



CLINICAL GUIDELINE

Daptomycin dosing in Adults 18 years or more

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Lead Author:	Ysobel Gourlay
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Important Note:

The Intranet version of this document is the only version that is maintained. Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Daptomycin Dosing in Adults ≥ 18 years



Daptomycin is a cyclic lipopeptide antibiotic that is only active against Gram positive bacteria. Daptomycin is a restricted antibiotic and should only be prescribed on the advice of an infection specialist (see NHS GGC's Adult Protected Antimicrobial Policy for more detail ([Adult Protected Antimicrobial Policy](#))).

Guidance on toxicity monitoring

- Creatine phosphokinase (CPK) levels must be measured at baseline and at regular intervals (at least weekly, and more frequently in those with renal impairment) during treatment.
- **Eosinophilic pneumonitis**; this can present with features of a pneumonia with cough, fever, raised inflammatory markers and breathlessness / hypoxaemia. Chest x-ray will show new pulmonary infiltrates, appearances can mimic those of covid-19 pneumonia. Peripheral eosinophilia only occurs in a minority of cases. Definitive diagnosis is by finding elevated eosinophils on bronchial lavage. Respiratory failure may be severe and rapidly progressive. Clinical or radiological suspicion of pneumonia in a patient on daptomycin warrants urgent consultation with ID / microbiology and respiratory medicine.

Daptomycin Dosing

The licensed doses are 4 mg/kg once daily (for complicated skin and soft tissue infection (SSTI)) or 6 mg/kg once daily (for SSTI with *Staphylococcus aureus* bacteraemia and right-sided endocarditis with *Staphylococcus aureus* bacteraemia).¹ However, increasing evidence and post marketing research supports higher (unlicensed) doses for both licensed and off-label indications.

Within NHS GGC it has been agreed between Microbiology and Infectious Diseases that doses outlined in Table 1 below should be prescribed. The dose is calculated using actual body weight unless the patient is obese with a BMI ≥ 30 kg/m².

If BMI is unknown it may be calculated using the following equation:

$$\text{BMI} = \text{Weight (kg)} / (\text{Height (m)})^2$$

If BMI ≥ 30 kg/m² an adjusted body weight (AdjBW) should be used to calculate the daptomycin mg/kg dose. See Table 2 to calculate AdjBW and dosing in renal impairment.

Table 1 Daptomycin dosing guidance

Infection indication	Daptomycin dose (See Table 2 below for additional dosing guidance)
Skin and Soft tissue Infection	6 mg/kg every 24 hours
Bone and Joint infection or Bacteraemia (excluding Enterococcal organisms)	*8 – 10 mg/kg every 24 hours
Infective Endocarditis or Infections involving Enterococcal organisms	*Minimum 10 mg/kg every 24 hours

*Please note these are unlicensed doses (see above).

Please see additional daptomycin dosing guidance in Table 2 below. Seek advice from the Antimicrobial Pharmacy team if dosing is unclear.

Table 2 Additional dosing guidance

Rounding of dose	<ul style="list-style-type: none"> ● Round the dose up to the nearest whole vial (350mg and 500mg vial strengths are available) unless: <ul style="list-style-type: none"> ◇ the calculated dose is $\leq 10\%$ above the available whole vial, in which case, round the dose down (e.g. calculated dose 530mg, prescribe 500mg) ◇ dose rounding results in a higher mg/kg dose than described above. Doses > 12 mg/kg are not recommended. Discuss with Antimicrobial Pharmacist if the dose is unclear.
Dosing in obesity² (BMI ≥ 30 kg/m²)	<ul style="list-style-type: none"> ● If BMI ≥ 30 kg/m² an adjusted body weight (AdjBW) should be used to calculate the daptomycin mg/kg dose. <ul style="list-style-type: none"> ◇ BMI equation: $\text{BMI} = \text{Weight (kg)} / (\text{Height (m)})^2$ ◇ Adjusted body weight equation: $\text{AdjBW} = (0.4 \times (\text{TBW} - \text{IBW})) + \text{IBW}$ (IBW; ideal body weight, TBW; total body weight) ◇ Ideal body weight (see table in link below)³: Ideal body weight table (SAPG)
Dosing in renal impairment⁴	<ul style="list-style-type: none"> ● CrCl < 30 ml/min; <ul style="list-style-type: none"> ◇ Calculate the mg/kg dose as above in Table 1 (use actual body weight or AdjBW if BMI ≥ 30 kg/m²). ◇ The dosage frequency should be reduced to 48 hourly and more frequent monitoring is required (see below)

	<ul style="list-style-type: none"> • Haemodialysis; If receiving regular thrice weekly haemodialysis (e.g. Mon/Wed/Fri): <ul style="list-style-type: none"> ◇ Calculate the mg/kg dose as above in Table 1 (use actual body weight or AdjBW if BMI \geq 30 kg/m²). ◇ Give on haemodialysis days only (after haemodialysis). ◇ Take a daptomycin 72 hour trough level (long dialysis interval) and send to microbiology. Daptomycin samples are sent to Bristol for analysis therefore may take 3 – 5 working days to be reported on clinical portal (under microbiology). ◇ Recommended daptomycin trough (pre-dose) concentration range; 5 – 20 mg/L (10 – 20 mg/L in severe sepsis). Seek advice from pharmacy if the reported trough concentration is out with this recommended target concentration range. If receiving irregular or daily haemodialysis: <ul style="list-style-type: none"> ◇ Seek advice from renal and antimicrobial pharmacy teams. • Please discuss dosing in continuous ambulatory peritoneal dialysis (CAPD), intermittent haemodiafiltration (HDF), continuous venovenous haemodialysis/ haemodiafiltration (CVV HD/HDF) and continuous arteriovenous haemodialysis/ haemodiafiltration (CAV HD/HDF) with renal and infection specialists.
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Drug interactions

- Please refer to the SPC for full prescribing information.
- Daptomycin may cause myopathy and rhabdomyolysis. Where possible, the drug's manufacturers recommend avoiding concomitant administration with other drugs which may also be associated with myopathies e.g. simvastatin, sodium fusidate etc. In NHS GGC there is local experience of continuing these drug combinations with patient counselling and weekly measurement of CPK levels to monitor for any potential toxicity.
- Daptomycin may interact with recombinant thromboplastin reagents leading to falsely elevated INR results. NHS GGC's haematology department use Recombiplastin 2G reagent which is not known to be affected by daptomycin.

References:

1. Merck Sharp & Dohme (UK) Limited. Cubicin 350 mg and 500 mg powder for solution for injection or infusion. Available at; <https://www.medicines.org.uk/emc>. Accessed 16/03/2021.
2. Meng L et al. Comprehensive Guidance for Antimicrobial Dosing in Obese Adults. *Pharmacotherapy* 2017; 37 (11): 1415 – 1431.

3. Health Improvement Scotland. Ideal Body Weight Table. Scottish Antimicrobial Prescribing Group, January 2015. Available at; <https://www.sapg.scot/media/4470/ideal-body-weight-tables.pdf>. Accessed 16/03/2021.
4. UK Renal Pharmacy Group. Daptomycin monograph. Available at; <https://renaldrugdatabase.com/>. Accessed 16/03/2021.