

Dalbavancin use in Southern Health and Social Care Trust 2021 - 2022

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Dalbavancin

- ▶ Novel lipoglycopeptide with a terminal half-life of 14.4 days.
- ▶ Same mechanism of action as vancomycin
- ▶ Activity against a wide spectrum of Gram-positive microorganisms, including MRSA.
- ▶ Bactericidal in vitro against *S.aureus* at therapeutically achievable concentrations through inhibition of peptidoglycan cross-linking in the cell wall.
- ▶ Indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults.
- ▶ The recommended dose of dalbavancin in adult patients with ABSSSI is 1,500 mg administered as either a single infusion of 1,500 mg or as 1,000 mg followed one week later by 500 mg.
- ▶ Manufacturer advises reduce dose to 1000 mg as a single infusion or reduce dose to 750 mg followed one week later by 375 mg if creatinine clearance less than 30 mL/minute. ^{1,2}

Dalbavancin

▶ Benefits:

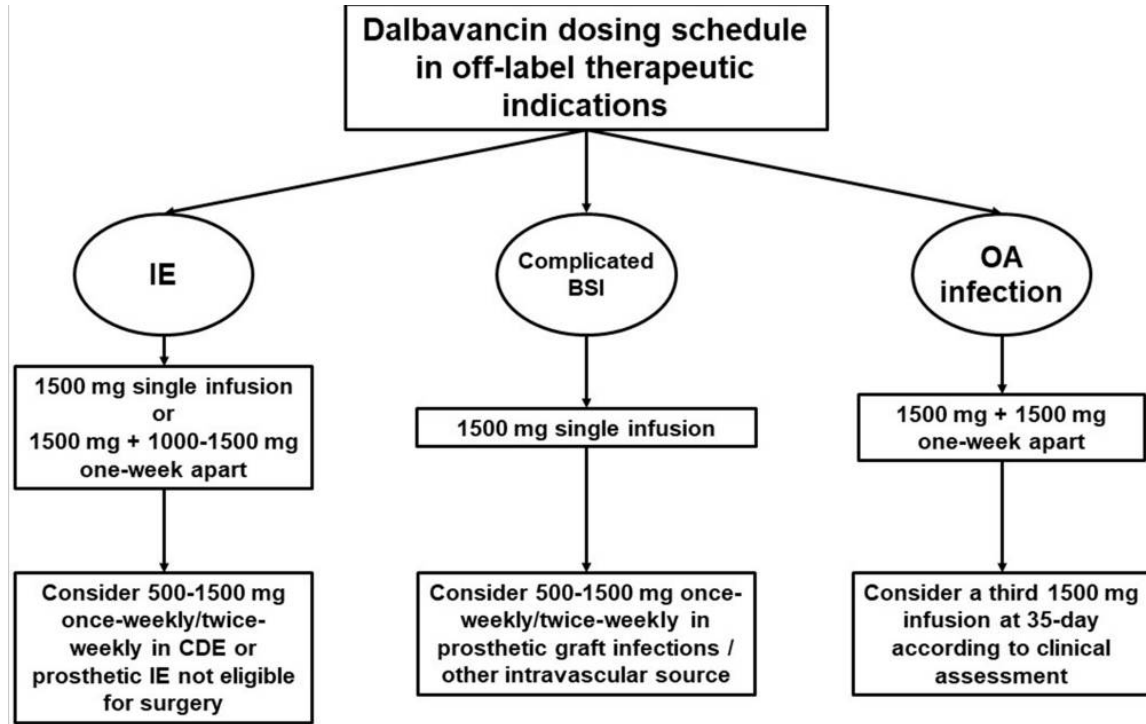
- ▶ Avoids daily administration
- ▶ No need for indwelling catheters
- ▶ No TDM
- ▶ Can speed up discharge
- ▶ Once weekly dosing
- ▶ Treat patients inappropriate for OPAT

● Limitations

- Only licensed ABSSSI
- Cost - Dalbavancin 1500 mg = £1674
 - 1 week daptomycin 1000 mg OD = £654
 - 1 week ceftriaxone 4 g OD = £28.42
- Long half-life if allergic / intolerant

A proposal of algorithm for dalbavancin dosing schedule in off-label therapeutic indications.

Real-world evidence showed a wide heterogeneity in dalbavancin dosing schedule and treatment duration in the different clinical scenarios. An attempt to standardise the therapeutic approach by Gatti et al.



