lasts 14 days for mucocutaneous (skin-eye-mouth) infections and 21 days for dissemination or central nervous system disease.

The duration of prophylactic administration of Zovirax IV is determined by the duration of the period at risk.

Table 1: Dosage for IV aciclovir in patients with normal renal function

Age group	Indication	Dosage
Adults and adolescents (≥12 years)	Immunocompetent and immunocompromised patients with *herpes simplex* (except herpes encephalitis) or immunocompetent patients with *varicella zoster*	5 mg/kg body weight every 8 hours

	Immunocompromised patients with *varicella zoster* infections or immunocompetent and immunocompromised patients with herpes encephalitis	10 mg/kg body weight every 8 hours
Infants and children (≥ 3 months to <12 years)	Immunocompetent and immunocompromised patients with *herpes simplex* (except herpes encephalitis) or immunocompetent patients with *varicella zoster*	10 mg/kg body weight every 8 hours
	Immunocompromised patients with *varicella zoster* infections or immunocompetent and immunocompromised patients with herpes encephalitis	20 mg/kg body weight every 8 hours
Neonates (<3 months)	Patients with known or suspected neonatal herpes (disseminated and CNS disease)	20 mg/kg body weight IV every 8 hours for 21 days
	Patients with known or suspected neonatal herpes limited to the skin and mucous membranes	20 mg/kg body weight IV every 8 hours for 14 days

Patients with impaired renal function require an appropriately modified dose, according to the degree of impairment (see Renal impairment)

In obese patients dosed with intravenous aciclovir based on their actual body weight, higher plasma concentrations may be obtained (see 5.2 Pharmacokinetic properties). Consideration should therefore be given to dosage reduction in obese patients and especially in those with renal impairment or the elderly.

Dosage in the elderly:
The possibility of renal impairment in the elderly must be considered and the dosage should be adjusted accordingly (see Renal impairment). Adequate hydration should be maintained.

Renal impairment:
Caution is advised when administering aciclovir IV for infusion to patients with impaired renal function. Adequate hydration should be maintained.

Dosage adjustment for patients with renal impairment is based on creatinine clearance, in units of mL/min for adults and adolescents and in units of mL/min/1.73m^2 for infants and children.

The following adjustments in dosage are recommended:

Table 2: Dosage adjustments for IV aciclovir in **adults and adolescents** 12 years or older with renal impairment for treatment of herpes simplex or varicella zoster virus infections

Creatinine Clearance	Dosage for herpes simplex infection (immunocompetent and immunocompromised patients) or varicella zoster (immunocompetent patients)	Dosage for herpes encephalitis (immunocompetent and immunocompromised patients) or varicella zoster (immunocompromised patients)
25 to 50 mL/min	5 mg/kg body weight given every 12 hours.	10 mg/kg body weight given every 12 hours.
10 to 25 mL/min	5 mg/kg body weight given every 24 hours.	10 mg/kg body weight given every 24 hours.
0 (anuric) to 10 mL/min	2.5 mg/kg body weight given every 24 hours.	5 mg/kg body weight given every 24 hours.

Patients on haemodialysis	2.5 mg/kg body weight given every 24 hours after dialysis.	5 mg/kg body weight given every 24 hours after dialysis.

Table 3: Dosage adjustments for IV aciclovir in **neonates, infants and children** <12 years with renal impairment for treatment of herpes simplex or varicella zoster virus infections

Creatinine Clearance	Dosage for herpes simplex infection (immunocompetent and immunocompromised patients) or varicella zoster (immunocompetent patients)	Dosage for herpes encephalitis (immunocompetent and immunocompromised patients) or varicella zoster (immunocompromised patients)
25 to 50 mL/min/1.73m^2	10 mg/kg body weight given every 12 hours.	20 mg/kg body weight given every 12 hours
10 to 25 mL/min/1.73m^2	5 mg/kg body weight given every 12 hours.	10 mg/kg body weight given every 12 hours
0 (anuric) to 10 mL/min/1.73m^2	2.5 mg/kg body weight given twice a day.	5 mg/kg body weight given every 12 hours
Patients on haemodialysis	2.5 mg/kg body weight given twice a day after dialysis.	5 mg/kg body weight given every 12 hours

Contraindications

Zovirax IV is contraindicated in patients known to be previously hypersensitive to aciclovir or valaciclovir or to any of the excipients listed in *List of excipients*.

Warnings and precautions

Use in patients with renal impairment and in elderly patients: Aciclovir is eliminated by renal clearance, therefore the dose must be adjusted in patients with renal impairment. Elderly patients are likely to have reduced renal function and therefore the need for dose adjustment must be considered in this group of patients. Both elderly patients and patients with renal impairment are at increased risk of developing neurological side effects and should be closely monitored for evidence of these effects. In the reported cases, these reactions were generally reversible on discontinuation of treatment.

Prolonged or repeated courses of aciclovir in severely immune-compromised individuals may result in the selection of virus strains with reduced sensitivity, which may not respond to continued aciclovir treatment (see section 5.1).

In patients receiving aciclovir IV for infusion at higher doses (e.g. for herpes encephalitis), specific care regarding renal function should be taken, particularly when patients are dehydrated or have any renal impairment.

Reconstituted Zovirax IV has a pH of approximately 11 and should not be administered by mouth.

