# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Aciclovir 25mg/ml concentrate for solution for infusion

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 25 mg aciclovir as aciclovir sodium.

Each vial of 10 ml of solution contains 250 mg aciclovir (sodium salt formed *in situ*)
Each vial of 20 ml of solution contains 500 mg aciclovir (sodium salt formed *in situ*)
Each vial of 40 ml of solution contains 1 g aciclovir (sodium salt formed *in situ*)

Excipient with known effect:

Each vial of 10 ml of solution contains 26.7 mg sodium.
Each vial of 20 ml of solution contains 53.4 mg sodium.
Each vial of 40 ml of solution contains 106.8 mg sodium.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate).

A clear, colourless or almost colourless solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is indicated for:

| **Immunocompetent Patients** | **Immunocompromised Patients** |
|---|---|
| Severe initial genital herpes | Herpes simplex infection |
| Recurrent *varicellazoster* virus infection | Primary and recurrent *varicellazoster* infection |
| | Prophylaxis of herpes simplex infection |
| Herpes simplex encephalitis | |
| Herpes simplex in neonates and infants up to 3 months of age | |

### 4.2 Posology and method of administration

The required dose of Aciclovir 25 mg/ml Concentrate for Solution for Infusion should be administered by slow intravenous infusion over 1 hour.

A course of treatment with Aciclovir 25 mg/ml Concentrate for Solution for Infusion 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 Aciclovir 25 mg/ml Concentrate for Solution for Infusion is determined by the duration of the period at risk.

<u>Dosage in adults:</u>

Patients with *Herpes simplex* (except herpes encephalitis) or *Varicella zoster* infections should be given Aciclovir 25 mg/ml Concentrate for Solution for Infusion 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 25 mg/ml Concentrate for Solution for Infusion 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 who received aciclovir intravenously based on their actual body weight, increased plasma concentrations may be obtained (see section 5.2 Pharmacokinetic properties). A dose reduction should therefore be considered in obese patients, especially in patients with renal impairment or in elderly patients.

Dosage for Neonates, Infants and Children:

The dose of Aciclovir 25 mg/ml Concentrate for Solution for Infusion for infants and children aged between 3 months and 12 years is calculated on the basis of body weight.

Infants 3 months of age and older and children with herpes simplex (except herpes simplex encephalitis) or *varicellazoster* infections should be given Aciclovir 25 mg/ml Concentrate for Solution for Infusion in doses of 10 mg/kg body weight every 8 hours if renal function is not impaired.

In immunocompromised infants aged 3 months and older and children with *varicellazoster* infections or infants and children with herpes encephalitis, Aciclovir 25 mg/ml Concentrate for Solution for Infusion should be given in doses of 20 mg/kg body weight every 8 hours if renal function is not impaired.

The dosage of Aciclovir 25 mg/ml Concentrate for Solution for Infusion in neonates and infants up to 3 months of age is calculated on the basis of body weight.

The recommended regimen for treatment for known or suspected neonatal herpes is aciclovir 20 mg/kg body weight intravenous (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.

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

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/1.73 $m^2$ for infants and children less than 12 years of age.

The following adjustments in dosage are suggested:

Table 1: 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 2: Dosage adjustments for IV aciclovir in **neonates, infants and children less than 12 years** of age with renal impairment for treatment of herpes simplex or varicella zoster virus infections.

| Creatinine Clearance (mL/min/1.73 $m^2$) | 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/1.73 $m^2$ | 10 mg/kg body weight given every 12 hours. | 20 mg/kg body weight given every 12 hours. |
| 10 to 25 mL/min/1.73 $m^2$ | 5 mg/kg body weight given every 12 hours. | 10 mg/kg body weight given every 12 hours. |
| 0 (anuric) to 10 mL/min/1.73 $m^2$ | 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. |

Method of administration

The required dose of Aciclovir 25 mg/ml Concentrate for Solution for Infusion should be administered by slow intravenous infusion over a one-hour period and adequate hydration should be established.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion may be administered by a controlled-rate infusion pump.

Refer to section 6.6 for instructions on use, preparation and handling.

**4.3 Contraindications**

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is contraindicated in patients known to be hypersensitive to aciclovir and valaciclovir or to any of the excipients as listed in section 6.1.

**4.4 Special warnings and precautions for use**

Solutions of aciclovir are alkaline (pH of approximately 11) and intended for intravenous infusion only and should not be used by any other route.

Contact with eyes or unprotected skin should be avoided.