Abbreviations: BSI, bloodstream infection; CDE, cardiac device-associated endocarditis; IE, infective endocarditis; OA, osteoarticular infection.⁴

Dalbavancin

▶ Osteomyelitis:

- ▶ 132 patient study (42 dalbavancin vs 90 standard of care).
- ▶ Equally efficacious after 1 year
- ▶ Safe and effective as alternative option to long-term IV antibiotics for the treatment of osteomyelitis^{1,5}

▶ Bacteraemia and Endocarditis:

- ▶ Retrospective study 1 November 2017 - 31 October 2019. University of Maryland Medical Centre. Salvage therapy e.g. IVDU.
- ▶ 4 Endocarditis and 14 Bacteraemia
 - ▶ 8 cured (1 IE (1 of 2 intended 1500mg) and 7 Bacteraemia)
 - ▶ 6 failed (1 IE (1 dose 1500mg) and 5 Bacteraemia)
 - ▶ 4 lost to follow-up (2 IE (1 dose 1500mg and 1 of 2 intended 1500mg) and 2 Bacteraemia)³

▶ Case reports

- ▶ Osteomyelitis with psoas abscess⁴
 - ▶ Cure. No relapse within 9 months of follow-up
- ▶ Spondylodiscitis D12-L1+ paravertebral abscess + ileo-femoral bypass vascular infection⁴
 - ▶ Cure, no follow-up

- ▶ Dalbavancin listed as additional alternative anti-MRSA agents immunocompetent adults with suspected septic bursitis on up-to-date.

Dalbavancin use in the Southern Trust 2021 - 2022

- ▶ For the year April 2021 - March 2022 twelve patients, with an average age of 61, were treated with dalbavancin.
- ▶ Indications for use:
 - ▶ 1 Cellulitis
 - ▶ 1 cellulitis with pre patellar bursitis
 - ▶ 1 Bursitis
 - ▶ 4 Bacteraemia
 - ▶ 1 Septic arthritis +/- osteomyelitis
 - ▶ 3 Osteomyelitis
 - ▶ 1 Brodie abscess and acute osteomyelitis

National Outcomes Registry System (NORS) criteria

Treatment Aim	
Cure	To complete an agreed OPAT duration of therapy on either intravenous and/or complicated oral antimicrobials* with no requirement for long term antimicrobial therapy.
Improvement	To complete an agreed OPAT duration of therapy on either intravenous and/or complicated oral antimicrobials (a) as part of an agreed surgical infection management plan with further surgery planned or (b) where there is a requirement for subsequent long term or an extended course of oral suppressive antimicrobial therapy, or (c) where potentially infective prosthetic material is still in situ.
Palliation	To undertake a course of OPAT on either intravenous and/or complicated oral antimicrobials where there are agreed ceilings of care due to co-morbidities with death being the likely outcome.

OPAT Service	
Treatment aim attained – uncomplicated	Completed OPAT therapy as per treatment aim with: <ul style="list-style-type: none"> • no unplanned changes in antimicrobial agent • no adverse events • no planned or unplanned readmission related to the current OPAT episode • no readmission of 24 hours or more for unrelated event (i.e. day case/ overnight stay for another medical problem allowed)
Treatment aim attained – complicated	Completed OPAT therapy as per treatment aim but with one or more of the following: <ul style="list-style-type: none"> • unplanned changes in antimicrobial agent • any adverse event including readmission for less than 24 hours related to the current OPAT episode
Treatment aim not attained	<ul style="list-style-type: none"> • Failure to complete planned OPAT therapy for any reason other than readmission due to unrelated event • Worsening of infection requiring readmission • Readmission for 24 hours or more for any cause related to OPAT including adverse events
Indeterminate	Readmission for 24 hours or more due to unrelated event
Death	Death due to any cause (except palliative)

Dalbavancin use in the Southern Trust 2021 - 2022

Diagnosis	Reason for using dalbavancin	INFECTION Outcome 30 days post discharge	OPAT Outcome 30 days post discharge	INFECTION Outcome 6 months discharge	OPAT Outcome 6 months post discharge
Right leg cellulitis	Single STAT dose of Dalbavancin 1500mg with no further treatment to facilitate discharge due to lack of District Nursing capacity.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated
Left leg cellulitis with pre patellar bursitis.	Not suitable for OPAT due to home circumstances. 3 days IV flucloxacillin then dose of dalbavancin 1500 mg given 9/3/22 and to returned to ambulatory 16/3/22 further 1000mg dose given. Reviewed 23/3/22, no further dose given.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated

