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*)

Excipients: 1 ml of solution contains 2.67 mg of sodium (approximately 0.116 mmol).

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 the treatment of severe initial genital herpes in the immunocompromised and the non-immunocompromised.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is indicated for the prophylaxis and treatment of Herpes simplex infections in immunocompromised patients.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is indicated for the treatment of Varicella zoster infections.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is indicated for the treatment of herpes encephalitis.

Aciclovir 25 mg/ml Concentrate for Solution for Infusion is indicated for the treatment of Herpes simplex infections in the neonate and infant up to 3 months of age.

4.2 Posology and method of administration

Posology
A course of treatment with Aciclovir 25 mg/ml Concentrate for Solution for Infusion usually lasts 5 days, but the duration of treatment 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 infections usually lasts for 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 25 mg/ml Concentrate for Solution for Infusion is determined by the duration of the period of risk.

Dosage in adults:

Patients with Herpes simplex (except herpes encephalitis) or Varicella zoster infections (with normal immune response) should be given Aciclovir 25 mg/ml Concentrate for Solution for Infusion in doses of 5 mg/kg bodyweight 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 bodyweight 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 5.2). Consideration should therefore be given to dosage reduction in obese patients and especially in those with renal impairment or the elderly.

Dosage in children:

Neonates and infants up to 3 months of age:

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 bodyweight.

The recommended regimen of Aciclovir 25mg/ml Concentrate for Solution for Infusion for known or suspected neonatal herpes infections is 20 mg/kg bodyweight every 8 hours for 21 days for disseminated and CNS disease, or for 14 days for disease limited to the skin and mucous membranes.

Children aged between 3 months and 12 years:

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

Children with Herpes simplex (except herpes encephalitis) or Varicella zoster infections (with normal immune response) should be given Aciclovir 25 mg/ml Concentrate for Solution for Infusion in doses of 250 mg/m2 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 25 mg/ml Concentrate for Solution for Infusion should be given in doses of 500 mg per square metre body surface area every 8 hours if renal function is not impaired.

Infants and children with impaired renal function:

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).

Adequate hydration should be maintained.

Dosage in renal impairment:

Caution is advised when administering Aciclovir 25 mg/ml Concentrate for Solution for Infusion to patients with impaired renal function since the drug is excreted through the kidneys. 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 adjustment in infants and children less than 13 years of age:

Dosage adjustments in adults and adolescents:

Creatinine clearance	**Dosage**
25 to 50 ml/min	The dose recommended above (5 or 10 mg/kg bodyweight) should be given every 12 hours.
10 to 25 ml/min	The dose recommended above (5 or 10 mg/kg bodyweight) 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 bodyweight) 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 adjustment in infants and children less than 13 years of age:

Creatinine clearance	Dosage
25 to 50 ml/min/1.73 m^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/1.73 m^2	The dose recommended above (250 or 500 mg/m2 body surface area or 20 mg/kg body weight) should be given every 24 hours.
0(anuric) to 10 ml/min/1.73 m^2	In patients receiving continuous ambulatory peritoneal dialysis (CAPD) the dose recommended above (250 or 500 mg/m2 body surface area or 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/m2 body surface area or 20 mg/kg body weight) should be halved and administered every 24 hours and after dialysis.

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 previously hypersensitive to aciclovir and valaciclovir or to any of the excipients 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, and therefore the dose of Aciclovir 25mg/ml Concentrate for Solution for Infusion must be adjusted in patients with impaired renal function in order to avoid accumulation of aciclovir in the body (see section 4.2, Dosage in 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. In patients receiving Aciclovir 25 mg/ml Concentrate for Solution 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.

Aciclovir should be used with caution in patients with underlying neurological abnormalities. 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 Undesirable effects).

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

Excipients in the formulation
This medicinal product contains 2.67 mg/ml (0.116 mmol/ml) sodium. To be taken into consideration by patients on a controlled sodium diet.

Other warnings and precautions:

The label shall contain the following statements:

For intravenous infusion only

Keep out of the sight and reach of children

Store below 25^{o}C

Prepare immediately before use

Discard unused solution

4.5 Interaction with other medicinal products and other forms of interactions

Aciclovir is mainly excreted renally as unchanged drug by active tubular secretion. Concomitantly administered agents, also eliminated via this pathway, may increase the plasma concentration of aciclovir. Probenecid and cimetidine, increase the area under the plasma concentration-time curve (AUC) of aciclovir by this mechanism and decrease its renal clearance. However, in these cases an adjustment of the aciclovir dosage is not thought to be necessary given the large therapeutic range of aciclovir.

In pateients 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 intravenous aciclovir, the lithium serum concentrations 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 changes in renal function) if administering Aciclovir 25 mg/ml Concentrate for Solution for Infusion with drugs that affect other aspects or renal physiology (e,g, cyclosporine, tacrolimus) as they may influence the nephrotoxic effect of aciclovir.

4.6 Fertility, pregnancy and lactation

Fertility
There is no information on the effect of aciclovir on human female fertility.

In a study of 20 male patients with normal sperm count, oral aciclovir administered at doses of up to 1 g per day for up to six months has been shown to have no clinically significant effect on sperm count, motility or morphology.

Pregnancy
Limited data are available on the use of aciclovir during pregnancy. A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of aciclovir. The registry findings have not shown an increase in the number of birth defects amongst aciclovir exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause. 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 uncertain.

Caution should therefore be exercised by balancing the potential benefits of treatment against any possible hazard. Findings from reproduction toxicology studies are included in section 5.3.

Breast-feeding
Following oral administration of 200 mg five times a day, aciclovir has been detected in human breast milk at concentrations ranging from 0.6 to 4.1 times the corresponding plasma levels. These levels would potentially expose nursing infants to aciclovir dosages of up to 0.3 mg/kg body weight/day. Caution is therefore advised if aciclovir is to be administered to a nursing woman.