Although the aqueous solubility of aciclovir exceeds 100 mg/ml, precipitation of aciclovir crystals in renal tubules and the consequent renal tubular damage can occur if the maximum solubility of free aciclovir (2.5 mg/ml at 37°C in water) is exceeded. Infusions of aciclovir must be given over a period of at least one hour in order to avoid renal tubular damage. Rapid or bolus injection should be avoided. Aciclovir infusions must be accompanied by adequate hydration. Since maximum urine concentration occurs within the first few hours following infusion particular attention should be given to establish sufficient urine flow during that period. Concomitant use of other nephrotoxic drugs, pre-existing renal disease and dehydration increase the risk of further renal impairment by aciclovir.

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 (see section 4.2).

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 section 4.8).

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 Aciclovir 25 mg/ml Concentrate for Solution for Infusion has a pH of approximately 11 and should not be administered by mouth.

Excipients

Each vial of 10 ml of solution contains 26.7 mg sodium equivalent to 1.34% of the WHO maximum recommended daily intake (RDI) of 2 g sodium for an adult.
Each vial of 20 ml of solution contains 53.4 mg sodium equivalent to 2.67% of the WHO maximum recommended daily intake (RDI) of 2 g sodium for an adult.

Each vial of 40 ml of solution contains 106.8 mg sodium equivalent to 5.34% of the WHO maximum recommended daily intake (RDI) of 2 g sodium for an adult.

This medicinal product may be further diluted with sodium-containing solutions (see section 6.6) and this should be considered in relation to the total sodium from all sources that will be administered to the patient.

**4.5 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 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.

If lithium is administered concurrently with high dose intravenous aciclovir, the lithium serum concentration should be closely monitored because of the risk of lithium toxicity and a reduced lithium dose may be needed.

When aciclovir isadministered concomitantly with theophylline, close monitoring of theophylline concentrations and possible theophylline dose reduction is recommended. A study has shown that when theophylline was given as single 320 mg doses before and with the sixth dose of aciclovir 800 mg five times daily for 2 days, the AUC of the theophylline was increased by 45% (from 189.9 to 274.9 micrograms.h/ml) and the total body clearance was reduced by 30%.

Care is also required (with monitoring for changes in renal function) if administering intravenous Aciclovir 25 mg/ml Concentrate for Solution for Infusion with drugs which affect other aspects of renal physiology (e,g., **cyclosporin, tacrolimus**).

**4.6 Fertility, pregnancy and lactation**

Pregnancy
A moderate amount of data on pregnant women (between 300-1,000 pregnancy outcomes, mostly orally given) indicate no malformative nor feto/neonatal toxicity. Animal studies do not indicate reproductive toxicity (see section 5.3).

The use of Aciclovir 25 mg/ml Concentrate for Solution for Infusion may be considered during pregnancy, if necessary.

Breast-feeding
Aciclovir is excreted in human milk, caution is therefore advised if aciclovir is to be administered to a nursing woman. It is unlikely that therapeutic doses of aciclovir have effects on the breastfed newborns/infants. Aciclovir may be considered for use during breast-feeding.

Fertility

There is no information on the effect of aciclovir on human female fertility. No effects were shown on male fertility. Animal studies do not show effects on fertility at relevant doses (see section 5.3).

**4.7 Effects on ability to drive and use machines**

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is generally used in an in-patient hospital population and information on ability to drive and operate machinery is not available. There have been no studies to investigate the effect of Aciclovir 25 mg/ml Concentrate for Solution for Infusion on driving performance or the ability to operate machinery.

**4.8 Undesirable effects**

The frequency categories associated with the adverse events below are estimates. For most events, suitable data for estimating incidence were not available. In addition, adverse events may vary in their incidence depending on the indication.

The following convention has been used for the classification of undesirable effects in terms of frequency: Very common (>1/10); common (>1/100 to < 1/10); uncommon (>1/1,000 to < 1/100); rare (>1/10,000 to < 1/1,000); very rare (< 1/10,000).

| **MedDRA System Organ Classes** | **Very common > 1/10,** | **Common 1/100 and < 1/10** | **Uncommon > 1/1,000 and < 1/100** | **Rare >1/10,000** | **Very rare < 1/10,000** |
|---|---|---|---|---|---|
| Blood and lymphatic system disorders | | | decreases in haematological indices (anaemia, thrombocytopenia, leukopenia) | | neutropenia |
| Immune system disorders | | | | | anaphylaxis |
| Psychiatric and nervous system disorders | | | | | headache, dizziness, agitation, confusion, tremor, ataxia, dysarthria, hallucinations, psychotic symptoms, convulsions, somnolence, encephalopathy, coma[$].<br><br>Lethargy, paraesthesia, and reversible psychiatric effect. |
| Vascular disorders | | phlebitis | | | |
| Respiratory, thoracic and mediastinal disorders | | | | | dyspnoea |
| Gastrointestinal disorders | | nausea, vomiting | | | diarrhoea, abdominal pain |
| Hepato-biliary disorders | | reversible increases in liver-related enzymes | | | reversible increases in bilirubin, jaundice, hepatitis |
| Skin and subcutaneous tissue disorders | | pruritus, urticaria, rashes (including photosensitivity) | | | angioedema |
| Renal and urinary disorders | | increases in blood urea and creatinine.* | | | renal impairment, acute renal failure[+] and renal pain[§] |
| General disorders and | | | | | fatigue, fever, local inflammatory reactions.[¥] |

| | | | | | |
|---|---|---|---|---|---|
| administration site conditions | | | | | |

