Package leaflet: Information for the user
Aciclovir 25 mg/ml Concentrate for solution for infusion
Aciclovir

The name of your medicine is Aciclovir 25 mg/ml Concentrate for solution for infusion, which will be referred to as Aciclovir throughout this leaflet.

Read all of this leaflet carefully before you start taking 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 Aciclovir is and what it is used for

Aciclovir contains a medicine called aciclovir,This belongs to a group of medicines called antivirals. It works by killing or stopping the growth of viruses.
Aciclovir can be used to:

- treat severe cases of genital herpes
- treat chickenpox
- 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.
- treat serious virus infections in children up to 3 months of age. This can rarely be caused by the virus responsible for cold sore infection and genital herpes.
- 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 use Aciclovir
Do not use Aciclovir :

If you are allergic to aciclovir or valaciclovir or any of the other ingredients of this medicine(listed in Section 6).

Do not take Aciclovir if the above applies to you. If you are not sure, talk to your doctor or pharmacist or nurse before taking Aciclovir.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Aciclovir if:

- you have kidney problems
- you are over 65 years of age
- you are suffering from dehydration

If you are not sure if the above apply to you, talk to your doctor, pharmacist or nurse before taking Aciclovir.
It is important that you drink plenty of water while taking Aciclovir.

Other medicines and Aciclovir

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines.
In particular tell your doctor or pharmacist if you are taking any of the following medicines:

- probenecid, used to treat gout
- cimetidine, used to treat stomach ulcers
- tracrolimus, ciclosporin or mycophenolate mofetil, used to stop your body rejecting transplanted organs.

Pregnancy and 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.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.

Aciclovir Contains Sodium
Aciclovir contains 0.116 mmol (or 2.67 mg) sodium per ml, 1.16 mmol (or 26.7 mg) sodium per 10 ml vial & 2.32 mmol (or 53.4 mg) sodium per 20 ml vial to be taken into consideration by patients on a controlled sodium diet.

3. How to use Aciclovir
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.
Aciclovir 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 duration of the dose will depend on:

- the type of infection you have
- your weight
- your age.

Your doctor may adjust the dose of Aciclovir if:

- you have kidney problems. If you have kidney problems, it is important you receive plenty of fluids while you are being treated with Aciclovir.

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

If you are given too much Aciclovir

If you think you have been given too much Aciclovir, talk to your doctor or nurse straight away.
If you have been given too much Aciclovir 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 Aciclovir and see a doctor straight away**. The signs may include:

- rash, itching or hives on your skin
- swelling of your face, lips, tongue or other parts of your body
- shortness of breath, wheezing or trouble breathing
- unexplained fever (high temperature) and feeling faint, especially when standing up.

Aciclovir 25 mg/ml Concentrate 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.

Excipients with known effect:
Sodium Hydroxide

Pharmaceutical form
Concentrate for solution for infusion

Therapeutic Indications
Aciclovir is indicated for the treatment of Herpes simplex infections in immunocompromised patients and severe initial genital herpes in the non-immunocompromised.
Aciclovir is indicated for the prophylaxis of Herpes simplex infections in immunocompromised patients.
Aciclovir is indicated for the treatment of Varicella zoster infections.
Aciclovir is indicated for the treatment of herpes encephalitis.
Aciclovir is indicated for the treatment of Herpes simplex infections in the neonate and infant up to 3 months of age.

Posology and method of administration
Route of administration: Slow intravenous infusion over 1 hour.

A course of treatment with Aciclovir 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 disseminated or central nervous system disease. The duration of prophylactic administration of Aciclovir is determined by the duration of the period at risk.

Dosage in adults:
Patients with Herpes simplex (except herpes encephalitis) or Varicella zoster infections should be given Aciclovir in doses of 5 mg/kg body weight every 8 hours provided renal function is not impaired (see Dosage in renal impairment).
Immunocompromised patients with Varicella zoster infections or patients with herpes encephalitis should be given Aciclovir in doses of 10 mg/kg body weight every 8 hours provided renal function is not impaired (see Dosage in renal impairment).
In obese patients dosed with intravenous aciclovir based on their actual body weight, higher plasma concentrations may be obtained (see SPC section 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 Children:
The dose of Aciclovir for children aged between 3 months and 12 years is calculated on the basis of body surface area.
Children 3 months of age or older with Herpes simplex (except herpes encephalitis) or Varicella zoster infections should be given Aciclovir in doses of 250 mg per square metre of body surface area every 8 hours if renal function is not impaired.
In immunocompromised children with Varicella zoster infections or children with herpes encephalitis, Aciclovir should be given in doses of 500 mg per square metre body surface area every 8 hours if renal function is not impaired.
The dosage of Aciclovir in neonates and infants up to 3 months of age is calculated on the basis of body weight.
The recommended regimen for infants treated for known or suspected neonatal herpes is aciclovir 20 mg/kg body weight IV every 8 hours for 21 days for disseminated and CNS disease, or for 14 days for disease limited to the skin and mucous membranes.
Infants and children with impaired renal function require an appropriately modified dose, according to the degree of impairment (see Dosage in renal impairment).

