Farmacia Hospitalaria xxx (xxxx) 1–11

Farmacia HOSPITALARIA
Órgano oficial de expresión científica de la Sociedad Española de Farmacia Hospitalaria
www.elsevier.es/farmaciahospitalaria

Review

[Translated article] Therapeutic drug monitoring of dalbavancin: A systematic review of strategies and clinical applications in the treatment of complex infections

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ARTICLE INFO

Article history:
Received 4 December 2024
Accepted 2 March 2025
Available online xxxx

Keywords:
Dalbavancin
Therapeutic drug monitoring
Pharmacokinetics/pharmacodynamics
Osteoarticular infections
Dose optimization

ABSTRACT

Introduction: dalbavancin is approved for treating acute bacterial skin and soft tissue infections, but its off-label use for treating complex chronic infections has become increasingly common. Currently, there is no established dosing regimen for such infections. Given the need for prolonged treatments, a dosing adjustment strategy based on therapeutic drug monitoring may optimize its use and allow for individualized regimens. This systematic review analyzes dalbavancin dosing in complex infections and TDM-based strategies to optimize treatment.
Materials and methods: A search was conducted in PubMed, Embase, Scopus, and the Cochrane Library (2014–2024) using the following keywords: "dalbavancin", "pharmacokinetics", "pharmacodynamics", "therapeutic drug monitoring", and "TDM". Three independent reviewers selected and evaluated the studies. Clinical studies related to the pharmacokinetics of dalbavancin and the use of TDM in complex infections requiring prolonged regimens were included. Due to the heterogeneity among the studies, a qualitative analysis of the data was performed.
Results: A total of 241 articles were identified. After removing duplicates and applying the inclusion and exclusion criteria, 10 studies were included. These studies exhibited heterogeneity in design (6 retrospective and 4 prospective) and sample size, encompassing 457 patients and 1.298 samples. Most studies focused on osteoarticular infections treated with dalbavancin using an initial two-dose regimen of 1,500 mg administered one week apart, followed by dose adjustments based on plasma level monitoring. The most commonly targeted pharmacokinetic/pharmacodynamic parameters were a trough concentration above 8 μg/ml and an area under the curve/minimum inhibitory concentration ratio greater than 111.1. Therapeutic Drug Monitoring-Guided strategies were found to optimize dosing and maintain adequate plasma levels. Significant interindividual variability in plasma concentrations was observed, influenced by factors such as renal function and body surface area.
Discussion: The use of Therapeutic Drug Monitoring in dalbavancin dosing optimizes the treatment of complex chronic infections by adjusting dosing intervals and maintaining adequate therapeutic levels over extended periods. However, further validation and definition of specific pharmacokinetic/pharmacodynamic targets is required.

Monitorización terapéutica de dalbavancina: revisión sistemática de estrategias y aplicaciones clínicas en el tratamiento de infecciones complejas

Palabras clave:
Dalbavancina
Monitorización terapéutica de fármacos
Farmacocinética/farmacodinámica
Infecciones osteoarticulares
Optimización de la dosificación

RESUMEN

Introducción: dalbavancina está aprobada para infecciones bacterianas agudas de la piel y las partes blandas, pero su uso fuera de ficha técnica en infecciones crónicas complejas se ha extendido. Actualmente, no hay una pauta establecida para este tipo de infecciones; al ser necesarios tratamientos muy prolongados, una estrategia basada en el ajuste de dosis mediante monitorización terapéutica de fármacos puede optimizar su uso e individualizar la pauta. Esta revisión sistemática analiza la dosificación de dalbavancina en infecciones complejas y las estrategias basadas en la monitorización terapéutica de fármacos para optimizar el tratamiento.

DOI of original article: https://doi.org/10.1016/j.farma.2025.03.002.
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https://doi.org/10.1016/j.farma.2025.08.003

Please cite this article as: Moñino-Dominguez L, et al.. [Translated article] Therapeutic drug monitoring of dalbavancin: A systematic review of strategies and clinical applications in the treatment of complex infections. Farmacia Hospitalaria. 2025. https://doi.org/10.1016/j.farma.2025.08.003

Material y métodos: se realizó una búsqueda en PubMed, Embase, Scopus y Cochrane Library (2014–2024) con las palabras clave: «dalbavancin», «pharmacokinetics», «pharmacodynamics» «therapeutic drug monitoring» y «TDM». Tres revisores independientes seleccionaron y evaluaron los estudios. Se incluyeron estudios clínicos relacionados con la farmacocinética de dalbavancina y el uso de monitorización terapéutica en infecciones complejas que requieren pautas prolongadas. Los datos se analizaron cualitativamente debido a la heterogeneidad entre estudios.

Resultados: se identificaron 241 artículos, de los cuales, tras eliminar duplicados y aplicar criterios de inclusión y exclusión, se incluyeron 10. Estos estudios presentaron heterogeneidad en el diseño (6 retrospectivos y 4 prospectivos) y el tamaño muestral, abarcando un total de 457 pacientes y 1.298 muestras. La mayoría se centraron en infecciones osteoarticulares, tratadas con dalbavancina en regímenes de 2 dosis iniciales de 1.500 mg separadas por una semana, con ajuste de dosis posteriores según la monitorización de los niveles plasmáticos. Los objetivos farmacocinéticos/farmacodinámicos más utilizados fueron una concentración mínima o valle por encima de 8 μg/ml y una relación entre área bajo la curva y concentración mínima inhibitoria superior a 111,1; observándose que las estrategias guiadas por monitorización farmacocinética optimizaron la dosificación y mantuvieron niveles plasmáticos adecuados. Se observó variabilidad interindividual significativa en las concentraciones plasmáticas, influenciada por factores como la función renal y la superficie corporal.

Discusión: el uso de la monitorización terapéutica de fármacos en la dosificación de dalbavancina optimiza el tratamiento de infecciones crónicas complejas, ajustando intervalos entre dosis y permitiendo mantener niveles terapéuticos adecuados durante largos periodos de tiempo, aunque se requiere validación y definición de objetivos farmacocinéticos/farmacodinámicos.

Introduction

Dalbavancin is a long-lasting parenteral lipoglycopeptide antibiotic[1] that mainly exerts its antimicrobial activity through interaction with the terminal D-alanyl-D-alanine residues of peptidoglycan precursors,[2] thereby inhibiting the activity of transpeptidase and transglycosylase enzymes.[3,4] It was approved by the US Food and Drug Administration (FDA) in 2014 and by the European Medicines Agency (EMA) in 2015 for the treatment of acute bacterial skin and skin structure infections (ABSSSI).[3,5]

Its off-label use is becoming increasingly common in the treatment of complex chronic infections caused by Gram-positive bacteria, including osteoarticular infections, periprosthetic joint infections, and endocarditis.[5–7]

Dalbavancin exhibits unique pharmacokinetic and pharmacodynamic (PK/PD) properties. Its long half-life means that a single 1500 mg dose is sufficient for the treatment of ABSSSI.Alternatively, a two-dose regimen of 1000 mg followed by 500 mg 1 week later can be used.[6–9] This extended half-life of at least 8.5 days[9] is attributable to its high plasma protein binding (mainly to albumin), which reaches 93% in humans.[8,9] Its volume of distribution is greater than 10 L,[8,9] with a clearance of 0.0473 mL/min.[9] It is widely distributed in the extracellular fluid of soft tissues,[8] and its elimination is both renal (up to 45%) and extrarenal.[8,9] No dose adjustment is recommended in cases of mild or moderate renal impairment or in hepatic impairment; however, a dose reduction is necessary in cases of severe renal impairment.[8] In addition, dalbavancin does not interfere with the activity of cytochrome P450 enzymes.[10–14] All these factors contribute to its ease of use.

