

# Daptomycin

## Adult outpatient parenteral antimicrobial therapy (OPAT) good practice prescribing guide

**Daptomycin** is a cyclic lipopeptide with activity against Gram-positive bacterial only. It is licensed for complicated skin and soft tissue infections (cSSTI) and right sided infective endocarditis as a result of *Staphylococcus aureus* including *Staphylococcus aureus* bacteraemia.

This guide shares practical experience of the use of daptomycin in an OPAT setting. We took an evidence based approach to create the guidance. We also used expert consensus and practical experience from across NHS Scotland.

This drug summary does not provide specific treatment guidance. Individual patient treatment should take into account the core principles of antimicrobial stewardship. This includes selection of the appropriate antimicrobial for the shortest duration with oral therapy being preferred, whenever possible. Please also refer to the British National Formulary (BNF) or Summary of Product Characteristics (SPC). These have more information on licensed use, drug interactions and use in pregnancy and breast feeding. When using unlicensed medicines, doses or indications, follow local health board governance processes.

It is strongly recommended that OPAT services in Scotland adhere to the [Key performance indicators for the management of patients in an outpatient parenteral antimicrobial therapy \(OPAT\) setting](#).

# Daptomycin

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## 1 Indication and dose

Licensed indication(s) in the OPAT setting	Dose
Complicated skin and soft tissue infection (cSSTI) without <i>Staphylococcus aureus</i> bacteraemia	Licensed dose is 4mg/kg but in practice some centres use off-label 6mg/kg (see cSSTI pathway below)
cSSTI with <i>Staphylococcus aureus</i> bacteraemia	6mg/kg 24 hourly
Right sided endocarditis	Licensed dose is 6mg/kg but in practice higher doses are frequently used (see off-label indications below)

## Off-label Indications

Off-label indications in the OPAT setting	Dose
Bone and joint infection <b>OR</b> Bacteraemia (excluding Enterococcal organisms)	8-10 mg/kg* 24 hourly
Right or left sided native/prosthetic valve or device related infective endocarditis <b>OR</b> Bacteraemia involving Enterococcal organisms	10-12 mg/kg* 24 hourly

\*Use total body weight total body weight (TBW) or adjusted body weight (AdjBW) if body mass index (BMI) of 30 kg/m<sup>2</sup> or over. (See also obesity section below)

## Complicated skin and soft tissue infections (cSSTI)

Daptomycin is used as an alternative to ceftriaxone in the [SAPG OPAT pathway for the management of adults with complicated skin and soft tissue infections \(SSTI\)](#) for patients with severe anaphylaxis or other life-threatening penicillin or beta-lactam allergy or *C. difficile* concern (including episode in previous 3 months).

This pathway supports reduced hospital admissions and promotes early discharge for patients with complicated skin and soft tissue infections,

### Suggested dosing guidance in (cSSTI)

Recommended dose of daptomycin IV is 4-6mg/kg and review daily

The following dosing advice for cSSTIs in the table below is an example of pragmatic dosing in practice based on a 6mg/kg (actual body weight) dosing regimen. It is for guidance only and may be locally adapted or modified.

Doses have been rounded up to the nearest 350mg or 500mg vials.

Table: Daptomycin SSTI 6mg/kg dosing regimen adapted from Greater Glasgow and Clyde OPAT

Body weight	6mg/kg dosing*
<59kg	350mg
59-83kg	500mg
84-117kg	700mg
118-142kg	850mg
>142kg	discuss with pharmacy

\*Dose rounded to nearest vial

## 2 Route and method of administration

Refer to Summary of Product Characteristics (SPC) or Medusa for further information

Each vial must be reconstituted and the total dose may be further diluted prior to administration as follows:

### Reconstitution

Reconstitute 350mg vial with 7ml and 500mg with 10ml NaCl 0.9 %

### Method of administration

Total dose may be administered via:

- Slow IV injection over minimum 2 minutes. No further dilution needed
- IV infusion over 30 minutes. Further dilute up to 50ml NaCl 0.9 %

Daptomycin has a low pH and may cause venous irritation and tissue damage in cases of extravasation

### Rounding of doses

- Where possible use whole vials (350mg and 500mg vial strengths are available).
- If the total calculated dose is  $\leq 10\%$  above the available whole vial round the dose down (eg calculated dose 530mg, prescribe 500mg).
- Dose rounding may result in a higher mg/kg dose than recommended above. Doses over 12mg/kg are not recommended. Discuss with pharmacy if the dose is unclear.

