

# Guideline

## Treatment Guideline for Infants with Congenital CMV Disease (cCMV)

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### Purpose and scope

This guideline is for the use of consultant paediatricians in consultation with Paediatric Infection Management Specialists at Queensland Children's Hospital (QCH), treating infants within the first 1 month of life with confirmed CMV disease.

### Related documents

- [CHQ-NS-60584 Cytotoxic Medication Administration– Non-Oncology Patients](#)
- [CHQ-PROC-60582 Management of Cytotoxic Drugs and Related Waste](#)
- [CHQ-PROC-60583 Management of Occupational Exposure to Cytotoxic Drugs and Related Waste](#)
- [CHQ-WI-60583 Cytotoxic Spill Management](#)
- [CHQ-PROC-01043 Medication - Administration](#)
- [CHQ-PROC-01036 Antimicrobial Prescribing and Management](#)
- [CHQ Antimicrobial restrictions](#)
- [VicTAG Handling of Hazardous Medicine Framework \(Nov 2021\)](#)

## List of abbreviations

cCMV	Congenital cytomegalovirus disease
CMV	Cytomegalovirus
CNS	Central nervous system
CSF	Cerebrospinal fluid
eLFTS	Electrolytes and Liver functions tests
FBC	Full blood count
GCV	Ganciclovir
ID	Infectious diseases
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IMPS	Infection Management and Prevention Service
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction
QCH	Queensland Children's Hospital
SNHL	Sensorineural hearing loss
TDM	Therapeutic drug monitoring
USS	Ultrasound
VGVC	Valganciclovir

## Treatment guideline for infants with congenital CMV disease (cCMV)

This guideline is for the use of consultant paediatricians, in consultation with Paediatric Infection Management team, for treating infants within the first 1 month of life with confirmed CMV disease.

### cCMV disease

CMV can infect babies in utero, in up to 7 per 1000 of all live births and can cause significant disease at birth including multi-system organ failure, growth retardation, neuro-developmental problems, and sensorineuronal hearing loss (SNHL). SNHL is the most common sequelae of cCMV, occurring in 10 to 15% of infected infants.

Both cCMV and SNHL in young children can have a profound and lifelong impact on development and quality of life, and incur a significant cost to the individual, health department and society. Early intervention is crucial in minimising the impact of SNHL on language development. Studies have shown that ganciclovir can reduce or stabilise the hearing impairment and improve neuro-developmental outcomes in infants with cCMV when treated within the first 4 weeks of life. Valganciclovir, (an oral prodrug of ganciclovir) is now available and an accepted alternative treatment option.

## Investigations

### Establish CMV disease and maternal risk:

- Urine CMV PCR from infant. Saliva CMV PCR is an alternative if urine unable to be obtained.
- If saliva or urine CMV PCR positive:
  - Blood CMV PCR quantitative (High CMV blood PCR may influence choice of cranial imaging)
  - CMV IgM and IgG
  - Maternal CMV serology (IgM, IgG, IgG avidity) – compare current and antenatal bloods.
  - Hearing screening test, if not passed requires urgent formal audiology
  - Ophthalmology: fundoscopy for CMV retinitis
  - Cranial imaging; MRI or cranial ultrasound. MRI preferred if concerns about symptomatic disease

Note: cCMV cannot be accurately diagnosed when CMV is detected on samples obtained after the first 21 days of life.

### Baseline blood tests:

- FBC
- eLFTs
- serum CMV quantitative PCR

## Treatment

### Asymptomatic infants

- Infants who are asymptomatic with no evidence of CMV disease on examination or imaging and with no hearing loss or retinitis do not require treatment of their cCMV. Ongoing follow up as below.
- However, if the viral load (quantitative CMV PCR) is  $\geq 10^5$  in an asymptomatic patient please refer to CHQ IMPS for consultation/discussion. Higher levels can be associated with greater risk of developing sequelae.

### Symptomatic Infants

Infants less than or equal to 30 days of age should be offered treatment as a standard of care if they have:

- Symptomatic focal organ disease (severe hepatitis, severe bone marrow suppression [anaemia, neutropenia, thrombocytopenia], colitis or pneumonitis) **or**
- CNS disease (microcephaly, radiological abnormalities on MRI or Cranial USS, abnormal CSF parameters or a positive CMV CSF PCR), chorioretinitis, **or**
- Sensorineural hearing loss.