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

Dosage in renal impairment:
Caution is advised when administering Aciclovir 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/1.73m2 for infants and children less than 13 years of age. The following adjustments in dosage are suggested:

Dosage adjustments in adults and adolescents:

Creatinine Clearance	Dosage
25 to 50 ml/min	The dose recommended above (5 or 10 mg/kg body weight) should be given every 12 hours.
10 to 25 ml/min	The dose recommended above (5 or 10 mg/kg body weight) should be given every 24 hours.
0(anuric) to 10 ml/min	In patients receiving continuous ambulatory peritoneal dialysis (CAPD) the dose recommended above (5 or 10 mg/kg body weight) should be halved and administered every 24 hours. In patients receiving haemodialysis the dose recommended above (5 or 10 mg/kg body weight) should be halved and administered every 24 hours and after dialysis.

Dosage adjustments in infants and children:

Creatinine Clearance	Dosage
25 to 50 ml/min/1.73m^2	The dose recommended above (250 or 500 mg/m^2 body surface area or 20 mg/kg body weight) should be given every 12 hours.
10 to 25 ml/min/1.73m^2	The dose recommended above (250 or 500 mg/m^2 20 mg/kg body weight) should be given every 24 hours.
0(anuric) to 10 ml/min /1.73m^2	In patients receiving continuous ambulatory peritoneal dialysis (CAPD) the dose recommended above (250 or 500 mg/m^2 20 mg/kg body weight) should be halved and administered every 24 hours. In patients receiving haemodialysis the dose recommended above (250 or 500 mg/m^2 20 mg/kg body weight) should be halved and administered every 24 hours and after dialysis.

Contraindications
Hypersensitivity to aciclovir or valaciclovir or to any of the excipients.

Special warnings and precautions for use
Use in patients with renal impairment and in elderly patients:

Other side effects include:

Common (may affect up to 1 in 10 people)

- feeling or being sick
- itchy, hive-like rash
- skin reaction after exposure to light (photosensitivity)
- itching
- swelling, redness and tenderness at the site of injection.
- Increase in the liver enzymes.

Uncommon (may affect up to 1 in 100 people)

- reduced numbers of red blood cells (anaemia)
- reduced numbers of white blood cells (leukopenia)
- reduced number of blood platelets (cells that help the blood to clot) (thrombocytopenia).

Very rare (may affect up to 1 in 10,000 people)

- headache or feeling dizzy
- diarrhoea or stomach pains
- feeling tired
- fever
- effects on some blood urine tests
- feeling weak
- feeling agitated or confused
- shaking or tremors
- hallucinations (seeing or hearing things that aren't there)
- fits
- feeling unusually sleepy or drowsy
- unsteadiness when walking and lack of coordination
- difficulty speaking
- inability to think or judge clearly
- unconsciousness (coma)
- paralysis of part or all of your body
- disturbances of behaviour, speech and eye movements
- stiff neck and sensitivity to light
- 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).

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.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

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

Store below 25°C. Do not refrigerate.
Store in the original carton in order to protect from light.

Do not use Aciclovir after the expiry date which is stated on the label and carton after Exp. The expiry date refers to the last day of that month.

Discard unused solution.

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.

Chemical and physical in-use stability has been demonstrated for 12 hours at 25 °C. 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.
Do not use Aciclovir if you notice any visible turbidity or crystallisation in the solution before or during infusion.

6. Contents of the pack and other information

What Aciclovir contains:
The active substance is Aciclovir.
Each 1 ml contains 25 mg of aciclovir as aciclovir sodium.
Each 10 ml vial contains 250 mg of aciclovir (sodium salt formed *in situ*)
Each 20 ml vial contains 500 mg of aciclovir (sodium salt formed *in situ*)
A clear, colourless solution, free from visible particles

The other ingredients are:
Water for Injections, Sodium hydroxide (for pH adjustment) and Hydrochloric acid (for pH adjustment)

For further information or if you have any questions about the use of this product, please contact on, telephone +44 (0)1270 582 255.

What Aciclovir looks like and contents of the pack
A clear, colourless solution, free from visible particles
Aciclovir comes in 10 ml and 20 ml clear glass vials.
Each pack contains 5, 10 and 20 vials of 10ml and 5, 10, 20 vials of 20ml.