[$] The events are generally reversible and usually reported in patients with renal impairment or with other predisposing factors (see section 4.4 Special Warnings and Precautions for Use).

* Rapid increases in blood urea and creatinine levels are believed to be related to the peak plasma levels and the state of hydration of the patient. To avoid this effect, when administered intravenously the drug should not be given as an intravenous bolus injection but by slow infusion over a one-hour period.

[+] Adequate hydration should be maintained. Renal impairment usually responds rapidly to rehydration of the patient and/or dosage reduction or withdrawal of the drug. Progression to acute renal failure, however, can occur in exceptional cases.

[§] Renal pain may be associated with renal failure.

[¥]Severe local inflammatory reactions sometimes leading to breakdown of the skin have occurred when Aciclovir for infusion has been inadvertently infused into extracellular tissues. In case of high doses thirst has been reported in patients who had been treated previously with Aciclovir.

Other less frequent adverse effects reported in patients receiving therapy with Aciclovir 25 mg/ml Concentrate for Solution for Infusion include:

Skin and subcutaneous disorders:
diaphoresis, leukocytoclastic vasculitis, erythema multiforme

Renal and urinary disorders:
haematuria

Vascular disorders:
hypotension

Blood and lymphatic system disorders:
haemolysis
In immunocompromised patients also: thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome (sometimes fatal)

Hepatobiliary disorders:
hyperbilirubinaemia.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

**4.9 Overdose**

Symptoms and Signs
Overdosage of intravenous 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
Adequate hydration is essential to reduce the possibility of crystal formation in the urine. 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.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: group Anti infective, ATC code: J05AB01

Mechanism of action:
Aciclovir is an antiviral agent which is highly active *in vitro* against Herpes simplex virus (HSV) types I and II and *Varicellazoster* virus. Toxicity to mammalian host cells is low.

Aciclovir is phosphorylated after entry into herpes infected cells to the active compound aciclovir triphosphate. The first step in this process is dependent on the presence of the HSV-coded thymidine kinase.

Aciclovir triphosphate acts as an inhibitor of and substrate for the herpes specified DNA polymerase preventing further viral DNA synthesis without affecting normal cellular processes.

**5.2 Pharmacokinetic properties**

Elimination

In adults, the terminal plasma half-life has been determined as about 2.9 hours.

Most of the drug is excreted unchanged in the kidney. Renal clearance of aciclovir is substantially greater than creatinine clearance, indicating that tubular secretion, in addition to glomerular filtration contributes to the renal elimination of the drug.

9-Carboxymethoxymethylguanine is the only significant metabolite of aciclovir, and accounts for 10-15% of the dose excreted in the urine.

When aciclovir is given one hour after 1 gram of probenecid, the terminal half-life and the area under the plasma concentration time curve, are extended by 18% and 40% respectively.

Absorption
In adults, mean steady state peak plasma concentrations ($C^{ss}_{max}$) following a one-hour infusion of 2.5 mg/kg, 5 mg/kg and 10 mg/kg were 22.7 micromolar (5.1 microgram/mL), 43.6 micromolar (9.8 microgram/mL) and 92 micromolar (20.7 microgram/mL) respectively. The corresponding trough levels ($C^{ss}_{min}$) 7 hours later were 2.2 micromolar (0.5 microgram/mL), 3.1 micromolar (0.7 microgram/mL) and 10.2 micromolar (2.3 microgram/mL) respectively. In children over 1 year of age similar mean peak ($C^{ss}_{max}$) and trough ($C^{ss}_{min}$) levels were observed when a dose of 250 mg/m$^2$ was substituted for 5 mg/kg and a dose of 500 mg/m$^2$ was substituted for 10 mg/kg. In neonates (0 to 3 months of age) treated with doses of 10 mg/kg administered by infusion over a one-hour period every 8 hours the $C^{ss}_{max}$ was found to be 61.2 micromolar (13.8 microgram/mL) and the $C^{ss}_{min}$ to be 10.1 micromolar (2.3 microgram/mL). A separate group of neonates treated with 15 mg/kg every 8 hours showed approximate dose proportional increases, with a $C_{max}$ of 83.5 micromolar (18.8 microgram/mL) and $C_{min}$ of 14.1 micromolar (3.2 microgram/mL).
The terminal plasma half-life in these patients was 3.8 hours. In the elderly, total body clearance falls with increasing age and is associated with decreases in creatinine clearance although there is little change in the terminal plasma half-life.