Treatment on advice of Infectious Diseases Paediatrician:

1. Valganciclovir oral 16 mg/kg/dose twice daily for at least 6 weeks (treatment will be extended to 6 months in most cases)

OR

2.

- Ganciclovir IV 6 mg/kg/dose twice daily

OR

- Ganciclovir IV at initiation (starting dose: 6mg/kg/dose IV twice daily) followed by oral Valganciclovir (VGCV) (16mg/kg/dose twice daily) (on advice of Infectious Diseases Paediatrician)

First line treatment is now preferentially oral valganciclovir unless severe symptomatic CNS disease or the baby is unable to tolerate oral medication.

## **Side effects**

Ganciclovir (GCV), and less frequently Valganciclovir, is associated with bone marrow suppression. Side effects include; neutropenia, anaemia, thrombocytopenia and less commonly raised liver enzymes, urea and creatinine. Reported symptoms in adults include mood changes, confusion, rash, tiredness, tremor, abdominal pain, diarrhoea and vomiting. These appear very uncommon in infants.

Animal data indicate that administration of Ganciclovir causes inhibition of spermatogenesis and subsequent infertility. These effects were reversible at lower doses and irreversible at higher doses. Ganciclovir causes tumors in animals, although there is no information from human studies, and no evidence to date of either effects on fertility or teratogenicity. Valganciclovir use is likely to be similar.

## **Monitoring**

Close monitoring of adverse effects including neutropenia, anaemia, thrombocytopenia, hepatitis is essential.

### **FBC, eLFTs (weekly for 6 weeks, then at 8 weeks, then monthly)**

- If the neutrophil count drops to less than  $0.2 \times 10^9/L$ ; cease until count recovers to more than  $0.5 \times 10^9/L$ .  
If the neutrophil count drops to between 0.2 and  $0.5 \times 10^9/L$  then recheck weekly and consider stopping if persistent.
- If the platelet count drops to less than  $50 \times 10^9/L$  then stop until the platelet count returns to more than  $50 \times 10^9/L$ .
- Changes in renal function with rising creatinine should be discussed with Pharmacy/Paediatric IMPS team and consideration given to changing to once daily dosing.

**CMV blood viral load – after first 2 weeks.**

**Therapeutic drug monitoring (TDM) – one test at end of first week of treatment; further testing only if indicated as advised by Paediatric ID.**

- If patient is receiving IV Ganciclovir, peak level should be taken one (1) hour after end of infusion in clotted serum bottles. (levels 7 to 9 mg/L) and a trough level taken 30 minutes pre-morning dose (trough level less than 3 mg/L).
- If patient is receiving oral Valganciclovir, peak level should be taken two (2) hours after administration in clotted serum bottles. (peak level 5 to 7 mg/L). and trough level taken 30 minutes pre-morning dose (trough level less than 3 mg/L).
- Adjusting dose according to peak levels should not be necessary in the presence of adequate trough levels and a good virological response.
- As GCV/VGCV is renally excreted, if the trough level exceeds 2 mg/L, a dosing interval adjustment may be required. GVC/VGCV trough levels often decrease during therapy due to newborn renal maturation and increasing renal drug clearance. Discuss with Paediatric IMPS team.

**Long term follow-up**

- Ophthalmological examination
  - Infants with symptomatic cCMV should have regular eye examinations for the first year of life (every 3 to 6 months depending on severity of cCMV disease and previous findings) and annually thereafter (until 5 years).
  - Infants with asymptomatic disease should have initial eye examination and then if normal and viral load low/ undetectable no further examinations are required.
- Fluctuation in hearing loss is common. All infants with cCMV should have audiological testing performed at 6-month intervals for the first 3 years of life, and annually thereafter to age 5 years. ([wi\\_00147.pdf](http://www.health.qld.gov.au/wi_00147.pdf) ([health.qld.gov.au](http://www.health.qld.gov.au))
- ENT review and assessment for cochlear implants should consider the following risks:
  - In children with symptomatic cCMV about 1 in 5 have delayed SNHL and 25-50% may progress from unilateral to bilateral HL over the first 2 years of life.
  - In children with SNHL as the only cCMV symptom (asymptomatic) up to 25% may progress from unilateral to bilateral HL over first 2 years.
- All infants with cCMV should be referred for General Paediatric review yearly for the first 3-5 years of life. Formal developmental assessments beginning at the first year of life might be helpful in some children with symptomatic congenital cytomegalovirus disease and should be requested on a case-by-case basis.