Marketing Authorisation Holder
United Kingdom:
Baxter Healthcare Limited
Caxton Way
Thetford, Norfolk IP24 3SE

Ireland:
Baxter Holding B.V.
Kobaltweg 49,
3542CE Utrecht, Netherlands

Manufacturer
UAB Norameda
Meistru 8a, 02189,
Vilnius, Lithuania

Or

Bieffe Medital S.P.A.,
Via Nuova Provinciale 23034
Grosotto (SO) - Italy

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

UK	Aciclovir 25mg/ml Concentrate for solution for infusion
Estonia	Aciclovir Baxter
Ireland	Aciclovir 25mg/ml Concentrate for solution for infusion
Lithuania	Aciclovir Baxter 25mg/ml Koncentratas Infuziniam tirpalui
Netherlands	Aciclovir Baxter 25mg/ml Concentraat voor oplossing voor intraveneuze infusie

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Adequate hydration should be maintained in patients given i.v. or high oral doses of aciclovir.
Intravenous doses should be given by infusion over one hour to avoid precipitation of aciclovir in the kidney; rapid or bolus injection should be avoided.
The risk of renal impairment is increased by use with other nephrotoxic drugs. Care is required if administering i.v. aciclovir with other nephrotoxic drugs.
Aciclovir is eliminated by renal clearance, therefore the dose must be adjusted in patients with renal impairment (see SPC section 4.2 Posology and method of administration). 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 (see SPC section 4.8 Undesirable effects). 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 SPC section 5.1).
In patients receiving Aciclovir 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.
Aciclovir should not be administered by mouth. Product contains sodium (26mg, approx. 1,13mmol). To be taken into consideration by patients on a controlled sodium diet.
Aciclovir contains no antimicrobial preservative. dilution should therefore be carried out under full aseptic conditions immediately before use and any unused solution discarded. Diluted solutions should not be refrigerated.

Interaction with other medicinal products and other forms of interaction
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. However no dosage adjustment is necessary because of the wide therapeutic index of aciclovir.
In patients receiving intravenous 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.
If lithium is administered concurrently with high dose aciclovir IV, the lithium serum concentration should be closely monitored because of the risk of lithium toxicity.
Care is also required (with monitoring for changes in renal function) if administering intravenous Aciclovir with drugs which affect other aspects of renal physiology (e.g. ciclosporin, tacrolimus).
An experimental study on five male subjects indicates that concomitant therapy with aciclovir increases AUC of totally administered theophylline with approximately 50%. It is recommended to measure plasma concentrations during concomitant therapy with aciclovir

Overdose
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. 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
Water for injections
Sodium Hydroxide (used to adjust pH)
Hydrochloric acid (used to adjust pH)

Incompatibilities

None known.

Nature and contents of container
Glass vials with Teflon coated rubber stopper and flip-off seal.
5, 10 and 20 x 10ml
5, 10 and 20 x 20ml
Not all pack sizes may be marketed.

Instructions for use and handling
For single use only.
Since no antimicrobial preservative is included, reconstitution and dilution must be carried out under full aseptic conditions, immediately before use, and any unused solution discarded.
Should any visible , turbidity or crystallisation appear in the solution before or during infusion, the preparation should be discarded.
Refrigeration is not recommended, because precipitation may occur.
Administration: The required dose of Aciclovir should be administered by slow intravenous infusion over a one-hour period.

Aciclovir product can be 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 Aciclovir product to the chosen infusion solution, as recommended below, and shake well to ensure adequate mixing occurs.

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 but a second bag must be used for doses between 500 and 1000 mg. Aciclovir 25 mg/ml Concentrate for solution for infusion should not be diluted to a concentration greater than 5 mg/ml (0.5%w/v) for administration by infusion. After addition of Aciclovir 25 mg/ml Concentrate for solution for infusion to an infusion solution, the mixture should be shaken to ensure thorough mixing.

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 of solution (100 mg aciclovir) added to 20 ml of infusion fluid.

When diluted in accordance with the recommended schedules, Aciclovir 25 mg/ml Concentrate for solution for infusion is known to be compatible with the following infusion fluids and stable for up to 12 hours at room temperature (15^0C to 25^0C) :
Sodium Chloride Intravenous Infusion BP (0.45% w/v and 0.9% w/v)
Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion BP;
Sodium Chloride (0.45% w/v) and Glucose (2.5% w/v) Intravenous Infusion BP;
Compound Sodium Lactate Intravenous Infusion BP (Hartmann's Solution).

Dilutions of Aciclovir in the above mentioned diluents have been demonstrated to be stable in Non polyvinyl chloride (Non-PVC) infusion bags.