Flucytosine Intravenous for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- **In worldwide short supply - consider oral use instead (April 2022)**
- **Must be approved by ID/microbiology**
- Not normally kept in stock in GUH- ordered on request of ID/microbiology
- Flucytosine is metabolised to 5-fluorouracil, therefore as a precaution all staff should **observe precautions recommended for handling waste products of patients receiving chemotherapy**
- Any women who is of child-bearing age or who is pregnant **should be informed of the risks of harm to a foetus** if the benefits of using flucytosine are considered to outweigh the risks of using it in such patients
- Consider an **IV to ORAL** switch as soon as the patient can tolerate oral medication. Studies show that the oral route compares favourably with the IV route in terms of efficacy (ref 2). Oral version will be made available on demand only (not kept in stock)
- **Crystals may form** if the product is stored at less than 18^{0}C
- See under 'Dose' for adjustments required in **renal** impairment

Available preparations

Ancotil **2.5g** per 250ml infusion bottle (10mg per ml)

Reconstitution

Already in solution

Infusion fluids

Not required

Methods of intravenous administration

Intravenous infusion

- **Inspect the bottle for crystals** prior to administration. See also under Storage information
- Remove the excess dose from the bottle and give the required dose over 20 to 40 minutes
- Glass bottles must be vented in one of two ways (ref 1)
  - Directly by means of a filter needle into the bottle which goes through the rubber stopper and opens into the air, or
  - Direct air vent on the air inlet of the administration set, located between the drip chamber and piercing pin, it is covered with a bacterial retentive filter to reduce the chance of contamination

Dose in adults

Dose

- Usual doseÂ 50mg/kg every 6 hours
- **Reduce** to 25mg/kg to 37.5mg/kg every 6 hours if an **extremely sensitive organism is identified or in cryptococcal meningitis if it is being used in combination with amphotericin**

Renal dose

- Dose adjust as per table below

eGFR (ml/min/1.73m^2)	Dose
Greater than 40	Dose as in normal renal function
20 to 40	Give 50mg/kg every 12 hours
10 to 20	Give 50mg/kg every 24 hours
Less than 10	Give 50mg/kg STAT, then dose according to levels Dose of 0.5g to 1g daily is usually adequate Monitor levels (but not routinely available) (ref 3) Trough levels of between 25-50microgram per ml are normally effective Avoid trough levels above 80microgram per ml

- Trough levels are to be taken just before the next dose is due

Monitoring

- Monitoring of drug levels is advised in patients who have **renal impairment or who are also taking cytarabine**
- **Weekly monitoring of full blood count, renal and hepatic function** is advised
- For recommended levels see under 'Renal dose' above. Contact biochemistry to arrange for levels as they may have to be sent away

Further information

- Each 250ml (2.5g) Ancotil bottle contains 35mmol of sodium
- Ancotil infusion may be given at the same time as sodium chloride 0.9%, glucose 5% or sodium chloride 0.18% with glucose 4%
- Take baseline cultures to allow sensitivity analysis before flucytosine is started (and also regularly throughout treatment)

Storage

- Ancotil must be stored **between 18^{0}C and 25^{0}C** in order to ensure that crystals do not form at lower temperatures and the product does not expire early at high temperatures

References

Ancotil SPC May 2021

1 Glass bottle venting: attached below

2. Brouwer, A et al. Oral versus intravenous flucytosine in patients with HIV-associated cryptococcal meningitis Antimicrobial agents and chemotherapy. March 2007,p1038-1042

3. GAPP accessed online 16th December 2021

4. Injectable Medicines Guide, Medusa, accessed online 16th December 2021

Therapeutic classification

Antifungal drug for highly resistant infections or those not responding to standard therapy