



## MONOGRAPH

# Flucytosine Monograph - Paediatric

<b>Scope (Staff):</b>	Medical, Pharmacy, Nursing
<b>Scope (Area):</b>	All Clinical Areas

### 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](#)

### QUICKLINKS

<a href="#">Dosage/Dosage Adjustments</a>	<a href="#">Administration</a>	<a href="#">Compatibility</a>	<a href="#">Monitoring</a>
---	--------------------------------	-------------------------------	----------------------------

### DRUG CLASS

Antifungal agent<sup>(1)</sup>

Flucytosine is also known as 5-FC or 5-fluorocytosine.<sup>(1, 2)</sup>

### INDICATIONS AND RESTRICTIONS

Flucytosine is indicated in the treatment of cryptococcal infections, Candida meningitis and Candida endocarditis in combination with another antifungal.<sup>(3, 4)</sup>

#### IV: Restricted (red) antifungal

ChAMP approval is required prior to prescription.

Special Access Scheme restrictions also apply. SAS [application/notification](#) must be completed online in accordance with the [TGA regulations](#).

## CONTRAINDICATIONS

- Hypersensitivity to flucytosine or any component of the formulation.<sup>(4)</sup>
- Flucytosine is contraindicated in patients with a history of hypersensitivity to flucytosine or any component of the preparation.
- Contraindicated in those with complete dihydropyrimidine dehydrogenase (DPD) deficiency due to increased risk of severe or fatal toxicity as DPD is a key enzyme involved in the metabolism of 5-fluorouracil, a metabolite of flucytosine.<sup>(1, 4-6)</sup> Pre-treatment testing for DPD deficiency is not required however, if drug toxicity is confirmed or suspected, testing of DPD activity and withdrawal of treatment should be considered.<sup>(1, 4-6)</sup>

## PRECAUTIONS

- Renal impairment can increase the risk of haematological toxicity; use with extreme caution dosage adjustments are required.<sup>(4)</sup>
- Concurrent treatment with nephrotoxic agents can reduce the excretion of flucytosine and increase the risk of toxicity, use with caution and monitor flucytosine serum concentration, blood count and renal function.<sup>(1)</sup>
- There is an increased risk of serious blood dyscrasia in patients with bone marrow suppression, those currently taking myelosuppressive medications, patients undergoing radiation therapy or patients with advanced HIV infection – use with extreme caution. Careful monitoring of hepatic function and the haematopoietic system is required as this may be irreversible.<sup>(4, 5, 7)</sup>
- Each 250 mL vial contains approximately 34 mmol of sodium.<sup>(2)</sup>

## FORMULATIONS

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

- 2.5 g/250 mL solution for infusion vial (SAS)
- 500 mg tablets (SAS)

Imprest location: [Formulary One](#)

## DOSAGE & DOSAGE ADJUSTMENTS

Neonates: [Refer to Neonatal Medication Protocols](#)

**Flucytosine should always be used in conjunction with another antifungal agent to prevent resistance.<sup>(1)</sup>**

**Children > 4 weeks to 18 years:**

**IV and oral:**

- **Standard dose:** 25 mg/kg/dose given 6 hourly. Dose may be increased to 37.5-50 mg/kg/dose given 6 hourly.<sup>(1, 4, 5)</sup> The lower dose may be sufficient for sensitive organisms.<sup>(5)</sup>

**Renal impairment:**

- [eGFR calculator](#)
- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 40 mL/min).
- CrCl  $\geq$  40 mL/minute: normal dosing
- CrCl 20 to 40 mL/minute: 100% of the normal dose given 12 hourly
- CrCl 10 to 20 mL/minute: 100% of the normal dose given 24 hourly<sup>(1, 5)</sup>
- CrCl < 10 mL/minute: 100% of the normal dose given 24 to 48 hourly – future doses should be based on plasma concentrations.<sup>(5)</sup>

**Hepatic impairment:**

- No dose adjustment required in hepatic impairment, use with caution and monitor liver function.<sup>(6)</sup>

**ADMINISTRATION****IV infusion:**

- Infuse undiluted over 20 to 40 minutes. A longer duration may be used in fluid restricted patients.<sup>(1, 2, 5)</sup>

**Oral:**

- Tablets should be taken with food to reduce stomach upset. If multiple tablets are required for each dose, they should be given over a period of 15 minutes to reduce stomach upset.<sup>(4, 7)</sup>

**COMPATIBILITY (LIST IS NOT EXHAUSTIVE)****Compatible fluids:**

- Glucose 5%
- Sodium Chloride 0.9%
- Glucose 4% with Sodium Chloride 0.18%<sup>(2)</sup>

**Compatible at Y-site:**

[Compatibilities of IV drugs](#) must be checked when two or more drugs are given concurrently.