### 3 Dose adjustments and monitoring

#### 3.1 Dose adjustments

##### Renal impairment

As renal function may fluctuate it is important to monitor renal function at least weekly and adjust dosing interval if required during the treatment course.

Information on optimal dosing and efficacy in CrCl <30 ml/min is limited. The following dose suggestions are unlicensed.

*Note:* Calculate the mg/kg dose using total body weight (TBW) or AdjBW if BMI is 30 kg/m<sup>2</sup> or over (see also obesity section below).

Renal function (Creatinine clearance (CrCl))	Dose adjustment
Less than 30 ml/min <b>OR</b> if patient is receiving irregular or daily haemodialysis	Reduce frequency to 48 hourly and more frequent monitoring is required (see below for monitoring requirements)
Regular three times weekly haemodialysis (eg Mon/Wed/Fri)	Give on haemodialysis days only (after haemodialysis)

##### Other dosage adjustments

Patient characteristic	Dosage advice
Hepatic impairment	No dose adjustment necessary
Obesity	<p>If BMI is 30 kg/m<sup>2</sup> or more use the patient's <b>adjusted body weight</b> (AdjBW) to calculate the daptomycin mg/kg dose:</p> <p><b>BMI is calculated using the following equation:</b>  <math display="block">\text{BMI} = \text{Weight (kg)} / (\text{Height (m)})^2</math></p> <p>If the patient's BMI is over 30 use <b>AdjBW equation</b> to calculate weight for daptomycin dosing.</p> <p><b>AdjBW equation</b>  <math display="block">\text{AdjBW} = (0.4 \times (\text{TBW} - \text{Ideal body weight (IBW)})) + \text{IBW}</math></p> <p><b>IBW is calculated using the following equation:</b>  <math display="block">\text{IBW} = ((\text{Ht (cm)} - 152.4\text{cm}) / 2.54) * 2.3 + 50\text{kg (male) or } 45.5\text{kg (female)}</math></p>

### 3.2 Monitoring requirements

Frequency	Recommended monitoring
<b>Baseline</b>	Urea and Electrolytes, LFTs, CRP and FBC, creatine phosphokinase (CPK)
<b>Weekly monitoring</b> ( <i>Note</i> this may be more frequent if clinically necessary)	<p>Urea and Electrolytes, LFTs, CRP, FBC, CPK (2-3 times weekly if poor renal function or receiving renal replacement therapy) For patients on higher doses consider more frequent monitoring</p> <p><b>Monitoring advice for patients that should be discussed at weekly appointment</b> Patients should be advised to report muscle pain Monitor for breathlessness or new cough as this may indicate eosinophilic pneumonitis (<i>Note</i> not usually associated with peripheral blood eosinophilia)</p>
<b>Therapeutic drug monitoring</b>	<p>Routine daptomycin therapeutic drug monitoring is not recommended because there is no clear evidence that links daptomycin concentration monitoring with clinical outcome. However, daptomycin trough concentrations may be useful in patients requiring renal replacement therapy to predict toxicity</p> <p>CPK should be measured at least weekly as a useful and easily measured surrogate marker of potential toxicity. More frequent monitoring may be required in renal impairment or those at risk of developing myopathy eg patients on statins. Please consider the following pragmatic approach.</p> <p>Daptomycin should be discontinued if:</p> <ul style="list-style-type: none"> <li>• Symptomatic rise in CPK observed (especially if CPK is more than 5 times upper normal limit)</li> <li>• Asymptomatic rise in CPK observed (CPK is more than 10 times upper limit normal)</li> </ul>

### Haemodialysis

The following table gives therapeutic drug monitoring guidance for patients on three times weekly haemodialysis

