ACICLOVIR: INTRAVENOUS - SCH

DRUG PROTOCOL©

DOCUMENT SUMMARY/KEY POINTS

- IV aciclovir kinetics have been investigated extensively in neonates and children.
- Intravenous aciclovir should be used in concordance with the recommendations made by the SCH Antimicrobial Subcommittee and all approval obtained through the electronic antimicrobial approval system GuidanceMS®.
- The recommended dose of IV aciclovir varies with indication, age, renal function and other patient specific factors.
- Dose adjustment and review of patient hydration status are necessary to reduce the risk of further renal impairment and accumulation of aciclovir in the body.
- Failure to use body surface area dosing in patients 3 months to 12 years can result in significant under or over-dosing. A single milligram per kilogram does not apply across all age groups.

CHANGE SUMMARY

- Updated dosing and indications based on best available evidence.
- Additional information for dosing in renal impairment and identification of patients at risk of acute kidney injury.

READ ACKNOWLEDGEMENT

- All SCH clinical staff involved in patient care where aciclovir may be in use should read and acknowledge they understand the contents of this document.

Note: Separate Practice Guidelines may be required to cover all aspects of management.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st October 2015	**Review Period**: 3 years
Team Leader:	Staff Specialist	**Area/Dept**: Infectious Diseases SCH

Date of Publishing: 21 September 2015 12:19 PM Date of Printing:

Introduction / Background

Aciclovir was discovered in the 1970s and first marketed in 1981.

Unlike most antimicrobials, IV aciclovir kinetics have been investigated extensively in neonates and children. Mean concentrations vary linearly with doses between 2.5 to 15 mg/kg and repeated 8-hourly intravenous doses providing clinically useful steady-state mean plasma levels ranging from 6.7 to 20.6 mg/L, respectively.

According to Ecksborg, Area Under the Curve (AUC) normalised for body weight or body surface area was independent of age [range 1.4 - 18 years]. **Dosing based on BSA gave a lower variability of target AUC than dosing based on body weight and is recommended due to an increased standardisation of drug exposure**.[2]

Approximate concentration of aciclovir in the CSF is 50% of plasma concentrations. Renal excretion is the major route of elimination. Up to 80% is excreted unchanged in the urine, with the remainder metabolised to inactive derivatives. In patients with end-stage renal disease, the half-life is extended to approximately 20 hours and mean peak plasma concentrations approximately doubled.[3] Most of the reported side effects of IV aciclovir are linked to high plasma concentration and/or inadequate hydration.

Contraindications

- Known hypersensitivity to aciclovir or valaciclovir.

Precautions

- Adequate hydration should be given to prevent the precipitation of crystals in the renal tubules, consideration should be given to whether fluid restriction allow for adequate hydration.[9]
- Renal impairment, concomitant use of nephrotoxins and dehydration increases risk of acute kidney injury and neurological adverse effects due to accumulation in the body; dose adjustment is required. See Table 1: Renal Dosing Adjustment in Children.

Table 1: Renal Dosing Adjustments in Children[1, 4,7,8,]

CrCl (mL/min1.73m^2)	Percentage dose (adjustment)	Frequency (adjustment)
Greater than 50	100%	8 hourly(No change necessary)
25-50	100%	12 hourly
10 to 25	100%	Daily
Less than 10	50%	Daily and after haemodialysis

Note: Seek renal advice for dosing in neonates with existing or at risk of renal impairment.

- Failure to use surface area dosing in patients 3 months to 12 years can result in significant under or overdosing. A single milligram per kilogram does not apply across all age groups.
- A reliable Body Surface Area (BSA) Calculator is available via CIAP: MedCalc Body Surface Area, Body Mass Index.
- To avoid excessive dose in obese patients parenteral dose should be calculated on the basis of ideal weight for height.[4] See Drug Dosing for Overweight and Obese Patients - SCH

Approved Indications and dosing[1,4]

Intravenous aciclovir should be used in concordance with the recommendations made by the SCH Antimicrobial Subcommittee and all approval obtained through the electronic antimicrobial approval system GuidanceMS®.

Patient Group	Indication	Dose
Neonates and infants under 3 months of age	Encephalitis – empiric therapy	*Post-conceptional age 32 weeks and over:* ACICLOVIR 20mg/kg/dose IV 8-hourly.[4,5,6,7,11]
	Herpes Simplex disseminated disease	
	Herpes Simplex Encephalitis	
	Herpes Simplex localised	
	Herpes Simplex Pneumonitis	
	Sepsis – empiric therapy	
Infants and Children - Immunocompetent	Encephalitis – empiric therapy	*Infants 3 months and over to children 12 years of age:* ACICLOVIR 500mg/m^2/dose IV 8-hourly.[4,5,6] *Children over 12 years of age:* ACICLOVIR 10mg/kg/dose IV 8-hourly.[4,7]
	Herpes Simplex Encephalitis	
	Herpes Simplex – severe mucocutaneous disease	*Infants 3 months and over to children 12 years of age:* ACICLOVIR 250 mg/m^2/dose IV 8-hourly.[4] *Children over 12 years of age:* ACICLOVIR 5 mg/kg/dose IV 8-hourly.[4,7]
	Varicella Encephalitis, or Pneumonitis	*Infants 3 months and over to children 12 years of age:* ACICLOVIR 500 mg/m^2/dose IV 8-hourly.[4,5] *Children over 12 years of age:* ACICLOVIR 10 mg/kg/dose IV 8-hourly.[4,5,7]
Infants and Children - Immunocompromised	Herpes Simplex	*Infants 3 months and over to children 12 years of age:* ACICLOVIR 500 mg/m^2/dose IV 8-hourly.[4] *Children over 12 years of age:* ACICLOVIR 10 mg/kg/dose IV 8-hourly.[4]
	Prophylactic use(Oncology/transplant)	*Children under 40 kg:* ACICLOVIR 250 mg/m^2/dose IV 8-hourly (up to 80 mg/kg/day).[8] *Children 40 kg and over:* ACICLOVIR 250 mg/m^2/dose IV 12-hourly.[8]
	Varicella Zoster (chickenpox)	*Infants 3 months and over to children 12 years of age:* ACICLOVIR 500 mg/m^2/dose IV 8-hourly.[4,5] *Children over 12 years of age:* ACICLOVIR 10 mg/kg/dose IV 8-hourly.[4,5]

*****Doses recommended for neonates under 35 weeks post-conception apply to those aged over 32 weeks with no renal impairment.*

Administration[1]

Dilute dose to a concentration of 5mg/mL or less (e.g. add no more than 250mg to 50mL, or no more than 500mg to 100mL) with a compatible fluid. Shake well to ensure thorough mixing. Should visible turbidity or crystallisation appear in the solution before or during infusion, the preparation should be discarded. Infuse diluted dose over 1 hour.[1]

A 25 mg/mL solution can be infused undiluted into a vein over a one hour period by a controlled rate infusion pump. However, the administration of the undiluted solution has also been advised against due to phlebitis and inflammation at the infusion site. A central line is preferred.

Use of concentrated solutions in fluid restricted patients should occur after discussion the Consultant.

Adverse Effects and monitoring

Reported adverse effects of IV aciclovir include changes in LFTs, phlebitis and injection site reactions, acute renal failure, dizziness, dysarthria, encephalopathy.[1]

Urinalysis, BUN, serum creatinine, urine output; liver enzymes, CBC; neutrophil count at least twice weekly have been recommended in neonates.[10]

Injection site should be reviewed regularly during administration for inflammation and phlebitis.

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