4.7 Effects on ability to drive and use machines

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. Furthermore, a detrimental effect on such activities cannot be predicted from the pharmacology of the drug.
Nevertheless, the clinical status of the patient and the adverse event profile of Aciclovir Concentrate for Solution for Infusion should be borne in mind when considering the patient's ability to drive or operate machinery.

4.8 Undesirable effects

The following convention has been used for the classification of undesirable effects in terms of frequency:− Very common ≥1/10, common ≥1/100 and < 1/10, uncommon ≥1/1,000 and < 1/100, rare ≥1/10,000 and < 1/1,000, very rare < 1/10,000. Not known (cannot be estimated from available data)

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. The above events are generally reversible and usually reported in patients with renal impairment or with other predisposing factors (see 4.4 Special Warnings and Precautions for Use).
Vascular disorders		phlebitis			
Respiratory, thoracic and mediastinal disorders					dyspnoea

Gastrointestinal disorders		nausea vomiting			Diarrhoea, abdominal pain
Hepatobiliary disorders		reversible increases in liver-related enzymes			Reversible increases in bilirubin, jaundice, hepatitis
Skin and subcutaneous tissue disorders		pruritus, urticarial, rashes (including photosensitivity)			angioedema

Renal and urinary disorders		Increases in blood urea and creatinine*			renal impairment, acute renal failure and renal pain, which may be associated with crystalluria
General disorders and administration site conditions					fatigue, fever, local inflammatory reactions. Severe local inflammatory reactions sometimes leading to breakdown of the skin have occurred when Aciclovir has been inadvertently infused into extracellular tissues.

*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 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.

Frequency is not known for the following undesirable effects:

General disorders and administration site conditions:
Local necrosis and inflammation have occurred when Aciclovir 25 mg/ml Concentrate for Solution for Infusion has been inadvertently infused into extravascular tissues. Severe local inflammatory reactions or phlebitis have occurred at the injection site sometimes leading to breakdown of the skin. These local effects occur more frequently following inadvertent infusion of Aciclovir into extravascular tissues.

In case of high doses thirst has been reported in patients who had been treated previously with Aciclovir

Psychiatric and nervous system disorders:

Lethargy, paraesthesia, and reversible psychiatric effects

Other:

Other less frequent adverse effects reported in patients receiving therapy with Aciclovir 25mg/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
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: http://www.hpra.ie/
e-mail: medsafety@hpra.ie

4.9 Overdose

Toxicity and treatment of overdosage

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. Adequate hydration is essential to reduce the possibility of crystal formation in the urine. Patients should be observed closely for signs of toxicity. Aciclovir can be removed from the circulation by haemodialysis which may, therefore, be considered an option in the management of overdose of this drug

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: – Direct acting antivirals – nucleosides and nucleotides excluding reverse transcriptase inhibitors.
ATC: J05A B01

Mode of action: Aciclovir is a synthetic acyclic purine nucleoside analogue with in vitro and in vivo inhibitory activity against human Herpes viruses, including Herpes simplex virus types 1 and 2 and Varicella zoster virus (VZV), Epstein Barr virus (EBV) and Cytomegalovirus (CMV). In cell culture aciclovir has the greatest antiviral activity against HSV-1, followed (in decreasing order of potency) by HSV-2, VZV, EBV, and CMV.

The inhibitory activity of aciclovir for HSV-1, HSV-2, VZV and EBV is highly selective. The enzyme thymidine kinase (TK) of normal, uninfected cells does not use aciclovir effectively as a substrate, hence toxicity to mammalian host cells is low; however, TK

encoded by HSV, VZV and EBV converts aciclovir to aciclovir monophosphate, a nucleoside analogue, which is further converted to the diphosphate and finally to the triphosphate by cellular enzymes. Aciclovir needs to be phosphorylated to the active compound aciclovir triphosphate, in order to become active against the virus. Aciclovir triphosphate acts as an inhibitor of, and a substrate for, the herpes specified DNA polymerase preventing further viral DNA synthesis.

5.2 Pharmacokinetic properties

In adults, the terminal plasma half-life of aciclovir after the administration of Aciclovir 25 mg/ml Concentrate for Solution for Infusion is about 3 hours. Aciclovir is widely distributed in tissues and body fluids. Approximately 75-80% of the drug is excreted unchanged by 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 major significant metabolite of aciclovir and accounts for 10 to 15% of the dose excreted in the urine.

In adults, mean steady state peak (C^{ss}_{max}) plasma concentrations following a one-hour infusion, and trough levels (C^{ss}_{min}) 7 hours later, were:

Dose	2.5 mg/kg	5 mg/kg	10 mg/kg	15 mg/kg
C^{ss}_{max} in µmol/L (µg/ml)	22.7 (5.1)	43.6 (9.8)	92 (20.7)	105 (23.6)
C^{ss}_{min}, after 7 hours, in µmol/L (µg/ml)	2.2 (0.5)	3.1 (0.7)	10.2 (2.3)	8.8 (2.0)

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 neonates was approximately 4 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 end stage renal failure the plasma half-life is increased, extending to a mean terminal half-life of approximately 20 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 diference in body weight between the two groups.

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

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.

Teratogenicity
Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rabbits, rats or mice. Animal studies indicate that at high dose aciclovir is cytotoxic.

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 uncertain.

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.

There is no experience of the effect of Aciclovir 25 mg/ml Concentrate for Solution for Infusion on human fertility. Aciclovir tablets have been shown to have no definitive effect upon sperm count, morphology or motility in man.

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 1 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.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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.

7 MARKETING AUTHORISATION HOLDER

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA000822/215/001

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

September 2018