In patients with chronic renal failure, the mean terminal half-life was found to be 19.5 hours. The mean aciclovir half-life during haemodialysis was 5.7 hours. Plasma aciclovir levels dropped approximately 60% during dialysis.

In a clinical study in which morbidly obese female patients (n=7) were dosed with intravenous aciclovir based on their actual body weight, plasma concentrations were found to be approximately twice that of normal weight patients (n=5), consistent with the difference in body weight between the two groups.

Distribution

Cerebrospinal fluid levels are approximately 50% of corresponding plasma levels.

Plasma protein binding is relatively low (9 to 33%) and drug interactions involving binding site displacement are not anticipated.

**5.3 Preclinical safety data**

Teratogenicity

Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rabbits, rats or mice. In a non-standard test in rats, foetal abnormalities were observed but only following such high subcutaneous doses that maternal toxicity was produced. The clinical relevance of these findings is probably low.

Mutagenicity
The results of a wide range of mutagenicity tests *in vitro* and *in vivo* indicate that aciclovir is unlikely to pose a genetic risk to man.

Carcinogenicity
Aciclovir was not found to be carcinogenic in long-term studies in the rat and the mouse.

Fertility
Largely reversible adverse effects on spermatogenesis in association with overall toxicity in rats and dogs have been reported only at doses of aciclovir greatly in excess of those employed therapeutically. Two-generation studies in mice did not reveal any effect of (orally administered) aciclovir on fertility.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Sodium hydroxide
Water for Injections.
In the manufacture of the finished product sodium hydroxide and / or hydrochloric acid are used for pH adjustment.

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Aciclovir sodium is reported to be incompatible with solutions of amifostine, amsacrine, aztreonam, diltiazem hydrochloride, dobutamine hydrochloride, dopamine hydrochloride, fludarabine phosphate, foscarnet sodium, idarubicin hydrochloride, meropenem, morphine sulphate, ondansetron hydrochloride, pethidine hydrochloride, piperacillin sodium - tazobactam sodium, sargramostim and vinorelbine tartrate.

Do not use bacteriostatic water for injection containing parabens or benzyl alcohol. Biologic or colloidal fluids (e.g. blood products, protein containing solutions) are incompatible with aciclovir sodium.

### 6.3 Shelf life

As packaged: 2 years.
After dilution: 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. When dilution is carried out under validated aseptic conditions, the product may be stored for a maximum of 12 hours at room temperature, below 25°C.

### 6.4 Special precautions for storage

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

### 6.5 Nature and contents of container

Clear, type I glass vials with butyl rubber stopper and an aluminium seal with a plastic 'flip-off' top. Packs of 5 vials (250 mg/10 mL) or (500 mg/20 mL) per carton, and as a single vial (1 g/40 mL) in a carton.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

Aciclovir 25 mg/ml Concentrate for Solution for Infusion contains no preservative. Dilution should therefore be carried out immediately before use under full aseptic conditions and any unused solution should be discarded.

Refrigeration is not recommended as precipitation may occur.

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 infusion fluids listed below:

Sodium Chloride Intravenous Infusion 0.9% w/v;

Sodium Chloride (0.18% w/v) and Glucose (4% w/v) Intravenous Infusion;

Sodium Chloride (0.9% w/v) and Glucose (5% w/v) Intravenous Infusion;

Sodium Chloride (0.45% w/v) and Glucose (2.5% w/v) Intravenous Infusion;

Compound Sodium Lactate Intravenous Infusion (Hartmann's Solution).

Aciclovir 25 mg/ml Concentrate for Solution for Infusion when diluted in accordance with the above schedule will give an aciclovir concentration not greater than 0.5% w/v.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion contains no preservative.

Should any visible turbidity or crystallisation appear in the solution before or during infusion, the preparation should be discarded.

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

**7 MARKETING AUTHORISATION HOLDER**

Pfizer Healthcare Ireland Unlimited Company
The Watermarque Building
Ringsend Road
Dublin 4
D04 K7N3
Ireland

**8 MARKETING AUTHORISATION NUMBER**

PA0822/215/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 22 January 1999
Date of last renewal: 24 June 2007

**10 DATE OF REVISION OF THE TEXT**

March 2026