## Drug administration

### Intravenous Ganciclovir:

Ganciclovir is manufactured utilising cytotoxic compounding techniques on-site by pharmacy or ordered by pharmacy from an external manufacturer and therefore arrives to ward in a premixed bag or prefilled infusion syringe. Contact pharmacy prior to initiation of IV Ganciclovir therapy to ensure timely compounding of this cytotoxic preparation. Ganciclovir is administered using cytotoxic precautions

### Oral Valganciclovir:

Valganciclovir is commercially available as a cytotoxic powder for oral solution. Valganciclovir should be prepared in a pharmacy utilizing cytotoxic precautions (preferably powder should be reconstituted in a cytotoxic isolator)

At home Valganciclovir should be kept in the provided container in a fridge.

When administered by a parent at home the parent should draw up the medication into an oral syringe as provided, wear gloves and dispose of syringe, gloves and any spills into containers provided. (see [Appendix 1: Homecare Guidelines – Administration of Oral Valganciclovir at Home](#))

**For further information on safe handling of cytotoxic medications, refer to [local policies and procedures](#).**

## Cost

Valganciclovir 50mg/mL solution 100mL bottle (note: once bottle is opened, expires 49 days from date of reconstitution) – store in fridge (2-8 degrees Celsius).

Example:

- For 3.5kg baby (16mg/kg/dose bd orally) = 56 mg orally twice daily – round dose to 60 mg (1.2 mL/dose) twice daily for ease of measurement and administration.
- A six-week course should be covered by one 100mL bottle
- Average Cost per course = \$450.00 (1 x 100mL bottle)

### Actual Cost to Patient at QCH:

Valganciclovir in this instance will need to be dispensed on a hospital prescription (non PBS- not funded) – cost to parent in a Queensland Health hospital will depend on the following:

- Cost to parent/carer (prices current for 2022/2023 Pharmaceutical benefits scheme co-payment- refer to [www.pbs.gov.au](http://www.pbs.gov.au) for current pricing):
- If they have a Medicare card: \$30-00
- If they have a Healthcare concession card and Medicare card: \$7-30
- If they don't have a Medicare card (i.e. overseas residents, not Aus. residents/citizens): Full price - \$450 + dispensing fee = approximately \$500
- Cost to Queensland Health hospital: \$450 per bottle (*current for 2023*)
- IV Ganciclovir cost will be site specific – there may be an additional fee for manufacturing on top of drug cost.

## References and suggested reading

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## Consultation

Key stakeholders who reviewed this version:

- Director, Infection Management and Prevention Service, Immunology and Rheumatology, QCH
- Paediatric Infection Specialist, QCH
- Pharmacist Advanced - Antimicrobial Stewardship, QCH
- Delegated Pharmacist Medicines Advisory Committee endorsed minor change 28/05/2024

## Guideline revision and approval history

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1.1	Pharmacist Antimicrobial Stewardship (CHQ)	Paediatric Infectious Diseases Specialist (CHQ)	Medicines Advisory Committee		
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5.0 22/07/2023	Paediatric Infectious Diseases Specialist (CHQ)  Pharmacist Advanced-Antimicrobial Stewardship (CHQ)	Medicines Committee	Advisory	Executive Services (QCH)	Director
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<b>Accreditation references</b>	National Safety and Quality Health Service Standards (1-8) Standard 3: Preventing and Controlling Healthcare-Associated Infection Standard 4: Medication Safety

## Appendix 1: Homecare Guidelines – Administration of Oral Valganciclovir at Home

### Giving Oral Valganciclovir solution at home.

#### What is oral Valganciclovir:

Oral VALCYTE (Valganciclovir) solution is a medicine that is used to prevent the growth of viruses such as cytomegalovirus or CMV (a type of Herpes virus). It prevents this virus from growing and multiplying in the body.