Dalbavancin is effective against Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus aureus* with intermediate sensitivity to vancomycin, multidrug-resistant coagulase-negative staphylococci, and vancomycin-resistant enterococci with the VanB phenotype.[11,15,16] Some complex infections, including bone and joint infections (BJI), prosthetic joint infections (PJI), and infective endocarditis (IE), are caused by *S. aureus* and other species of staphylococci and streptococci.[17,18] These infections are more difficult to treat due to biofilm formation and the variable penetration of antibiotics into bone and joint structures. This penetration can be particularly limited in bone tissue and in the presence of biofilms.[19] This challenge necessitates long-term treatment with drugs that have good tissue distribution, as has been demonstrated for dalbavancin in tissue distribution studies.[20] Therefore, dalbavancin has great potential as an antibiotic in these cases. However, these indications are not included in the current authorisation for use.

Due to its activity against Gram-positive cocci—including MRSA—its prolonged half-life, and favourable safety profile, dalbavancin is considered a potential alternative to the daily IV administration of other antibiotics, which typically necessitates prolonged hospitalisation for patients with osteoarticular, periprosthetic, and vascular graft infections.[11–13,15–19,21]

There is growing evidence supporting the prolonged use of dalbavancin in complex chronic infections, with published case series demonstrating favourable clinical outcomes.[13,18,20,22–26] However, dosing strategies vary widely between studies, and there are no clear recommendations or published guidelines on extended dosing regimens. Therefore, dosing is frequently informed by therapeutic drug monitoring (TDM).

Because of this unmet need, we conducted a systematic review to identify existing studies proposing dalbavancin administration guidelines based on TDM for complex infections. The aim was to find potential regimens that extend treatment beyond the approved dosing regimen for ABSSSI.[3,4]

In a mouse model of *S. aureus* infection, the mean free-drug area under the concentration-time curve at 24 h/minimum inhibitory concentration (24-h *f*AUC/MIC) required to achieve a 2-log reduction in *S. aureus* bacterial load (equivalent to a 100-fold decrease in the number of bacteria, or 99% reduction of the initial inoculum) was 111.1 ± 51.81.[27] This indicates that, in infected mice, the drug needed to maintain a 24-h AUC/MIC ratio greater than 111.1 is necessary to achieve a significant reduction in bacterial load. Subsequently, using population pharmacokinetic simulations, it was determined that a 24-h AUC/MIC ratio greater than 111.1 corresponded to a trough concentration of 8.04 mg/L for a MIC of 0.125 mg/L. This value was derived from the previously calculated 24-h *f*AUC/MIC thresholds in order to achieve the optimal PK/PD target against *S. aureus*, based on the most commonly observed MIC values (0.0625 mg/L and 0.125 mg/L). The 24-h *f*AUC/MIC thresholds were 6.94 mg·h/L and 13.89 mg·h/L. Taking into account the high plasma protein binding of dalbavancin, these values corresponded to total 24-h AUC values of 99.2 mg·h/L and 198.3 mg·h/L, respectively. Plasma concentrations were validated as a reliable estimate of 24-h AUC values, enabling the determination of trough thresholds of 4.02 mg/L and 8.04 mg/L for MICs of 0.0625 mg/L and 0.125 mg/L, respectively.[28]

To date, there are no systematic reviews have analysed the optimal dosing regimen for dalbavancin in treating complex chronic infections caused by Gram-positive microorganisms. Our objective was to review the current literature in order to summarise the most common dosing regimens for dalbavancin in treating this type of infection, assess whether the PK/PD objectives reported in the literature are achieved with these regimens, and explore TDM-based strategies used to optimise treatment. In addition, we aimed to describe the interindividual variability observed in plasma concentrations and the patient characteristics that may influence it.

Materials and methods

The protocol for this review was registered in the PROSPERO database (registration number: CRD42024622177).[29] The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[30] statement (see Fig. 1).

Search strategy and article selection

A systematic search of the PubMed, Embase, Scopus, and Cochrane Library databases was conducted for articles published between 2014 and 2024. The search strategy was designed using the following keywords: 'dalbavancin', 'pharmacokinetics', 'pharmacodynamics', 'therapeutic drug monitoring', and 'TDM'. The following search strategy was used: ((dalbavancin) AND (pharmacokinetics OR pharmacodynamics)) AND (therapeutic drug monitoring OR TDM). This strategy was applied to all searchable fields, including the title, abstract, and full text. Articles in both English and Spanish were eligible for inclusion. Studies conducted on animals were excluded from the review.

Two review authors (Laura Moñino-Dominguez and Alicia Aguado-Paredes) independently screened the titles and abstracts of the identified references using Rayyan. The full texts of relevant titles and abstracts were then evaluated independently to identify studies that met the inclusion criteria. Any discrepancies were resolved by consensus between the 2 reviewers: if consensus could not be reached, a third reviewer (Jaime Cordero-Ramos) was consulted.

Inclusion criteria

The following were included: randomised clinical trials; prospective studies; retrospective studies; case series; and case reports. These were published in peer-reviewed medical journals and were related to the pharmacokinetics of dalbavancin, as well as the application of TDM to personalise treatment for complex infections involving prolonged