Product contains sodium (28.03mg)

Other warnings and precautions

The labels shall contain the following statements:

For intravenous infusion only
For single use only
Keep this medicine out of the sight and reach of children
Discard if, before or during infusion, turbidity or crystallisation occurs
Do not store above 25°C
Prepare immediately prior to use
Any portions of the contents remaining after use should be discarded

Interaction with other medicinal products and other forms of interaction

No clinically significant interactions have been identified.

Aciclovir is eliminated primarily unchanged in the urine via active renal tubular secretion. Any drugs administered concurrently that compete with this mechanism may increase aciclovir plasma concentrations. **Probenecid** and **cimetidine** increase the AUC of aciclovir by this mechanism and reduce aciclovir renal clearance. Similarly increases in plasma AUCs of aciclovir and of the inactive metabolite of **mycophenolate mofetil**, an immunosuppressant agent used in transplant patients, have been shown when the drugs are coadministered. However no dosage adjustment is necessary because of the wide therapeutic index of aciclovir.

In patients receiving IV aciclovir, caution is required during concurrent administration with drugs which compete with aciclovir for elimination, because of the potential for increased plasma levels of one or both drugs or their metabolites. Increases in plasma AUCs of aciclovir and of the inactive metabolite of mycophenolate mofetil, an immunosuppressant agent used in transplant patients have been shown when the drugs are coadministered.

Care is also required (with monitoring for changes in renal function) if administering intravenous Zovirax with drugs which affect other aspects of renal physiology (e.g. **ciclosporin, tacrolimus**).

Overdose

Symptoms and Signs
Overdosage of intravenenous aciclovir has resulted in elevations of serum creatinine, blood urea nitrogen and subsequent renal failure. Neurological effects including confusion, hallucinations, agitation, seizures and coma have been described in association with overdosage.

Treatment
Patients should be observed closely for signs of toxicity. Haemodialysis significantly enhances the removal of aciclovir from the blood and may, therefore, be considered an option in the management of overdose of this drug.

List of excipients

Sodium hydroxide (used to adjust pH)

Incompatibilities

This medicinal product should not be mixed with other medicinal products except those mentioned in ***Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product***.

Shelf life

5 years

From a microbiological point of view, the reconstituted 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 12 hours at room temperature, unless reconstitution has taken place in controlled and validated aseptic conditions.

Following further dilution to give a concentration not greater than 0.5% w/v of aciclovir, Zovirax is known to be compatible and stable for up to 12 hours (in the named infusion fluids listed in section 6.6) when stored at room temperature (15ºC to 25ºC).

The reconstituted or diluted solutions should not be refrigerated.

Special precautions for storage

Do not store above 25°C.

For in-use storage conditions, see ***Shelf life***

Nature and contents of container

Clear colourless, Type I glass bottle (Ph. Eur.) with bromobutyl rubber stoppers or with a bromobutyl rubber stopper with a fluorinated polymer coating and aluminium collars with a polypropylene flip-top cover.

Pack size: 5 vials.

Special precautions for disposal and other handling

Prepare immediately prior to use. Discard any unused solution. Any unused product or waste materials should be disposed of in accordance with local requirements.

For intravenous infusion only.

For single use only.

Reconstitution: Each vial (containing the equivalent of 250 mg aciclovir) should be reconstituted by the addition of 10 mL of either Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9% w/v). This provides a solution containing 25 mg aciclovir per mL.

From the calculated dose, determine the appropriate number of vials to be used. To reconstitute each vial, add the recommended volume of Infusion fluid and shake gently until the contents of the vial have dissolved completely.

Zovirax IV for Infusion contains no antimicrobial preservative. Reconstitution and dilution should therefore be carried out either under full aseptic conditions or immediately before use and any unused solution should be discarded.

The reconstituted or diluted solutions should not be refrigerated. Should visible turbidity or crystallisation appear in the solution, before or during the infusion, the mixture should be discarded.

Administration: The required dose of Zovirax IV for infusion should be administered by slow intravenous infusion over a one-hour period. After reconstitution Zovirax IV for Infusion may be administered by a controlled-rate infusion pump. Alternately, the reconstituted solution may be further diluted to give an aciclovir concentration of not greater than 5 mg/mL (0.5% w/v) for administration by infusion.

Add the required volume of reconstituted solution to the chosen infusion solution, as recommended below, and shake well to ensure adequate mixing occurs. For children and neonates, where it is advisable to keep the volume of infusion fluid to a minimum it is recommended that dilution is on the basis of 4 mL reconstituted solution (100 mg aciclovir) added to 20 mL of infusion fluid.

For adults, it is recommended that infusion bags containing 100 mL of infusion fluid are used, even when this would give an aciclovir concentration substantially below 0.5% w/v. Thus one 100 mL infusion bag may be used for any dose between 250 mg and 500 mg aciclovir (10 and 20 mL of reconstituted solution), but a second bag must be used for doses between 500 and 1000 mg. Zovirax when diluted in accordance with the above schedules to give a concentration not greater than 0.5% w/v of aciclovir, is known to be compatible with the following infusion fluids and stable for up to 12 hours at room temperature (15ºC to 25°C).

Sodium Chloride Intravenous Infusion BP (0.45% and 0.9% w/v).
Sodium Chloride (0.18% w/v) and Dextrose (4% w/v) Intravenous Infusion BP.
Sodium Chloride (0.45% w/v) and Dextrose (2.5% w/v) Intravenous Infusion BP.
Compound Sodium Lactate Intravenous Infusion BP (Hartmann's solution).

Marketing Authorisation Holder

GlaxoSmithKline (Ireland) Ltd., 12 Riverwalk, Citywest Business Campus, Dublin 24, Ireland

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