**MONITORING****General Therapeutic Drug Monitoring**

- Monitoring of flucytosine levels is essential in all patients, especially in patients with renal impairment due to the increased risk of bone marrow suppression.<sup>(1, 4)</sup>
- Initial peak and trough levels should be taken 3-5 days after commencing therapy or any dose change. Once the dose is within the therapeutic range, weekly trough levels are required for ongoing monitoring.<sup>(7)</sup>

- Peak levels should be taken 2 hours after an oral dose. Trough levels should be taken immediately prior to the next dose.<sup>(7)</sup>
- Trough levels should be maintained between 25 and 50 mg/L with levels above 25 mg/L required for efficacy.<sup>(1, 4, 6)</sup>
- Recommended peak levels are 30 - 80 mg/L. Toxicity, including bone marrow toxicity, is associated with peak levels of more than 100 mg/L.<sup>(1, 4, 6)</sup>

**Collection tubes:**

- Serum, no gel (RED) or Lithium heparin no gel (DKGNLITH)<sup>(8)</sup>  
Minimum volume required: 2mL<sup>(8)</sup>

**Additional Monitoring:**

- At a minimum, renal, hepatic and haematological monitoring is required at baseline, and regularly throughout therapy. Monitoring should be done daily initially and then at least twice weekly.<sup>(1, 5, 6)</sup>

**ADVERSE EFFECTS**

**Common:** anaemia, leucopenia, thrombocytopenia (risk increased with plasma concentrations of more than 100 mg/L), diarrhoea, nausea, vomiting, elevated liver enzymes (dose related), rash.<sup>(1, 5)</sup>

**Infrequent or Rare:** headache, sedation, vertigo, hepatic necrosis, agranulocytosis, gastrointestinal haemorrhage, allergic reactions, toxic epidermal necrolysis, seizures, confusion, hallucinations, cardiotoxicity, aplastic anaemia, confusion, ventricular dysfunction.<sup>(1, 5)</sup>

**STORAGE**

- The vials should be stored between 15°C and 25 °C. At temperatures greater than 25°C, flucytosine is converted to 5-fluorouracil (a cytotoxic) and at temperatures below 15°C, it may precipitate.<sup>(1, 2)</sup>
- The tablets should be stored at 25°C preferably (allowed range 15°C to 30°C) and kept protected from light.<sup>(6)</sup>

**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 **flucytosine**. 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](#)

## References

1. Australian Medicines Handbook. Adelaide, S. Aust.: Australian Medicines Handbook; 2022 [cited 2022 6th Dec]. Available from: [https://amhonline-amh-net-au.pklibresources.health.wa.gov.au/](https://amhonline-amh-net.au.pklibresources.health.wa.gov.au/).
2. Symons K. Ermer J. (editors). Australian injectable drugs handbook. Collingwood: The Society of Hospital Pharmacists of Australia; 2022.
3. Antibiotic Writing Group. Therapeutic Guidelines - Antibiotic. West Melbourne: Therapeutic Guidelines Ltd; 2022. Available from: <https://tguidcdp-tg-org-au.pklibresources.health.wa.gov.au/etgAccess>.
4. Clinical Pharmacology powered by ClinicalKey [Internet]. Elsevier. 2022 [cited 2023 Jan 19th]. Available from: <http://www.clinicalpharmacology-ip.com.pklibresources.health.wa.gov.au/default.aspx>.
5. Paediatric Formulary Committee. BNF for Children: 2022. London: BMJ Group Pharmaceutical Press; 2022.
6. Up To Date - Paediatric Drug information [Internet]. Lexicomp. 2022 [cited 2023 Jan 19th]. Available from: <https://www.uptodate-com.pklibresources.health.wa.gov.au/contents/table-of-contents/drug-information/pediatric-drug-information>.
7. Miller J, editor. AHFS Drug Information. Maryland: American Society of Health-System Pharmacists; 2022.
8. PathWest. PathWest - test directory Perth2023 [cited 2023]. Available from: <https://pathwesttd.health.wa.gov.au/testdirectory/>.

**This document can be made available in alternative formats on request for a person with a disability.**

<b>File Path:</b>	<a href="W:\Paediatrics\PMH\ChAMP\Monographs\FINALISED\00 Current version 00">W:\Paediatrics\PMH\ChAMP\Monographs\FINALISED\00 Current version 00</a>		
<b>Document Owner:</b>	Head of Department – Infectious Diseases		
<b>Reviewer / Team:</b>	Children’s Antimicrobial Management Program Pharmacist		
<b>Date First Issued:</b>	October 2013	<b>Last Reviewed:</b>	January 2023
<b>Amendment Dates:</b>	January 2023	<b>Next Review Date:</b>	January 2026
<b>Approved by:</b>	Drugs and Therapeutics Committee	<b>Date:</b>	February 2023
<b>Endorsed by:</b>	Chair, Drugs and Therapeutics Committee	<b>Date:</b>	February 2023
<b>Standards Applicable:</b>	NSQHS Standards:  NSMHS: N/A Child Safe Standards: N/A		

**Printed or personally saved electronic copies of this document are considered uncontrolled**



## Healthy kids, healthy communities

Compassion
Excellence
Collaboration
Accountability
Equity
Respect

Neonatology | Community Health | Mental Health | Perth Children’s Hospital