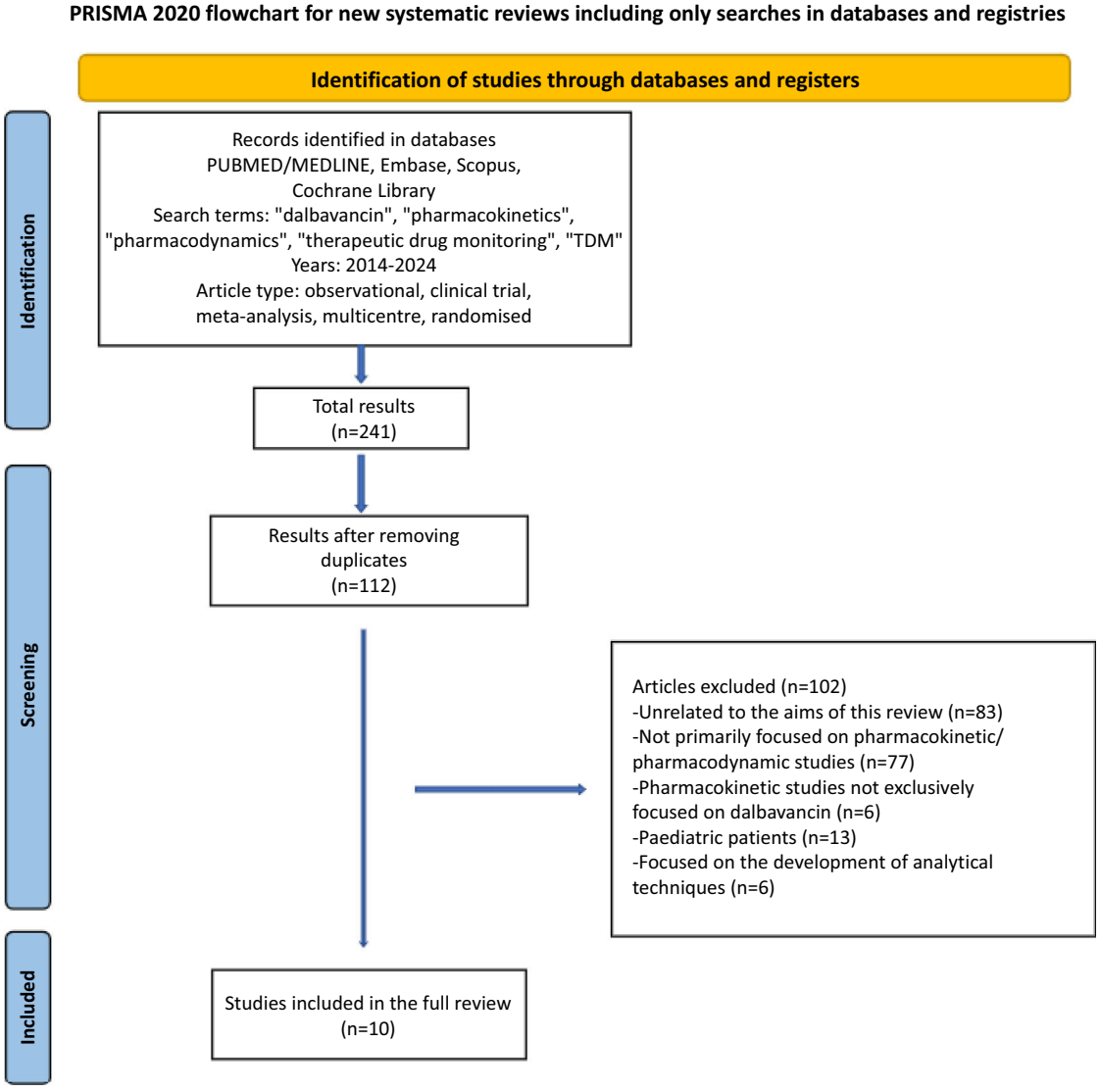

Figure 1. PRISMA flow diagram illustrating the study selection process.

treatment regimens. These infections include osteoarticular infections, infective endocarditis, and prosthetic infections (whether vascular or orthopaedic).

Exclusion criteria

The following were excluded: editorials, comments, and letters to the editor; case reports and case series involving fewer than 10 participants; studies involving animals or focusing on animal data; in vitro studies; studies whose primary objective was not the pharmacokinetic analysis of dalbavancin; pharmacokinetic studies that did not focus exclusively on dalbavancin; studies focusing on analytical techniques for determining plasma concentrations of dalbavancin; and articles whose full text was published in languages other than English or Spanish.

The exclusion of case series with fewer than 10 participants was based on the need to include only studies with a sufficiently representative sample size to allow for more reliable and generalizable conclusions.

Data extraction

Two reviewers (Laura Moñino-Dominguez and Alicia Aguado-Paredes) independently extracted relevant data from all included studies using a customised data extraction form.

They also assessed the risk of bias independenty. The Newcastle-Ottawa Scale was used to assess the quality of observational studies. This scale ranges from 0 to 9, with higher scores indicating higher quality. We chose a cut-off score of 6 or more to define studies of good quality. Any disagreements were resolved through discussion with a third review author (Jaime Cordero-Ramos).

We conducted a qualitative analysis of the included studies. A meta-analysis was not performed due to significant heterogeneity among the studies, including variability in populations, differences in interventions, and measured outcomes.

Relevant data from each study were extracted and analysed qualitatively. To provide a comprehensive overview of the available evidence, the main characteristics and findings of the studies were organised and presented in tables alongside a descriptive narrative.

Results

The initial search yielded a total of 241 articles. After removing duplicates, 112 unique articles remained. The titles and abstracts of these 112 articles were reviewed, of which 102 were excluded for not meeting the inclusion criteria. Of these 102 articles, 83 were excluded because they were unrelated to the aims of this review: 77 did not primarily analyse the pharmacokinetics of dalbavancin, while 6 analysed the pharmacokinetics of dalbavancin alongside those of other drugs. Thirteen articles were excluded because they involved studies conducted in paediatric patients, and 6 because they focused on the development of analytical techniques for determining dalbavancin concentrations in blood. Finally, 10 studies were included in the systematic review (Fig. 1).

Studies with variability in both design and sample size were included. Six of the included studies were retrospective observational,[31–36] and 4 were prospective observational[37–40] (Table 1). Nine of these were single-centre studies, and 1 was conducted in 2 centres.[36] Table 1 presents the characteristics of the reviewed studies.

A total of 1298 samples from 457 patients were included in the analysed studies. The number of samples per study ranged from 34 to 336, and the number of patients per study ranged from 14 to 133. However, some studies did not provide this information.

The reviewed studies addressed various complex infections, the most frequent of which wereosteoarticular infections (such as osteomyelitis, septic arthritis, prosthetic infections, and spondylodiscitis). These infections were reported in 9 of the 10 studies. They accounted for all (100%) infections in 5[32–34,38,40] of the studies, and 79%,[37] 76.8%,[31] and 80%[36] of infections in 3 other studies. One other study did not report the percentage of osteoarticular infections.[39]

Other types of complex infection included vascular prosthetic infections and endocarditis. However, these studies also described patients with osteoarticular infections, which were generally more prevalent.[31,36,37,39]

The main objectives of the studies included in this systematic review were to evaluate the appropriate dosage of dalbavancin for treating complex infections (particularly osteoarticular infections), describe actual dalbavancin plasma concentrations, and determine whether these concentrations exceed the therapeutic targets established in the literature. Our review also aimed to assess the usefulness of TDM in achieving PK/PD targets and optimising dosing regimens, and to describe interindividual variability in dalbavancin plasma concentrations.

Dose and administration interval

The majority of the reviewed studies used a regimen of two 1500 mg doses administered 1 week apart.[31,33–35,37,40] In some cases, patients received additional doses guided by TDM.[33–35,40]

In 2 studies, the dalbavancin regimen was adjusted for patients with severe renal impairment (glomerular filtration rate [GFR] <30 mL/min): in 1 study, two 1000 mg doses were administered 1 week apart,[31] and in the other, a regimen of 1000 mg dose was administered on day 1 was followed by a 500 mg dose guided by TDM.[33]

Another study included 2 different dosing strategies: 40.5% of patients received a single 1500 mg dose, while the remaining 58.5% received two 1500 mg doses with 1-week, 2-week, or 3-week intervals, according to the investigator's discretion. However, the basis for this was not described.[39]

In 1 study, the regimen was chosen based on previous antibiotic treatment. Patients who had previously received another antibiotic were treated with 1500 mg on days 1 and 15. Those who started with dalbavancin received doses on days 1, 15, and 42 (93.3% of patients).[36]

Another study found that 35 out of 133 patients received a single dose, while 98 received multiple dose at an average interval of 14 days. Although the exact doses were not specified, the analysis of plasma concentrations focused on patients treated with two 1500 mg doses administered 1 week apart.[32] Finally, 1 study evaluated 6 different dalbavancin administration regimens: 1500 mg on day 1 + 1500 mg on day 8; 1000 mg on day 1 + 500 mg on day 8; 1500 mg on day 1; 1500 mg on day 1 + 1500 mg on day 8 + 1500 mg on day 36; 1500 mg on day 1 + 1500 mg on day 8 + 1000 mg on day 36; 1500 mg on day 1 + 1500 mg on day 8 + 500 mg on day 36.[37]

Table 1 summarises all these regimens.

Pharmacokinetic and pharmacodynamic objectives and overall distribution of dalbavancin concentrations

The most commonly used PK/PD objective was C_{min} (trough). While most studies aimed to maintain a C_{min} of more than 8 μg/mL,[31,33–35,40] others defined thresholds of 4 μg/mL[34] or 10 μg/mL.[36] Two studies used the AUC/MIC ratio as the target: one aimed for a 24-h AUC/MIC ratio greater than 111.1,[38] and the other for an AUC/MIC ratio greater than 1000.[37]

In 1 study, Monte Carlo simulations were used to estimate the concentrations achieved after two 1500 mg doses (or 1000 mg in patients with GFR <30 mL/min) administered 1 week apart, according to GFR. This regimen was considered sufficient to maintain C_{min} greater than 8 μg/mL for the following periods:

- 4 weeks in patients with creatinine clearance (ClCr) of 90–120 mL/min.
- 5 weeks in patients with ClCr of 60–90 mL/min.
- 6 weeks in patients with ClCr of 30–60 mL/min.

