MONOGRAPH

Valaciclovir Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas (Perth Children's Hospital)

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

DRUG CLASS

Guanine analogue antiviral. Valaciclovir is a prodrug of aciclovir.[1-4]

Valaciclovir is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Valaciclovir is used in the treatment and prevention of herpes simplex virus (HSV), varicella-zoster virus (VZV).[1, 3]

Oral: Monitored (orange) antiviral

As per indications stipulated in Formulary One. For any other use, phone approval must be obtained from ChAMP before prescribing as per the Antimicrobial Stewardship Policy.

CONTRAINDICATIONS

- Hypersensitivity to valaciclovir, aciclovir or any component of the formulation.[1, 2, 5-8]

PRECAUTIONS

- Use with caution in renal impairment due to increased risk of neurological adverse effects, dose adjustment is required.[6, 8]
- Patients should be instructed to drink plenty of fluids whilst prescribed valaciclovir. If dehydrated, precipitation of aciclovir may occur in the renal tubules if the solubility is exceeded in the intratubular fluid.[2, 5-9]
- CNS adverse effects have been reported in children with and without renal impairment receiving high dose therapy. These adverse effects include agitation, dysarthria, hallucinations, confusion, impaired consciousness and seizures.[6, 8]
- Thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (HUS) have been associated with high dose, prolonged use of valaciclovir in immunocompromised patients (e.g., post-transplant or HIV positive patients). Treatment with valaciclovir should be ceased immediately if clinical signs, symptoms, and laboratory abnormalities consistent with TTP/HUS occur.[2, 5, 7, 8]

FORMULATIONS

Listed below are products available at PCH. Other formulations may be available, check with pharmacy if required:

- Valaciclovir 500mg tablet

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

- Although valaciclovir is not licensed for use in children in Australia it is thought to be a safe alternative to aciclovir as it is a prodrug of aciclovir and may be preferred for its more convenient dosing schedule and greater bioavailability. Valaciclovir is licensed for use internationally in children >2 years.[4]

Neonates and children <3 months of age:

Valaciclovir is not routinely used in neonates or children < 3 months of age and has limited data on use in children under 2 years of age. Contact the Infectious Diseases or Clinical Microbiology service for advice. Aciclovir is preferred in those <3 months of age.

Refer to: Aciclovir Monograph – Paediatric **OR** Neonatal Medication Protocol - Aciclovir

Dosing in Overweight and Obese Children: There is minimal information regarding the dosing of valaciclovir in overweight or obese patients. Given valaciclovir is a pro-drug of aciclovir which should be dosed on ideal body weight, valaciclovir should also be dosed based on ideal body weight.[10]

Immunocompromised patients:

Indication	Age and / or weight	Dose	Duration
Prophylaxis			
Prophylaxis – HSV Seropositive haematopoietic stem cell transplant (HSCT) recipients.[8, 11]	< 3 months	IV aciclovir is preferred – refer to Aciclovir monograph - Paediatric	
	≥ 3 months and <40kg	250 mg twice daily[8]	Variable – up to 12 months post HSCT[8]
	≥ 3 months and ≥40kg	500 mg twice daily[8]	Variable – up to 12 months post HSCT[8]
Treatment			
HSV disease in immunocompromised patients. (e.g., skin, eye, or mouth disease)	< 2 years old	IV aciclovir is preferred – refer to Aciclovir monograph - Paediatric	
	In majority of cases, initial IV therapy is required with aciclovir for immunocompromised patients. Oral switch to valaciclovir may be considered following improvement (see dose below).		
	≥ 2 years	20 mg/kg/dose (to a maximum of 1000 mg) three times a day.[8, 12]	10 to 14 days[8]
VZV (chickenpox) in immunocompromised patients.[6, 8]	< 3 months	IV aciclovir is preferred – refer to Aciclovir monograph - Paediatric	
	≥ 3 months[8]	20 mg/kg/dose (to a maximum of 1000 mg) three times a day.[8]	7 to 14 days[8]
Shingles in immunocompromised patients	< 2 years old	Discuss with Infectious Diseases	
	≥ 2 years[8]	In many cases, initial IV therapy with aciclovir is recommended. Discuss with Infectious Diseases.[8]	
		20 mg/kg/dose (to a maximum of 1000 mg) three times a day.[8]	7 to 10 days – longer therapy may be required if lesions are slow to respond.[8]

Immunocompetent patients:

