MONOGRAPH	
Flucloxacillin Monograph - Paediatric	
Scope (Staff):	Clinical Staff – Medical, Nursing, Pharmacy
Scope (Area):	Perth Children's Hospital (PCH)

This document should be read in conjunction with this DISCLAIMER

DESCRIPTION	• Flucloxacillin is a bactericidal penicillin antibiotic with a narrow spectrum of activity specific to Gram positive organisms, excluding methicillin resistant *staphylococcus aureus* (MRSA). It interferes with the bacterial cell wall peptidoglycan synthesis resulting in cell lysis.(1)
INDICATIONS AND RESTRICTIONS	• Flucloxacillin is indicated for the treatment of confirmed or suspected methicillin susceptible *Staphylococcus aureus* infections (MSSA) e.g. bacteraemia, osteomyelitis, pneumonia, cellulitis.(1, 2) **IV and Oral: Unrestricted (green) antibiotic:** • This is not a restricted agent. Follow standard ChAMP guidelines where appropriate.
CONTRAINDICATIONS	• Flucloxacillin is generally contraindicated in patients with a history of high risk allergy to penicillins.(1-4)
PRECAUTIONS	• Flucloxacillin may be prescribed in selected patients with high risk allergy to another Beta-lactam sub-class (e.g. some cephalosporins, carbapenems) in discussion with immunology. • In patients with a previous low risk reaction to flucloxacillin or another penicillin (delayed rash [>1hr after initial exposure] without mucosal or systemic involvement) the risk of subsequent reaction is low. Re-challenge may be acceptable in discussion with immunology.(2) • Use with extreme caution in jaundiced neonates or premature infants as it reduces albumin bound bilirubin to 50 – 70% of the baseline concentration.(2) • Pain and phlebitis are common and may be severe. Consider a central line if prolonged treatment or a continuous infusion is required.(3)
FORMULATIONS	**Available at PCH:** • 250mg/5mL oral liquid

	• 250mg and 500mg capsules • 1000mg powder for injection vial **Other formulations available:** • 500mg and 1000mg powder for injection vial – multiple generic brands • 250mg and 500mg capsules – multiple generic brands
DOSAGE	**Neonates (less than 30 days of age):** • Please refer to Neonatal Medication Protocols **Children (>1month to 18 years):** **IV:** • Usual dose: 50mg/kg/dose (to a maximum of 1 gram) 6 hourly[1, 5] • Severe infections (including osteomyelitis): 50mg/kg/dose (to a maximum of 2 grams) 4 to 6 hourly. Four hourly dosing should be used in critically unwell patients, those with CNS infections and/or endocarditis.[1, 5] **Oral:** • Usual dose: 12.5mg/kg/dose (to a maximum of 500mg) 6 hourly.[1, 5] • Severe infections (including osteomyelitis): 25mg/kg/dose (to a maximum of 1 gram) 6 hourly.[1, 5] • Although 6 hourly dosing is preferred, giving the four doses evenly spaced throughout the waking hours has been used in children.[6]
DOSAGE ADJUSTMENT	**Dosage adjustment required in renal impairment:** • Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 10mL/min). • To calculate the estimated glomerular filtration rate (eGFR) use the following formula[6]: $eGFR\ (mL/min/1.73m^2) = \frac{36.5 \times height\ (in\ cm)}{Serum\ creatinine\ (micromol/L)}$ • CrCl ≥10mL/minute: normal dose • CrCl <10mL/minute: 100% dose 8 hourly.[4] **Dosage adjustment in hepatic impairment:** • There is no dosage adjustment required in hepatic impairment. However, flucloxacillin is contraindicated in patients with a history of jaundice or hepatic dysfunction associated with dicloxacillin or flucloxacillin.[2, 4]

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- Flucloxacillin can cause cholestatic hepatitis. The risk is increased for patients on courses longer than 2 weeks. Pre-existing hepatic impairment is not a risk factor.[1]

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<tr><td>RECONSTITUTION</td><td>

IV: Reconstitute each vial with the volume of water for injection in the table below. Further dilution with a compatible fluid to a concentration of 50mg/mL is required prior to administration.[3]

<table>
<tr><td>Vial strength</td><td>Volume of water for injection required</td><td>Resulting concentration</td></tr>
<tr><td>1 gram</td><td>9.3mL</td><td>100mg/mL</td></tr>
</table>

Oral (250mg/5mL strength):

- Open foil packaging and reconstitute as per the product information with water as follows:
- Tap bottle until all powder flows freely; add approximately half the total volume of water for reconstitution and shake vigorously to suspend powder.
- Add remainder of the water and again shake vigorously.
- Store reconstituted solution in the refrigerator (between 2 and 8ºC) and discard any remaining suspension after 14 days.[2]
- Refer to packaging for the reconstitution instructions for alternative brands and strengths.