Table 1
Main characteristics of the studies reviewed.

Main characteristics of the articles reviewed							
Author and year/type of study	Objective	Samples obtained/ population	Type of infection (% of patients)	Dalbavancin regimen	Type of sample/ collection time	PK/PD target	Results
Cojutti et al., 2021[31]*/ retrospective observational*	Define how to appropriately manage dalbavancin dosage regimens and TDM for optimal long-term treatment of subacute and chronic infectious diseases	289/69	Osteoarticular infections (76.8%), endocarditis endocarditis (NA), and vascular prosthetic infections (NA)	1500 mg on day 1 and day 8 (84.4%), or 1000 mg on day 1 and day 8	Plasma/different time points after the second dose, at trough	C_{min} ≥ 8.04 mg/L	**Maintaining C_{min} higher than target according to renal function** 1500 mg × 2, 1 week apart: – ClCr 90–120 mL/min: C_{min} > 8 μg/mL 4 weeks. – ClCr 60–90 mL/min: C_{min} > 8 μg/mL 5 weeks. – ClCr 30–60 mL/min: C_{min} > 8 μg/mL 6 weeks. – 1000 mg × 2, 1 week apart: C_{min} > 8 μg/mL up to 5 weeks if ClCr <30 mL/min. **Recommended timing for monitoring C_{min}:** – If ClCr 30–59 mL/min: Day 35 ± 3 – If ClCr 60–89 mL/min: Day 28 ± 3 – If ClCr 90–120 mL/min: Day 21 ± 3
Hervochon et al., 2023[32]*/ retrospective observational*	Describe the actual plasma concentrations of dalbavancin	313/133	Osteoarticular infections (100%)	1500 mg, according to clinical practice	Plasma/ concentrations 1, 2, 3, 4, 6, and 8 weeks after the 1500 mg dose	NA	**Median concentration**: – 1 week after first dose: 40.00 mg/L; after second or subsequent doses: 37.60 mg/L – 2 weeks after first dose: 25.00 mg/L; after second or subsequent doses: 34.55 mg/L – 3 weeks after first dose: 14.80 mg/L; after second or subsequent doses: 22.60 mg/L – 4 weeks after first dose: 9.24 mg/L; after second or subsequent doses: 19.20 mg/L – 6 weeks after first dose: 11.55 mg/L; after second or subsequent doses: 13.26 mg/L – 8 weeks after first dose: 9.60 mg/L; after second or subsequent doses: 7.60 mg/L GFR <60 mL/min: Higher trough concentrations than with GFR > 60 mL/min (29.4 vs 22.4 μg/mL, $p = 0.01$). **Weight** < 75 kg: higher trough concentrations than with weight > 75 kg (25.9 vs 22.2 μg/mL, $p = 0.02$)
Cattaneo et al., 2023[33]*/ retrospective observational*	Evaluate the usefulness of TDM-guided dosing to achieve PK/PD targets	336/81	Osteoarticular infections (100%)	Two 1500 mg doses 1 week apart, followed by TDM-guided doses based on C_{max} or TDM based on C_{min}	Plasma/just before the dose and after completion of the dose infusion	C_{min} ≥ 8.04 mg/L	C_{min} between 5.3 and 56 mg/L (group with C_{min}-based TDM) and 5.4 and 57.3 mg/L (group with C_{max}-based TDM) 1 week after the first dose. – C_{min} > 8 mg/L for 42–48 days after the second dose. – 8.7% of patients C_{min} < 8 mg/L **Average number of injections required**: – C_{min}-based TDM: 7.3 ± 2.6 – C_{max}-based TDM: 5.2 ± 1.8 ($p < 0.0001$)

(continued on next page)

Table 1 (*continued*)

Main characteristics of the articles reviewed

Author and year/type of study	Objective	Samples obtained/ population	Type of infection (% of patients)	Dalbavancin regimen	Type of sample/ collection time	PK/PD target	Results
							Interval between doses: – C_{min}-based TDM: 29 ± 14 days – C_{max}-based TDM: 40 ± 10 days ($p = 0.013$)
Gatti et al., 2023[34]/ *retrospective observational*	Describe the relationship between maintaining dalbavancin PK/PD efficacy thresholds and clinical outcomes	NA/17	Osteoarticular infections (100%)	Two 1500 mg doses dalbavancin, 1 week apart, followed by TDM-guided doses	Plasma/just before the second dose	C_{min} ≥ 4.02 mg/L and ≥ 8.04 mg/L	Percentage of time **≥ 4.02 mg/L**: – 100% in 13 cases – 75–99.9% in 2 cases – 50–74.99% in 2 cases Percentage of time **≥ 8.04 mg/L**: – 100% in 8 cases – 75–99.9% in 4 cases – 50–74.99% in 4 cases – <50% in 1 case
Gallerani et al., 2023[35]/ *retrospective observational*	Describe the experience of dalbavancin use in complicated cardiovascular infections with TDM support	34/21	Osteoarticular cardiovascular infections	Two 1500 mg doses 1 week apart, followed by TDM-guided doses	Plasma/NA	C_{min} ≥ 8.04 mg/L	– 85.3% of concentrations were >8.04 μg/mL – 14.7% of concentrations were 4.02–8.04 μg/mL – The next dose based on TDM between 4 and 9 weeks – Clinical success in 87.5% of patients treated with TDM vs –60% without TDM (not statistically significant)
Lafon-Desmurs et al., 2024[36]/ *retrospective observational*	Describe dalbavancin use in patients with implant-associated infections, including TDM data	94/15	Osteoarticular infections (vascular, 20% or orthopaedic, 80%)	Patients initially treated with dalbavancin: 1500 mg on days 1, 15, and 42. Patients who received dalbavancin as subsequent therapy: 1500 mg on days 1 and 15. Subsequent 1500 mg doses based on TDM	Plasma/just before next dose	C_{min} ≥ 10 mg/L	Plasma concentrations of dalbavancin before the second dose: – 69% >10 mg/L – 85% >8 mg/L – 97.9% >4 mg/L Dalbavancin plasma concentrations with dosing intervals of 4–12 weeks: – 96.7% >4 mg/L – 68.3% >10 mg/L
De Nicolo et al., 2021[37]/ *prospective observational*	Describe the long-term pharmacokinetic profile of dalbavancin in a real-life clinical setting	112/14	Osteoarticular infections (79%) and ABSSSI (21%)	Single dose of 1500 mg or 1500 mg × 2, 1 week apart	Plasma/0 h (pre-dose), 0.5 h (end of infusion), 1 h, 1 week, 2 weeks, 3 weeks, 1 month, Every 2 months	AUC/MIC >1000	**Single-dose** group: – AUC weeks 0–1: 27.230 h × mg/L (AUC/MIC: 16.246) – AUC weeks 0–2: 35,647 h × mg/L (AUC/MIC: 19.959) – AUC 0–∞: 54.666 h × mg/L (AUC/MIC: 30.680) – Median T > MIC (0.125 mg/L): 11.9 weeks – C_{max}: 390.1 μg/mL **Double dose** group: – AUC weeks 0–1 (1st dose): 2.110 h × mg/L (AUC/MIC: 18.422) – AUC weeks 0–2 (1st and 2nd doses): 58.012 h × mg/L (AUC/MIC: 32.481) – AUC 0–∞: 116.196 h × mg/L (AUC/MIC: 65.059) – Median T > MIC (0.125 mg/L): 13.7 weeks – C_{max}: 431.2 μg/mL Inverse correlation with body surface area: – AUC and T > MIC ($R = -0.881$, $p = 0.004$) – C_{max} ($r = -0.924$, $p = 0.002$)