Dalbavancin use in the Southern Trust 2021 - 2022

Diagnosis	Reason for using dalbavancin	INFECTION Outcome 30 days post discharge	OPAT Outcome 30 days post discharge	INFECTION Outcome 6 months discharge	OPAT Outcome 6 months post discharge
Bacteraemia / blood stream infection/ Septicaemia (MSSA)	IV drug user - 1 week of IV flucloxacillin in hospital then one dose dalbavancin 1500 mg used (poor access).	Cure	Aim attained - uncomplicated	Cure	<u>Indeterminate</u> (Readmitted within 6 months (14 - 21 May 22) for a stab wound to left anterior chest and another to left posterior chest.)
Bacteraemia / blood stream infection/ Septicaemia (MSSA)	Nursing Home resident. No District Nursing capacity. Received 6 days of IV flucloxacillin then 1 dose of dalbavancin 1500 mg prior to discharge and received 1500 mg dose one week later.	Cure	Aim attained - uncomplicated	Cure	<u>Indeterminate</u> (Readmitted within 6 months (20/3/22 - 30/3/22) for Hyponatremia and AKI secondary to dehydration. Lower respiratory tract infection.
Bacteraemia / blood stream infection/ Septicaemia (MSSA)	5 days IV flucloxacillin/ ceftriaxone. Patient pulling out cannulas. Received one dose of dalbavancin 1500 mg to complete bacteraemia treatment.	Cure	Aim attained - uncomplicated	Cure	<u>Death</u> (cause of death pneumonia secondary to dementia)
Bacteraemia / blood stream infection/ Septicaemia (MSSA)	IV drug user. MSSA Bacteraemia with extensive DVT in left arm. Flucloxacillin given for 28 days and then stat of Dalbavancin 1500 mg prior to discharge.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated

Dalbavancin use in the Southern Trust 2021 - 2022

Diagnosis	Reason for using dalbavancin	INFECTION Outcome 30 days post discharge	OPAT Outcome 30 days post discharge	INFECTION Outcome 6 months post discharge	OPAT Outcome 6 months post discharge
Septic Arthritis + /- Osteomyelitis - non surgical (left foot 5th metatarsal head septic arthritis +/- OM)	4 days benzylpenicillin and flucloxacillin. Patient commenced on dalbavancin as unable to get PICC line for OPAT. Given 1500 mg prior to discharge and further 1500mg dose after one week.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated
Osteomyelitis - non surgical (Left second toe)	Nursing Home resident. No District Nursing capacity. 8 days of IV flucloxacillin and teicoplanin then switched dalbavancin 1500 mg received as an inpatient. Further dose of dalbavancin 1500 mg in Day Clinical Centre one week later.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated
Osteomyelitis - non surgical (osteomyelitis and septic arthritis of the left 2nd toe)	Prevention of admission. Lives in a rural hilltop farm and refuses to come into hospital. MSSA from a toe swab and MRI had shown osteomyelitis and septic arthritis of the left 2nd toe. Dose was 1500 mg repeated one week later.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated
Osteomyelitis - non surgical (Left second toe)	Background motor neurone disease. One dose of daptomycin and rifampicin then dalbavancin 1500 mg which was repeated one week later.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated

Dalbavancin use in the Southern Trust 2021 - 2022

Diagnosis	Reason for using dalbavancin	INFECTION Outcome 30 days post discharge	OPAT Outcome 30 days post discharge	INFECTION Outcome 6 months post discharge T	OPAT Outcome 6 months post discharge
Brodie abscess and acute osteomyelitis at the distal tibia	During treatment with ceftriaxone WCC dropped 3.3 and neutrophils to 0.53. 7 days of 6 weeks treatment remaining. Decision to stop ceftriaxone and give stat dose of dalbavancin 1500mg to complete course.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated
Bursitis (Infective bursitis of right elbow)	No District Nurse Capacity and unable to get appropriate line inserted as IV co-ordinators on leave. Received dalbavancin 1500 mg on discharge and further 1000 mg one week later.	Cure	Aim attained - uncomplicated	Cure	Aim attained - uncomplicated

Outcome discussion

- ▶ Twelve patients were treated with dalbavancin from April 21 - March 22. Of those patients all were deemed to have been cured of the infection that dalbavancin was used to treat at 6 months after the completion of treatment.
- ▶ Nine patients aim attained (uncomplicated) 6 months after completion of treatment.
- ▶ Two patients had a treatment aim of indeterminate and one patient died.

Two Indeterminate outcomes:

- ▶ One patient treated for a bacteraemia was re-admitted within 6 months of treatment for a stab wound to left anterior chest and another to left posterior chest.
- ▶ One patient treated for a bacteraemia was re-admitted within 6 months of treatment due to hypernatremia and AKI secondary to dehydration and a lower respiratory tract infection.

One Death

- ▶ One patient passed away approximately 3 months after treatment with dalbavancin for a bacteraemia. Cause of death documented as pneumonia secondary to dementia.

Adverse events

- ▶ No adverse event recorded for 2021 - 2022
- ▶ In 2022 - 2023 Dalbavancin used for 11 patients.
 - ▶ One patient with sacral ulcer with osteomyelitis had urticarial rash with 1500 mg dalbavancin and was switched to Levofloxacin and Rifampicin to complete the 6 week course.
 - ▶ One patient with osteomyelitis left index finger. Received 1000mg dalbavancin (renal dose) experienced vomiting and diarrhea which settled the next day. Received second dose 7 days later with antiemetic prescribed.

Summary

Dalbavancin appears to offer an effective, safe, and convenient treatment option for patients with gram-positive microorganisms.

References

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