MONOGRAPH

Daptomycin 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

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Cyclic lipopeptide antibiotic[1]

INDICATIONS AND RESTRICTIONS

- Daptomycin is used in the treatment of complicated skin and soft tissue infections, bacteraemia, infective endocarditis and osteomyelitis due to Gram positive bacteria (such as Methicillin Resistant *Staphylococcus aureus* (MRSA), Methicillin Sensitive *Staphylococcus aureus* (MSSA) or Vancomycin Resistant Enterococci (VRE)) in patients intolerant to other agents or where first line therapy has failed.[2-4]
- Daptomycin is inactivated by lung surfactant and is therefore **not** recommended for the treatment of pneumonia.[3, 4]
- **IV: Restricted (red) antibiotic**

ChAMP approval is required prior to prescribing

CONTRAINDICATIONS

- Hypersensitivity to daptomycin or any component of the formulation. [2, 3, 5]

PRECAUTIONS

- Daptomycin has been shown to increase creatine kinase (CK) levels and increase the risk of myopathy. Care should be taken in patients who have a pre-existing increased risk of myopathy (e.g. currently being treated with a statin); in these patients consideration should be given to withholding the contributing agents and CK should be measured more frequently (see monitoring section for further information).[2-4]
- Daptomycin has been associated with the development of eosinophilic pneumonia, generally after courses of 2 to 4 weeks. Patients should be monitored for signs and symptoms of eosinophilic pneumonia (see monitoring section for further information).[3, 4]
- Cases of peripheral neuropathy have been reported with daptomycin. Care should be taken in patients with pre-existing peripheral neuropathy. Patients should be monitored for signs and symptoms of neuropathy whilst on treatment and advised to report any numbness, tingling, muscle pain or tenderness, weakness or cramps. Consider ceasing daptomycin if any signs of peripheral neuropathy occur.[3, 4]
- A high MIC to vancomycin may reflect a high MIC to daptomycin; confirm susceptibility to daptomycin in this setting before altering treatment.[6]

FORMULATIONS

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

- 500mg powder for injection vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates:

- Daptomycin is not routinely used in neonates due to the musculoskeletal, neuromuscular and nervous system effects seen in canine models.[3, 4]
- There is very limited information regarding neonatal dosing. Case studies have suggested a dose of 6mg/kg/dose given 12 hourly has been used successfully. Discussion with Infectious Diseases is required.[3, 4]

Children 1-12 months old:

- Daptomycin is not routinely used first line in children <12 months old due to the musculoskeletal, neuromuscular and nervous system effects seen in canine models.[3, 4]
- Limited data is available for those infants 1-12 months of age the following doses have been suggested:
    - General dosing: 8-10mg/kg/dose IV given 24 hourly.[3, 4]

Children >12 months old:

- The doses listed below fall within the standard range.
- Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

Treatment of MRSA bacteraemia, endocarditis, bone and joint infections:[4, 5, 7, 8]

Children 1 to <7 years	12mg/kg/dose IV given 24-hourly
Children ≥7 to<12 years	9 mg/kg/dose IV given 24-hourly
Adolescents ≥12 to <18 years	7 mg/kg/dose IV given 24-hourly

Treatment of complicated MRSA skin & soft tissue infections:[5, 7]

Infants ≥1 to <2 years	10mg/kg/dose IV given 24-hourly
Children ≥2 to <7 years	9mg/kg/dose IV given 24-hourly
Children ≥7 to <12 years	7mg/kg/dose IV given 24-hourly
Adolescents ≥12 to <18years	5mg/kg/dose IV given 24-hourly

Treatment of infections due to VRE:[4]

Infants & Children 1-18 years	8-10mg/kg/dose IV given 24-hourly

Renal impairment:

- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 30mL/min).
- eGFR calculator (Google Chrome®)
- There is limited information about dose adjustment in paediatric patients with impaired renal function.

eGFR	**Recommended dose**[2, 4, 9]
≥ 30mL/minute:	normal dose
≥10 to <30mL/minute	67% of the normal dose 24 hourly
<10mL/minute	67% of the normal dose 48 hourly.
Intermittent haemodialysis	67% of the normal dose 48 hourly after dialysis
Peritoneal dialysis	67% of the normal dose 48 hourly
Continuous renal replacement therapy	8mg/kg/dose given every 48 hours.