Table 1 (*continued*)

Main characteristics of the articles reviewed							
Author and year/type of study	Objective	Samples obtained/ population	Type of infection (% of patients)	Dalbavancin regimen	Type of sample/ collection time	PK/PD target	Results
Cojutti et al., 2021[38]*/ prospective observational*	Conduct a population pharmacokinetic analysis of dalbavancin and use Monte Carlo simulations to identify effective dosing regimens for the long-term treatment of staphylococcal osteoarticular infections	120/15	Osteoarticular infections (100%)	Six dosing regimens: 1500 d1 + 1500 d8; 1000 d1 + 500 d8 1500 d1; 1500 d1 + 1500 d8 + 1500 d36; 1500 d1 + 1500 d8 + 1000 d36; 1500 d1 + 1500 d8 + 500 d36	Plasma/at the end of the first dose infusion (day 1), before and at the end of the second dose infusion (day 8) and weekly for 6 week intervals	24-h AUC/MIC >111.1	Two 1500 mg doses 1 week apart achieved an: – 24-h AUC/MIC >111.1 for 5 weeks **Additional** doses prolong the duration of the target: – 500 mg: Maintains the target for 7 weeks – 1000 mg: Maintains target for 8 weeks – 1500 mg: Maintains target for 9 weeks
Stroffolini et al., 2022[39]*/ prospective observational*	Evaluate the role of a TDM-based approach to optimise the use of dalbavancin, focusing on PK/PD parameters and their relationship to clinical outcomes	NA/76	Osteoarticular infections, ABSSSI, and endocarditis	Single dose of 1500 mg or two 1500 mg doses at 1-week, 2-week, or 3-week intervals	Plasma/0 h (pre-dose), 0.5 h (end of infusion), 1 h, 1 week, 2 weeks, 3 weeks, 1 month, Every 2 months, for 6 months	NA	Group 0 (**One 1500 mg dose**): – C_{max} first dose: 41.6 mg/L – AUC weeks 0–4: 41.681 mg·h/L Group 1 (**two 1500 mg doses 1 week apart**): – C_{max} first dose: 347.0 mg/L – C_{max} second dose: 420.6 mg/L – AUC weeks 0–4: 79.486 mg·h/L Group 2 (**two 1500 mg doses 2 weeks apart**): – C_{max} first dose: 323.3 mg/L – C_{max} second dose: 337.0 mg/L – AUC weeks 0–4: 62.432 mg·h/L Group 3 (**two 1500 mg doses, 3 weeks apart**): – C_{max} first dose: 383.8 mg/L – C_{max} second dose: 432.4 mg/L – AUC weeks 0–4: 68.835 mg·h/L
Cattaneo et al., 2024[40]*/ prospective observational*	Demonstrate that proactive TDM based on C_{min}/C_{max} can optimise the use of dalbavancin in the prolonged treatment of osteoarticular infections	NA/16	Osteoarticular infections (100%)	Two 1500 mg doses 1-week apart, followed by TDM-guided doses	Plasma/before and after the second dose	C_{min} ≥ 8.04 mg/L	C_{min}: – Range: 5–68 mg/L – Interindividual coefficient of variation: 33% – 8% of concentrations were < 8 mg/L Injections: – Administered every 39–47 days

ABSSSI, acute bacterial skin and skin structure infections; ClCr, creatinine clearance; C_{min}, minimum (trough) concentration; C_{max}, maximum concentration; d, day; GFR, glomerular filtration rate; NA, not specified; PK/PD, pharmacokinetic-pharmacodynamic; TDM, therapeutic drug monitoring.

In patients with a ClCr of less than 30 mL/min, reduced doses maintained a C_{min} of over 8 μg/mL for 5 weeks.[31]

Another study which used a 24-h AUC/MIC ratio greater than 111.1 as the PK/PD target demonstrated that the 2-dose regimen of 1500 mg on days 1 and 8 maintained this target over a 5-week period. Furthermore, administering additional doses of 500 mg, 1000 mg, and 1500 mg on day 36 (week 5) prolonged this period to 7, 8, and 9 weeks, respectively. However this study did not include patients with impaired renal function.[38] Similar results were observed in another study, where C_{min} remained greater than 8 μg/mL for up to 6 weeks after the second 1500 mg dose.[33]

Another study found that 1 week after the initial 1500 mg dose, 69% of C_{min} concentrations were greater than 10 μg/mL, 85% were greater than 8 μg/mL, and 97.9% were greater than 4 μg/mL. Administered additional 1500 mg doses administered at 4- to 12-week intervals based on TDM resulted in 96.7% of C_{min} concentrations exceeding 4 μg/mL and 68.3% exceeding 10 μg/mL.[36]

Another study used AUC and MIC to evaluate the difference in dalbavancin exposure between patients treated with a single 1500 mg dose and those treated with two 1500 mg doses administered 1 week apart. The results showed that the double-dose group had a greater cumulative exposure (AUC 0–∞: 116.196 h·mg/L vs 54.666 h·mg/L),

remained above the MIC for a longer period (13.7 weeks vs 11.9 weeks), and had a greater maximum plasma concentration (C_{max}: 431.2 μg/mL vs 390.1 μg/mL). Although both groups exceeded the established cut-off point of an AUC/MIC ratio greater than 1000, exposure was significantly higher with 2 doses.[37]

Similarly, another study used by using minimum (trough) concentrations to compare exposure between patients who received a single dose versus those who received successive doses. Table 1 shows that these concentrations were higher in patients who received successive doses than in those treated with a single dose, when measured at the same time interval after the last dose in both groups.32

Finally, 1 study evaluating C_{max} found that patients who received two 1500 mg doses administered 1 week apart had a significantly greater C_{max} (420.6 μg/mL, $p = 0.05$) and cumulative AUC (79.486 mg·h/L, $p < 0.001$) values in the first 4 weeks (AUC 0–4 weeks) than those who received doses 2 or 3 weeks apart. In addition, a significant correlation was found between C_{max} after the first dose and the cumulative AUC in the first 4 weeks ($p = 0.018$). Patients with a C_{max} of less than 313 μg/mL after the first dose were at an increased risk of therapeutic failure (sensitivity: 100%; specificity: 78%; $p = 0.035$).[39] Table 1 shows the C_{max} and AUC values for the different groups.

Therapeutic drug monitoring of dalbavancin

Five studies evaluated adjustments to the TDM-based dalbavancin dosage regimens. In these studies, the frequency of additional doses was optimised after an initial regimen involving two 1500 mg doses administered 1 week apart.