Indication	Age and / or weight	Dose	Duration
Prophylaxis			
Oral mucocutaneous or skin HSV - frequent and severe recurrences	< 3 months	Aciclovir is preferred – refer to Aciclovir monograph - Paediatric or discuss with Infectious Diseases	
	≥ 3 months	Minimal information regarding this indication – dose has been extrapolated from adult data.[4]	
		10 mg/kg/dose (to a maximum of 500 mg) once daily.[12]	Variable
Treatment			
Uncomplicated VZV (chickenpox) in immunocompetent patients.[6, 8]	• Unvaccinated adolescents and patients with chronic pulmonary disorders (including those on inhaled steroids) are recommended therapy due to an increased risk of developing complications.[13] • Children with pre-existing skin disease (e.g. eczema) require antiviral therapy due to greater risk of severe varicella including extensive cutaneous varicella and complications of varicella (e.g. pneumonia, encephalitis and hepatitis).[4] • Children without significant pre-existing skin disease do not require antiviral therapy for varicella as the benefits of treatment are only marginal.[4]		
	< 3 months	IV aciclovir is preferred – refer to Aciclovir monograph - Paediatric	
	≥ 3 months	20 mg/kg/dose (to a maximum of 1000 mg) three times a day.[3, 6, 8] Commenced within 24 hours of rash onset	5 days[3, 6, 8]
Uncomplicated VZV (shingles) in immunocompetent patients.[6, 8]	≥ 2 years	20 mg/kg/dose (to a maximum of 1000 mg) three times a day.[8] Commenced within 24 hours of rash onset	7 days[4, 8]
Severe primary HSV gingivostomatitis[8]	< 3 months	IV aciclovir is preferred – refer to Aciclovir monograph - Paediatric	

	≥ 3 months	20 mg/kg/dose (to a maximum of 1000 mg) twice daily.[8]	5 to 7 days[8]
Oral mucocutaneous or skin HSV - infrequent and severe recurrences[1, 3, 4]	< 12 years	20 mg/kg/dose (to a maximum of 1000 mg) twice daily.[8]	5 to 7 days[8]
	Adolescents ≥ 12 years	2000 mg dose taken 12 hours apart at earliest symptoms of a cold sore.[1, 3, 4]	1 day[1, 3, 4]

Renal impairment:

- eGFR calculator
- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 50mL/min) due to increased risk of neurological adverse effects.[1]

Treatment dosing:

- The below dose adjustments are based on an initial treating dose of 20mg/kg/dose given three times a day.[6]

	Treatment dosing	
eGFR	Standard treatment dose of 20 mg/kg/dose given three times daily.[6]	Standard treatment dose of 2000 mg given 12 hourly for 1 day.[8]
≥ 50 mL/minute/1.73m^2	No dose adjustment required	No dose adjustment required
≥ 30 to <50 mL/minute/1.73m^2	20 mg/kg/dose given twice daily	1000 mg given 12 hourly for 2 doses
≥ 10 to <30 mL/minute/1.73m^2	20 mg/kg/dose given once daily	500 mg given 12 hourly for 2 doses
<10 mL/minute/1.73m^2	10 mg/kg/dose given once daily	500 mg as a single dose

Prophylaxis dosing:

- There is limited information available regarding dose adjustments in paediatric patients for prophylaxis. The below recommendations are extrapolated from adult data.[8]

	Prophylaxis dosing[8]	
eGFR	Standard prophylaxis dose: 10 mg/kg/dose once daily	Standard prophylaxis dose: 10 mg/kg/dose twice daily
≥ 50 mL/minute/1.73m^2	No dose adjustment required	No dose adjustment required
≥ 30 to <50 mL/minute/1.73m^2	No dose adjustment required	No dose adjustment required
≥ 10 to <30 mL/minute/1.73m^2	100% dose given every 48 hours	100% dose given every 24 hours
<10 mL/minute/1.73m^2	100% dose given every 48 hours	100% dose given every 24 hours

Hepatic impairment:

- No dose reduction is required in patients with hepatic impairment.[6-8]

ADMINISTRATION

- May be administered without regard to food intake.[6, 7]
- The tablets may be crushed and mixed with water, yoghurt or apple puree, however they have a very unpleasant taste.[14]
- Patients should be instructed to drink plenty of fluids whilst undergoing treatment with valaciclovir.[1, 2, 7]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

- Not applicable

MONITORING

- Hepatic, haematological, and renal function including urea and electrolytes should be monitored with prolonged therapy (longer than 7 days).[6-8]

ADVERSE EFFECTS

As aciclovir is the active metabolite of valaciclovir, adverse effects seen with aciclovir are likely to occur with valaciclovir.[1, 15]

Common: diarrhoea, skin reactions, photosensitivity reactions, dizziness, nausea, vomiting, headache.[1, 9]

Infrequent: agitation, vertigo, urticaria, renal impairment, confusion, dyspnoea, haematuria, abdominal discomfort, hallucination.[5, 9, 15]

Rare: neurological effects (more likely in patients with renal impairment or taking high doses include; coma, encephalopathy, psychotic symptoms, delirium, seizure),leucopenia, thrombocytopenia, tremor, ataxia, thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome and multi-organ hypersensitivity syndrome, angioedema, renal impairment, nephrolithiasis.[1, 2, 9, 15]

STORAGE

Valaciclovir tablets should be stored below 30°C.[5]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **valaciclovir.** Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Antimicrobial Stewardship Policy

ChAMP Empiric Guidelines and Monographs

KEMH Neonatal Medication Protocols

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