Hepatic impairment:

- No dosage adjustment is required in patients with mild to moderate hepatic impairment. There is limited information on patients with severe impairment however available information suggestions no dose adjustment is necessary.[3, 4, 10]

Dosage adjustment required in cases of elevated creatine kinase (CK):

- An increase in CK levels has been demonstrated in 6-7% of paediatric patients who receive daptomycin [4]
    - CK >5 times the upper limit of normal: reconsider the need for treatment (or consider alternative agent) and monitor CK more frequently.[2, 4]
- CK >10 times the upper limit of normal, **OR** >5 times the upper limit of normal with signs of myopathy: daptomycin should be ceased.[2]

RECONSTITUTION & ADMINISTRATION

- To reconstitute daptomycin, **slowly** add the required volume of sodium chloride 0.9% as per the table below via a 21 gauge (or smaller) needle.[1, 3, 9]
- Rotate the vial to wet the powder. **DO NOT SHAKE**.
- Allow the vial to stand for 10 minutes then rotate again to ensure complete dissolution of the powder.
- This will result in a 50mg/mL solution.[1, 3, 9]
- Further dilution is required prior to administration.[1, 2]

Vial strength	**Volume of sodium chloride 0.9% required**	**Resulting concentration**[1, 9]
500mg	10mL	50mg/mL

IV infusion:

- **Children 1 to <7years**: Add the required dose to 25mL of compatible fluid and infuse over 60 minutes.[1, 9, 10]
- **Children ≥7 to 18 years**: Add the required dose to 50mL of compatible fluid and infuse over 30 minutes.[1, 9, 10]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Hartmann's
- Sodium chloride 0.9%[9]

Compatible at Y-site:

- *Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.*

Incompatible drugs:

- Daptomycin is not compatible with glucose containing solutions.[1, 9]

MONITORING

- Patients should have their CK measured at baseline and weekly throughout treatment. More frequent monitoring is required if:
  - There are signs of myopathy (muscle pain or weakness, especially in the extremities) and/or an elevation in CK level less than 5 times above the upper limit of normal has been detected. For elevations greater than 5 times the upper limit of normal, reconsider the need for treatment with daptomycin. Refer to the Dosage/Dosage Adjustments for further information.[2]
  - The patient is currently being treated with other agents that can cause myopathy (e.g. statins).
  - The patient is at increased risk of myopathy (e.g. renal impairment).[3, 10]
- Full blood count, hepatic and renal function should be measured regularly throughout therapy, as should signs of peripheral neuropathy.
- Eosinophilic pneumonia may develop whilst on daptomycin (usually after 2 to 4 weeks).[3]
  - Patients should be monitored for new onset or worsening of fever, dyspnoea, new infiltrates on chest imaging, and/or >25% eosinophils on BAL.
  - Daptomycin should be discontinued if signs of eosinophilic pneumonia develop.
  - Re-exposure may result in reoccurrence, so documentation of a drug allergy (Clinical Alert) should be made.[3]

ADVERSE EFFECTS

Common: headache, nausea, vomiting, diarrhoea, constipation, flatulence, rash, pruritus, injection site reactions, increased creatine kinase (CK), increased liver enzymes, hypotension, hypertension, abdominal pain, anaemia, anxiety, asthenia, dizziness, insomnia.[2, 10]

Infrequent: paraesthesia, myalgia, muscle weakness, renal impairment, reduced appetite, arrhythmias, arthralgia, electrolyte imbalance, flushing, glossitis, hyperglycaemia, altered taste, thrombocytosis, tremor, vertigo.[2, 10]

Rare: dyspepsia, eosinophilia, hypersensitivity, eosinophilic pneumonia, rhabdomyolysis, hepatotoxicity, *Clostridium difficile*-associated disease, multi-organ hypersensitivity syndrome .[2, 10]

STORAGE

- Store vials and products prepared by PCS at 2 to 8˚C.[1, 3, 9]

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 **daptomycin.** 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

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