One of these studies, based on a population pharmacokinetic model, suggested different time points at which to measure trough concentrations according to the dosing regimen and renal function. For patients with CrCl of 30–59, 60–89, and 90–120 mL/min, TDM was recommended 35 ± 3, 28 ± 3, and 21 ± 3 days after the first 2 doses were administered, respectively.[31]

One study found that a TDM-guided strategy enabled additional dalbavancin doses to be administered at intervals of 4- to 9-week, adjusted according to the patient's renal function. The timing of the next dose was determined using the aforementioned population pharmacokinetic model.[31] This strategy resulted in 85.3% of plasma concentrations exceeding 8 μg/mL, with clinical success rate of 87.5% in patients with TDM compared to 60% in those without TDM, although this difference was not statistically significant.[35]

Another study evaluated the long-term outcomes of incorporating TDM into routine clinical practice. The optimal timing of the next dose was estimated using logarithmic models based on C_{min} and C_{max}. The aim was to maintain C_{min} greater than 8 μg/mL, and 82% of the measurements showed that this target had been achieved. Additional doses were administered at an average interval of 39–47 days, depending on plasma concentrations.[40]

One study compared a TDM approach based on C_{min} with one based on C_{max}. There were no statistically significant differences in mean C_{min} between the 2 groups (Table 1). Less than 10% of C_{min} values were less than 8 μg/mL, and none were less than 4 μg/mL. The C_{max}-based approach achieved longer intervals between administrations, requiring fewer doses and demostrating statistically significant differences. The mean number of injections required was 5.2 ± 1.8 with the C_{max}-based approach, compared to 7.3 ± 2.6 with the C_{min}-based approach ($p < 0.0001$). The mean interval between doses was 40 ± 10 days with the C_{max}-based approach, compared to 29 ± 14 days with the C_{min}-based approach ($p = 0.013$).[33]

Finally, another study found that a TDM-guided strategy enabled dosing intervals to be increased to between 4 and 12 weeks. This resulted in 96.7% of concentrations exceeding 4 μg/mL and 68.3% exceeding 10 μg/mL. However, the method used to determine the timing of the next dose was not specified.[36]

Interindividual variability

Considerable interindividual variability in trough concentrations was observed. One study found values ranging from 5.3 to 56 mg/L (C_{min}-based TDM group) and from 5.4 to 57.3 mg/L (C_{max}-based TDM group).[33] Another study found that trough concentrations fluctuated between 5 and 68 μg/mL, with a coefficient of variation of 33%.[40]

The variability of dalbavancin concentrations was largely due to renal impairment. Concentrations were significantly higher in patients with a GFR of less than 60 mL/min than in those with a GFR of greater than 60 mL/min (29.4 μg/mL vs 22.4 μg/m, $p = 0.01$).[32] One study identified ClCr as the only variable associated with dalbavancin elimination ($p = 0.041$), showing an inverse relationship.[31] TDM-adjusted dosing intervals ranged from 4 to 9 weeks, depending on renal function.[35] Dose adjustment using Monte Carlo simulations enabled adequate plasma concentrations to be maintained in patients with renal impairment.[31]

Body weight also had a significant impact on dalbavancin concentrations. Patients weighing more than 75 kg had significantly lower plasma concentrations than those weighing less than 75 kg (22.2 μg/mL vs 25.9 μg/mL, $p = 0.02$).[32]

Body surface area was another important factor influencing drug exposure. One of the studies found an inverse relationship between body surface area and total AUC during the first 2 weeks of treatment (AUC 0–2 weeks: 58.012 h × mg/L, $r = -0.881$, $p = 0.004$), as well as with time above the MIC (T > MIC, $r = -0.881$, $p = 0.004$), and with C_{max} ($r = -0.924$, $p = 0.002$).[37] These findings were confirmed in another study that identified a significant inverse correlation between body surface area and AUC in the first week ($p = 0.006$), AUC in the first month ($p = 0.004$), and C_{max} ($p = 0.002$). This suggests that doses need to be adjusted for patients with a larger body surface area to achieve adequate therapeutic concentrations.[39]

Discussion

This systematic review is the most comprehensive analysis to date of dalbavancin plasma concentration monitoring in patients with complex infections. It includes 10 observational studies, comprising 1298 samples from 457 patients. The results highlight the usefulness of TDM in optimising dalbavancin dosing regimens and achieving pharmacokinetic/pharmacodynamic goals, particularly in settings characterised by high inter-individual variability in plasma concentrations.

Most of the reviewedstudies used a 2-dose regimen of 1500 mg administered 1 week apart. This regimen, which is based on population pharmacokinetic models, maintains adequate concentrations for 5 weeks.[38] However, considerable flexibility in dosing regimens was observed, with TDM being used to determine the optimal timing of additional doses,[33–36,40] and dose adjustments being made in patients with renal impairment.[31,33]

Based on studies by Lepak[27] and Cojutti,[28] the most common PK/PD targets were maintaining trough concentrations greater than 8 μg/mL[31,33–35,40] or achieving an AUC/MIC ratio greater than 111.1. However, although 1 study proposed a more restrictive threshold of 10 μg/mL,[36] no justification was provided for this, raising questions about its clinical relevance.

While most of the reviewed studies used C_{min} or the AUC/MIC ratio as PK/PD targets, some evaluated C_{max} as an exposure parameter, justifying its use as an alternative for assessing dalbavancin pharmacokinetics and predicting its behaviour.[33,39] This parameter has been shown to be related to early clinical response, with a correlation was found between values of less than 313 mg/mL after the first dose and a higher

risk of therapeutic failure.[39] In addition, patients who received two 1500 mg doses administered 1 week apart achieved significantly higher C_{max}, which translated into greater cumulative exposure (AUC 0–4 weeks).[39] Another study used C_{max} as an alternative to C_{min} to guide TDM and adjust dosing intervals.[33] However, the AUC/MIC ratio and C_{min} remain the most well-established PK/PD targets for assessing the long-term effectiveness of dalbavancin.

Another study set an AUC/MIC ratio threshold of greater than 1000,[37] based on a dalbavancin pharmacokinetic model.[41] This threshold was determined using Monte Carlo simulations and PK/PD models, and represents the cumulative exposure to dalbavancin throughout the course of treatment. It complements the 24-h AUC/MIC ratio threshold greater than 111.1, as maintaining this value over time enables a total AUC/MIC ratio greater than 1000 to be achieved.[41]

Most of the studies reviewed found that administering two 1500 mg doses 1 week apart was an effective regimen for achieving PK/PD targets.[31,33–35,40]

Five studies used TDM to adjust the dalbavancin dosing regimen following the initial doses,[33–36,40] using strategies such as Monte Carlo simulations or adjustments based on trough or C_{max} concentrations. These strategies enabled therapeutic concentrations to be maintained for prolonged periods and reduced the frequency of dalbavancin administration, particularly in patients with renal impairment.[33,38,40] It was also demonstrated that administering additional doses at specific times could extend the period during which trough concentrations remain above the therapeutic target. This suggests that TDM can be used to to extend the interval between doses without compromising clinical outcomes. These results are important because standard regimens approved for treating ABSSSI maintain adequate plasma concentrations for approximately 3 weeks. While this timeframe is generally sufficient for treating these infections, it is insufficient for treating complex or chronic infections.

Although no statistically significant differences in clinical success were found between patients with and without TDM,[35] this result may be due to the small sample size. Further research is needed to confirm this finding.

Another key finding of the reviewed studies was that plasma dalbavancin concentrations varied between individuals and were influenced by factors including renal function, weight, and body surface area.[31,32,37,39] Patients with a GFR of less than 60 mL/min showed significantly higher concentrations, while those weighing more than 75 kg or with a larger body surface area—for which no specific threshold was identified—showed lower exposure to the drug. These findings reinforce the importance of individualised dose adjustment for patients with significant variations in renal function or body weight.

Conclusions

Based on the available evidence, we recommend therapeutic monitoring of dalbavancin between 3 and 5 weeks after the initial treatment, depending on renal function, to determine whether a further dose is required.

For patients with a GFR of 60 mL/min or more, trough concentrations greater than 8 μg/mL are usually maintained for 4–5 weeks after two 1500 mg doses have been administered 1 week apart. If TDM is unavailable and treatment requires extension, an additional 500 mg, 1000 mg, or 1500 mg dose may be administered at week 5. This will prolong exposure by 1, 2 or 3 additional weeks, respectively, depending on the expected duration of treatment.