Haemodialysis dosing regimen	Target trough concentration
Regular three times weekly haemodialysis (eg Mon/Wed/Fri)	<p>Take a daptomycin 72 hour trough level (long dialysis interval)</p> <p>Recommended daptomycin trough concentration is 5-20mg/L (10 – 20mg/L in severe sepsis)</p> <p>Seek advice from pharmacy if the reported trough concentration is out with this recommended target concentration range</p> <p>Daptomycin samples are sent to North Bristol Antimicrobial Reference Laboratory for analysis; therefore, these may take 3-5 working days to be reported</p>

### Follow up

Ensure follow up is arranged with referring specialty or an infection specialist

## 4 Contraindications, cautions and adverse effects

### 4.1 Contraindications

History of severe hypersensitivity (eg anaphylactic reaction) to daptomycin or excipients.

### 4.2 Cautions

- Daptomycin may interact with recombinant thromboplastin reagents leading to falsely elevated international normalised ratio (INR) test results. Most haematology departments use RecombiPlasTin 2G reagent, which is not known to be affected by daptomycin. Please check with your haematology department and if any concerns use a capillary INR test, which is not known to interfere.
- Higher daptomycin plasma concentrations and total exposure may be observed in patients with pre-existing chronic renal impairment, which may increase risk of myopathies.
- Most brands of daptomycin vials must be kept in the fridge but please check storage instructions on individual vials as there is at least one brand on the market that requires room temperature storage. Please refer to guidance provided by the manufacturer regarding disruption of the cold chain.

### 4.3 Adverse effects

Please note that this is not an exhaustive list. Refer to the BNF or SPC

Common
gastrointestinal disturbance abnormal liver function tests
Uncommon
myopathy and rhabdomyolysis
Advise patient to report any new muscle symptoms. Where possible, the drug's manufacturers recommend avoiding concomitant administration with other drugs, which may also be associated with myopathies, eg simvastatin, sodium fusidate, etc. However, there is Scottish experience of continuing these drug combinations with patient counselling and weekly measurement of CPK levels to monitor for any potential toxicity.
Rare but serious
eosinophilic pneumonitis
Advise patients of this potential side effect and monitor for new onset respiratory symptoms (fever, cough, dyspnoea and hypoxia) or new infiltrates on chest x-ray. Peripheral eosinophil count may be normal or raised. If this reaction is suspected, stop daptomycin and discuss with an infection specialist immediately.
Unknown frequency
peripheral neuropathy severe cutaneous adverse reaction

### 5 Interactions

Please note that this is not an exhaustive list. Refer to the BNF or SPC

Interaction	Details
<b>Statins</b>	Where possible the manufacturers of daptomycin recommend avoiding concomitant administration with any other drug, which may enhance the risk of myopathies and rhabdomyolysis. However, marketing research supports the continued prescription of statins together with daptomycin.  If statin continues consider twice weekly CPK monitoring.
<b>Warfarin</b>	Must ensure follow up with anticoagulant service (or GP as per local arrangement) for INR monitoring and any necessary dosage adjustments. Patients should also be counselled on signs of over anticoagulation (eg bruising, bleeding).
<b>Hormonal contraception</b>	Additional precautions are no longer necessary when daptomycin (a non-enzyme inducing drug) is taken with combined or progestogen-only contraceptive preparation, unless diarrhoea or vomiting occurs. See manufacturer's guidance.
<b>Drug or food interactions</b>	No known serious interactions with food.

For the use of other antibiotics in an OPAT setting please refer to the [SAPG website](#)

## Table of abbreviations

AdjBW	Adjusted body weight
ASAP	Association of Scottish Antimicrobial Pharmacists
BMI	Body mass index
BNF	British National Formulary
CPK	Creatine phosphokinase
CrCl	Creatinine clearance
CRP	C-reactive protein
cSSTI	Complicated skin and soft tissue infections
FBC	Full blood count
INR	International normalised ratio
LFTs	Liver function tests
OPAT	Outpatient parenteral antimicrobial therapy
SAPG	Scottish Antimicrobial Prescribing Group
SPC	Summary of Product Characteristics
TBW	Total body weight

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