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<tr><td>ADMINISTRATION</td><td>

IV infusion (preferred):

- Dilute to a final concentration of 50mg/mL or weaker and infuse over 30 to 60 minutes.[3, 4]
- Rapid administration of large doses has also been associated with seizures.[1]

IV push:

- Administer a 50mg/mL or weaker solution over 3 to 4 minutes. Pain and inflammation are more common with IV push administration and may be severe.[3, 7]
- Doses greater than 25mg/kg are best given via IV infusion to reduce the risk of phlebitis.[1]

Continuous infusion:

- May be given over 24 hours by continuous infusion. Contact Pharmacy for advice.[3]

Oral:

- Give on an empty stomach at least 30 minutes before food or 2 hours after food.[1]

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MONITORING	• Renal, hepatic and haematological function should be monitored weekly with prolonged therapy (i.e. longer than 7 days).[1] • Hepatic adverse effects are more likely with larger doses or long treatment courses (greater than 2 weeks).[1, 2] • Patients should also be monitored for phlebitis if being administered via a peripheral IV catheter.[1, 3]
ADVERSE EFFECTS	**Common:** transient increases in liver enzymes and bilirubin, diarrhoea, nausea, pain and inflammation at injection site, allergy.[1] **Rare:** cholestatic hepatitis (more common in females and in treatment courses >2weeks), black tongue, vomiting, *Clostridium difficile*-associated disease, electrolyte disturbances, neurotoxicity (usually with high doses, e.g. drowsiness, hallucinations, coma, seizures), bleeding, blood dyscrasias (e.g. neutropenia-related to dose and duration of treatment, thrombocytopenia).[1]
COMPATIBLE FLUIDS	• Glucose 5% • Glucose/sodium chloride solutions • Sodium chloride 0.9% • Hartmann's[3]
STORAGE	**Oral:** • 250mg and 500mg capsules – store below 25ºC and protect from light .[2] • 250mg/5mL oral liquid – store un-reconstituted bottle below 25ºC and protect from light. After reconstitution, store in the refrigerator (between 2 and 8ºC) and discard any remaining solution after 14 days.[2] **IV:** • 500mg and 1g powder for injection vial – store below 25ºC and protect from light. Use immediately after reconstitution.[2]
INTERACTIONS	**Flucloxacillin interacts with other medications. Please consult PCH approved references (e.g. Clinical Pharmacology), your ward pharmacist or Pharmacy on 63546 for more information** • IV aminoglycoside antibiotics are inactivated by IV penicillins and cephalosporins. Aminoglycoside antibiotics are rapidly bactericidal and should be administered first. The line should then be flushed well with a compatible fluid and the flucloxacillin administered.[2, 3, 7] • Probenecid inhibits excretion of penicillins which may increase flucloxacillin levels and increase the risk of seizures in certain patients.[1, 2]

	• Flucloxacillin may inhibit platelet aggregation and therefore prolong bleeding time. Care should be taken with other drugs (e.g. warfarin) that affect the clotting process.(1) • Flucloxacillin may increase the concentration and risk of toxicity with methotrexate if used concurrently.(1)
COMMENTS	• Each 1 gram of flucloxacillin contains 2.2mmol of sodium.(3)
MANUFACTURER SAFETY DATA SHEET (SDS)	To access to the Manufacturer SDS for this product, use the following link to ChemAlert.

Please note: The information contained in this guideline is to assist with the preparation and administration of **flucloxacillin.** 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 and related external legislation, policies, and guidelines

1. Rossi S, editor. Australian Medicines Handboook. Adelaide, S. Aust.: Australian Medicines Handbook; 2020.
2. MIMS Australia. MIMS online [full product information]. St Leonards, N.S.W: CMP Medica Australia.; 2019. p. 1v. (various pagings).
3. Symons K. Ermer J. (editors). Australian injectable drugs handbook. Collingwood: The Society of Hospital Pharmacists of Australia; 2020.
4. Paediatric Formulary Committee. BNF for Children: 2019. London: BMJ Group Pharmaceutical Press; 2019.
5. Royal Australian College of General Practitioners, Pharmaceutical Society of Australia, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists. AMH: Children's Dosing Companion. Adelaide: Australian Medicines Handbook Pty Ltd; 2018.
6. Antibiotic Writing Group. eTG complete. West Melbourne: Therapeutic Guidelines Ltd; 2020. Available from: https://tgldcdp-tg-org-au.pklibresources.health.wa.gov.au/etgAccess.
7. Lilley L, Legge D. Paediatric Injectable Guidelines 5th ed. Melbourne: Royal Children's Hospital Melbourne; 2016.

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