If TDM is available, management can be adjusted according to plasma concentrations:

- Adequate concentrations (greater than 8 μg/mL): If treatment needs to be extended, continue clinical monitoring and consider repeating TDM in 2 weeks.
- Concentrations 6–8 μg/mL: repeat TDM in 1 week. Consider a 500 mg dose if concentrations fall or there are signs of therapeutic failure. Repeat TDM in 2 weeks.
- Concentrations 4–6 μg/mL: administer 1000 mg and repeat TDM in 2 weeks.
- Concentrations of less than 4 μg/mL: administer 1500 mg and repeat TDM in 2 weeks.

As the effects of additional doses has not been studied in patients with a ClCr of less than 60 mL/min, their empirical administration is not recommended. If subtherapeutic concentrations are detected, redosing should be based exclusively on TDM; therefore, monitoring may be performed at 5 or 6 weeks. If a significant decrease in concentrations is confirmed and an additional dose is deemed necessary, the most prudent option may be to administer a 500 mg dose with reassessment using TDM at 2 weeks.

In patients with severe renal impairment (a ClCr <30 mL/min), administering two 1000 mg doses on days 1 and 8 may be an appropriate strategy.

These recommendations are based on the best available evidence to date, but they should be interpreted with caution and adapted to each patient's individual clinical situation. The final decision on redosing should take clinical progress into account and, whenever possible, be supported by TDM.

Larger sample size studies and randomised designs are essential to validate and develop dosing recommendations for complex Gram-positive infections treated with dalbavancin. It would also be desirable to standardise PK/PD endpoints and evaluate the impact of TDM on broader clinical parameters, such as infection clearance.

In summary, this review demonstrates that a TDM-based approach not only ensures adequate drug exposure but also enables personalised dosing according to patient characteristics. Although the results are promising, further evidence from clinical trials is needed to establish these strategies as standard clinical practice.

Limitations

This review has the following limitations:

- Study design: all of the reviewed studies were observational, which introduces potential biases and limits the possibility of establishing causal relationships.
- Small sample size: the results of several studies are difficult to generalise due to their small sample size.
- Heterogeneity in methods and objectives: the results are difficult to compare due to a lack of consensus on PK/PD cut-off points.
- Single-centre setting: most studies were conducted in a single centre, which limits the applicability of the findings to different clinical settings.

Strengths

This review provides a comprehensive and up-to-date overview of studies published on the therapeutic monitoring of dalbavancin since 2021, emphasising its relevance and novelty in the clinical context of treating infections that require prolonged management with this antibiotic.

Despite the limitations inherent to observational studies, this review represents a significant advance in understanding the pharmacokinetics of dalbavancin and its application in complex infections.

This review also identifies emerging areas of research that could address gaps in the current literature. Although the sample size of the included studies is limited, this issue has been addressed through

detailed analysis and a focus on consistent patterns within the samples analysed.

Funding

None declared.

Conflicts of interest

None declared.

CRediT authorship contribution statement

Laura Moñino-Dominguez: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Alicia Aguado-Paredes:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Jaime Cordero-Ramos:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization.