Valganciclovir is a medicine that requires a prescription from your doctor. Valganciclovir is classed as a cytotoxic medicine and will therefore require special handling. These medications are often identified by a **purple** label and the nurses/pharmacists at your hospital/pharmacy will also identify them for you. Be careful when handling these drugs, avoid contact with the skin.

#### How does it come:

VALCYTE (Valganciclovir) solution 50 mg/mL comes in a bottle which is reconstituted and dispensed by your pharmacist.

**All doses should be administered using appropriate oral dispensers which will be provided by the Pharmacy. Do not use oral dispensers for measuring doses of any other medicines.**

#### How is it given:

Valganciclovir can be given by mouth, nasogastric (NG) tube or gastrostomy tube (G tube, PEG tube).

It is recommended that you wear disposable purple gloves when handling or giving this solution. These will be provided by the hospital.

- Draw up the required amount of syrup into the oral dispenser provided.
- Give the dose of medicine directly into mouth and swallow. Do not mix with any liquid before giving the dose.
- Close the bottle with child-resistant bottle cap after each use.
- After giving the medicine, take apart (disassemble) the oral dispenser right away and rinse under running tap water. Then air dry before next use.
- Avoid skin contact with Valcyte for oral solution. If you come in contact with Valcyte for oral solution, wash the area well with soap and water.

#### Safe storage:

It is recommended you use a plastic lunchbox or container or zip lock sealable plastic bag with a **purple** label marked “**CYTOTOXIC-handle with care**” to store the medication.

Keep this medicine out of reach of other children and pets.

Store this medication in the original bottle in the refrigerator (between **(2 to 8 degrees Celcius. Do not freeze)**

**How to dispose of Valganciclovir:**

- Return the bottle (even if empty) to a pharmacy.
- If your doctor tells you to stop taking VALCYTE (Valganciclovir), or the solution has passed its expiry date, ask your pharmacist what to do with any solution that is left over.

**Do not use VALCYTE (Valganciclovir) solution after its expiry date (49 days after it has been made up by your pharmacy).**

Your pharmacist will have written the expiry date on the bottle for you.

**Missing a dose:**

Always give the dose exactly as the doctor prescribes. Please try not to skip any doses. If you do forget, give the dose as soon as you remember. If it is time for the next dose, do not double up, just do not give the forgotten dose, make a record of any missed doses, and tell your doctor.

While a patient is receiving treatment and for 7 days after receiving Valganciclovir, some small amounts of the drug or broken-down products may be detected in urine, faeces and vomitus. Therefore, exposure to cytotoxic drugs may occur through contamination with body waste from a treated patient. Exposure to those body wastes should be avoided.

**Nausea and vomiting:**

If your child vomits a dose within 15 minutes of taking, give the dose again. If it is after 15 minutes, please do not repeat the dose, make a note and let the doctor know.

**Spitting out doses:**

If your child spits out the medication regularly, or you are concerned they are not swallowing the whole dose, please contact your nurse/doctor. Please ensure you wear purple gloves when cleaning up any medicine that is spat out.

**Cleaning up a spill:**

If your child spits out a dose, vomits, or you accidentally spill the medication put on a pair of purple gloves to clean up the spill and discard any fluids in a plastic bag. If the spill gets on you or your child's clothes, please wash in hot water separately from other clothing. Use a disposable cloth to clean up the spill.

**Nappies:**

Wear purple gloves when changing nappies. Place soiled nappies in a plastic bag that can be tied closed and discard in regular waste.

**Urine and stools:**

Use the full flush to flush the toilet after each time your child uses the bathroom.

**Linen and clothing:**

Unsoiled clothing and linens can be washed normally. Soiled linen and clothing should be washed immediately in hot water on their own in the washing machine. Do not hand-wash soiled linens.

**Pregnancy:**

It is recommended that pregnant women or adults trying to conceive avoid handling, preparing or administering this medicine. Please talk to your doctor/nurse if you have concerns regarding this.

**Food:**

Valganciclovir doses should be given with or soon after food/feed. This will be indicated on the label or in printed information from the pharmacist.

If you have any questions, please do not hesitate to contact your child's treating Doctor or Pharmacist at your local hospital or the Queensland Children's Hospital (contact via the hospital switchboard (07) 3068 1111).