References

1. Malabarba A, Goldstein BP. Origin, structure, and activity in vitro and in vivo of dalbavancin. J Antimicrob Chemother. 2005;55(Suppl 2):ii15–20. doi:10.1093/jac/dki005.
2. Nagarajan R. Structure-activity relationships of vancomycin-type glycopeptide antibiotics. J Antibiot (Tokyo). 1993;46(8):1181–95. doi:10.7164/antibiotics.46.1181.
3. EMA. *Annex 1. Summary of product characteristics*. European Medicines Agency; Amsterdam, the Netherlands. [accessed 08 Sep 2024]; 2015. Available from: https://ec.europa.eu/health/documents/community-register/2015/20150219130765/anx_130765_en.pdf.
4. Ramdeen S, Boucher HW. Dalbavancin for the treatment of acute bacterial skin and skin structure infections. Expert Opin Pharmacother. 2015;16(13):2073–81. doi:10.1517/14656566.2015.1075508.
5. Lovatti S, Tiecco G, Mulé A, Rossi L, Sforza A, Salvi M, et al. Dalbavancin in bone and joint infections: a systematic review. Pharmaceuticals (Basel). 2023;16(7):1005. doi:10.3390/ph16071005.
6. De Vito A, Fiore V, Colpani A, Zauli B, Fanelli C, Tiseo G, et al. The current and future off-label uses of dalbavancin: a narrative review. Eur Rev Med Pharmacol Sci. 2023;27(3):1222–38. doi:10.26355/eurrev_202302_31233.
7. Simon S, Frank BJH, Hartmann S, Hinterhuber L, Reitsamer M, Aichmair A, et al. Dalbavancin in gram-positive periprosthetic joint infections. J Antimicrob Chemother. 2022;77(8):2274–7. doi:10.1093/jac/dkac178.
8. Molina KC, Miller MA, Mueller SW, Van Matre ET, Krsak M, Kiser TH. Clinical pharmacokinetics and pharmacodynamics of dalbavancin. Clin Pharmacokinet. 2022;61(3):363–74. doi:10.1007/s40262-021-01088-w.
9. Dash RP, Babu RJ, Srinivas NR. Review of the pharmacokinetics of dalbavancin, a recently approved lipoglycopeptide antibiotic. Infect Dis (Lond). 2017;49(7):483–92. doi:10.1080/23744235.2017.1296968.
10. Soriano A, Rossolini GM, Pea F. The role of dalbavancin in the treatment of acute bacterial skin and skin structure infections (ABSSSIs). Expert Rev Anti Infect Ther. 2020;18(5):415–22. doi:10.1080/14787210.2020.1746643.
11. Righi E, Visentin A, Meroi M, Carrara E, Tacconelli E. Dalbavancin in the treatment of acute bacterial skin and skin structure and other infections: a safety evaluation. Expert Opin Drug Saf. 2022;21(9):1171–81. doi:10.1080/14740338.2022.2122437.
12. Simonetti O, Rizzetto G, Molinelli E, Cirioni O, Offidani A. Review: a safety profile of dalbavancin for on- and off-label utilization. Ther Clin Risk Manag. 2021;17:223–32. doi:10.2147/TCRM.S271445.
13. Gatti M, Andreoni M, Pea F, Viale P. Real-world use of dalbavancin in the era of empowerment of outpatient antimicrobial treatment: a careful appraisal beyond approved indications focusing on unmet clinical needs. Drug Des Devel Ther. 2021(15):3349–78. doi:10.2147/DDDT.S313756.
14. Sader HS, Streit JM, Mendes RE. Update on the in vitro activity of dalbavancin against indicated species (*Staphylococcus aureus*, *Enterococcus faecalis*, β-hemolytic streptococci, and *Streptococcus anginosus* group) collected from United States hospitals in 2017-2019. Diagn Microbiol Infect Dis. 2021;99(1):115195. doi:10.1016/j.diagmicrobio.2020.115195.
15. Weber RE, Fleige C, Layer F, Neumann B, Kresken M, Werner G. Determination of a tentative epidemiological cut-off value (ECOFF) for dalbavancin and *Enterococcus faecium*. Antibiotics (Basel). 2021;10(8):915. doi:10.3390/antibiotics10080915.
16. Mendes R, Mariana C, David JF, Robert K, Helio S, Ronald N. Update on dalbavancin activity tested against gram-positive clinical isolates responsible for documented skin and skin-structure infections in US and European hospitals (2011–2013). J Antimicrob Chemother. 2016;71(1):276–8. doi:10.1093/jac/dkv303.
17. Talha KM, Baddour LM, Thornhill MH, Arshad V, Tariq W, Tleyjeh IM, et al. Escalating incidence of infective endocarditis in Europe in the 21st century. Open Heart. 2021;8(2):e001846. doi:10.1136/openhrt-2021-001846.
18. Morata L, Cobo J, Fernández-Sampedro M, Guisado Vasco P, Ruano E, Lora-Tamayo J, et al. Safety and efficacy of prolonged use of dalbavancin in bone and joint infections. Antimicrob Agents Chemother. 2019;63(5):e02280–318. doi:10.1128/AAC.02280-18.
19. Landersdorfer CB, Bulitta JB, Kinzig M, Holzgrabe U, Sörgel F. Penetration of antibacterials into bone: pharmacokinetic, pharmacodynamic and bioanalytical considerations. Clin Pharmacokinet. 2009;48(2):89–124.
20. Dunne MW, Puttagunta S, Sprenger CR, Rubino C, Van Wart S, Baldassarre J. Extended-duration dosing and distribution of dalbavancin into bone and articular tissue. Antimicrob Agents Chemother. 2015;59(4):1849–55. doi:10.1128/AAC.04550-14.
21. Durante-Mangoni E, Gambardella M, Iula VD, De Stefano GF, Corrado MF, Esposito V, et al. Current trends in the real-life use of dalbavancin: report of a study panel. Int J Antimicrob Agents. 2020;56(4):106107. doi:10.1016/j.ijantimicag.2020.106107.
22. Buzón-Martín L, Zollner-Schwetz I, Tobudic S, Cercenado E, Lora-Tamayo J. Dalbavancin for the treatment of prosthetic joint infections: a narrative review. Antibiotics (Basel). 2021;10(6):656. doi:10.3390/antibiotics10060656.
23. Rappo U, Puttagunta S, Shevchenko V, Shevchenko A, Jandourek A, Gonzalez PL, et al. Dalbavancin for the treatment of osteomyelitis in adult patients: a randomized clinical trial of efficacy and safety. Open Forum Infect Dis. 2018;6(1):ofy331. doi:10.1093/ofid/ofy331.
24. Courjon J, Dinh A, Lemaignen A, Senneville E, Robineau O, Carles M. Comment on: Dalbavancin in gram-positive periprosthetic joint infections. Antimicrob Chem. 2023;78(2):561. doi:10.1093/jac/dkac417.
25. Matt M, Duran C, Courjon J, Lotte R, Moing VL, Monnin B, et al. Dalbavancin treatment for prosthetic joint infections in real-life: a national cohort study and literature review. J Glob Antimicrob Resist. 2021;25:341–5. doi:10.1016/j.jgar.2021.03.026.
26. Courjon J, Senneville E, Illes HG, Pavese P, Boutoille D. Daoud FC, el al. Effectiveness and safety of dalbavancin in France: a prospective, multicentre cohort study. Int J Antimicrob Agents. 2023 Oct;62(4):106945.
27. Lepak A, Marchillo K, VanHecker J, Andes D. Impact of glycopeptide resistance in *Staphylococcus aureus* on the dalbavancin *in vivo* pharmacodynamic target. Antimicrob Agents Chemother. 2015;59(12):7833–6. doi:10.1128/AAC.01717-15.
28. Cojutti PG, Rinaldi M, Gatti M, Tedeschi S, Viale P, Pea F. Usefulness of therapeutic drug monitoring in estimating the duration of dalbavancin optimal target attainment in staphylococcal osteoarticular infections: a proof-of-concept. Int J Antimicrob Agents. 2021;58(5):106445. doi:10.1016/j.ijantimicag.2021.106445.
29. Moñino-Dominguez L, Paredes AA. Therapeutic drug monitoring of dalbavancin: a systematic review of strategies and clinical applications in the treatment of complex infections. PROSPERO. 2024:CRD42024622177 [accessed 02 Feb 2025]. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024622177.
30. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;29(372):n71.
31. Cojutti PG, Tedeschi S, Gatti M, Zamparini E, Meschiari M, Siega PD, et al. Population pharmacokinetic and pharmacodynamic analysis of dalbavancin for long-term treatment of subacute and/or chronic infectious diseases: the major role of therapeutic drug monitoring. Antibiotics (Basel). 2022;11(8):996. doi:10.3390/antibiotics11080996.
32. Hervochon C, Hennart B, Leroy AG, Corvec S, Boutoille D, Senneville É, et al. Dalbavancin plasma concentrations in 133 patients: a PK/PD observational study. J Antimicrob Chemother. 2023;78(12):2919–25. doi:10.1093/jac/dkad331.
33. Cattaneo D, Fusi M, Colaneri M, Fusetti C, Genovese C, Giorgi R, et al. Therapeutic drug monitoring of dalbavancin in real life: a two-year experience. Antibiotics (Basel). 2023;13(1):20. doi:10.3390/antibiotics13010020.
34. Gatti M, Viale P, Cojutti PG, Zamparini E, De Paolis M, Giannella M, et al. A descriptive case series of the relationship between maintenance of conservative PK/PD efficacy thresholds of dalbavancin over time and clinical outcome in long-term treatment of staphylococcal osteoarticular infections. Int J Antimicrob Agents. 2023;61(5):106773. doi:10.1016/j.ijantimicag.2023.106773.
35. Gallerani A, Gatti M, Bedini A, Casolari S, Orlando G, Puzzolante C, et al. Long-term suppressive therapeutic-drug-monitoring-guided dalbavancin therapy for cardiovascular prosthetic infections. Antibiotics (Basel). 2023;12(11):1639. doi:10.3390/antibiotics12111639.
36. Lafon-Desmurs B, Gachet B, Hennart B, Valentin B, Roosen G, Degrendel M, et al. Dalbavancin as suppressive therapy for implant-related infections: a case series with therapeutic drug monitoring and review of the literature. Eur J Clin Microbiol Infect Dis. 2024;43(7):1475–80. doi:10.1007/s10096-024-04849-0.
37. De Nicolò A, Stroffolini G, Antonucci M, Mula J, De Vivo ED, Cusato J, et al. Long-term pharmacokinetics of dalbavancin in ABSSSI and osteoarticular settings: a real-life outpatient context. Biomedicines. 2021;9(10):1288. doi:10.3390/biomedicines9101288.
38. Cojutti PG, Rinaldi M, Zamparini E, Rossi N, Tedeschi S, Conti M, et al. Population pharmacokinetics of dalbavancin and dosing consideration for optimal treatment of adult patients with staphylococcal osteoarticular infections. Antimicrob Agents Chemother. 2023;65(5):e02260–320. doi:10.1128/AAC.02260-20.

39. Stroffolini G, De Nicolò A, Gaviraghi A, Mula J, Cariti G, Scabini S, et al. Clinical effectiveness and pharmacokinetics of dalbavancin in treatment-experienced patients with skin, osteoarticular, or vascular infections. Pharmaceutics. 2022;14(9):1882. doi:10.3390/pharmaceutics14091882.
40. Cattaneo D, Fusi M, Galli L, Genovese C, Giorgi R, Matone M, et al. Proactive therapeutic monitoring of dalbavancin concentrations in the long-term management of chronic osteoarticular/periprosthetic joint infections. Antimicrob Agents Chemother. 2024;68(4):e0002324. doi:10.1128/aac.00023-24.
41. Dowell JA, Goldstein BP, Buckwalter M, Stogniew M, Damle B. Pharmacokinetic-pharmacodynamic modeling of dalbavancin, a novel glycopeptide antibiotic. J Clin Pharmacol. 2008;48:1063–8.