



# Left ventricular assist device-associated driveline infections as a specific form of complicated skin and soft tissue infection/acute bacterial skin and skin structure infection – issues and therapeutic options

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## Purpose of review

This review comments on the current guidelines for the treatment of wound infections under definition of acute bacterial skin and skin structure infections (ABSSSI). However, wound infections around a catheter, such as driveline infections of a left ventricular assist device (LVAD) are not specifically listed under this definition in any of the existing guidelines.

## Recent findings

Definitions and classification of LVAD infections may vary across countries, and the existing guidelines and recommendations may not be equally interpreted among physicians, making it unclear if these infections can be considered as ABSSSI. Consequently, the use of certain antibiotics that are approved for ABSSSI may be considered as 'off-label' for LVAD infections, leading to rejection of reimbursement applications in some countries, affecting treatment strategies, and hence, patients' outcomes. However, we believe driveline exit site infections related to LVAD can be included within the ABSSSI definition.

## Summary

We argue that driveline infections meet the criteria for ABSSSI which would enlarge the 'on-label' antibiotic armamentarium for treating these severe infections, thereby improving the patients' quality of life.

## Keywords

acute bacterial skin and skin structure infection, driveline infections, heart assist devices, skin and soft tissue infections, wound infections

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## KEY POINTS

- Current guidelines regarding the treatment of left ventricular assist device left ventricular assist device-related infections and their possible classification as ABSSSI are not always clear, and are interpreted differently between physicians, institutions and regulators.
- As a result, patients with these types of infections may not always receive the most appropriate treatment.
- In our opinion, driveline infections (DLIs) can be considered as part of the acute bacterial skin and skin structure infections (ABSSSI) spectrum, thereby allowing the on-label use of novel antibiotics approved for ABSSSI.
- In patients with DLIs, outpatient parenteral antimicrobial therapy can be a patient-friendly and resource-saving treatment option due to the long therapy cycles that are required.

## INTRODUCTION

Heart failure is a leading cause of morbidity and mortality worldwide, affecting 1–3% of the adult population in industrialized countries, and its prevalence is expected to increase substantially in the future [1]. The use of a left ventricular assist device (LVAD) has revolutionized the treatment of end-stage heart failure. LVADs are used as a bridge to recovery or bridge to transplantation for patients waiting for a donor heart, or as a destination therapy for patients who are ineligible for heart transplant [2,3<sup>■</sup>]. A major complication can be LVAD-related infections. However, current treatment guidelines and regulations for these infections are not always clear, and can be improved. As patients should receive the best possible care, especially in palliative care settings, access to appropriate and effective treatment is of crucial importance.

An LVAD is an electromechanical pump, which assists cardiac circulation and can partially or completely replace a failing ventricle. The device consists of an internal pump and an extracorporeal controller unit with batteries. A percutaneous wire, known as the driveline, connects both components [4]. Infections affecting the soft tissues around the driveline outlet, so-called driveline infections (DLIs), are the most common complications, with a reported incidence range among LVAD recipients of 10–52% [3<sup>■</sup>,4–6,7<sup>■</sup>,8–10,11<sup>■</sup>]. Although most DLIs are local, they may also extend into the pump pocket, heart or chest wall, or spread into the bloodstream, leading to potentially life-threatening infections [4]. DLIs are also a major risk factor for additional complications such as sepsis or stroke,

hospital readmissions and mortality [4]. Since the number of patients who require LVAD support for longer periods of time is rising and the incidence of DLIs increases with the duration of support [5,9,12], the need for outpatient care of LVAD patients with DLIs is increasing.

The majority of LVAD infections are caused by Gram-positive bacteria. *Staphylococcus aureus* and *S. epidermidis* are the most commonly identified organisms, together accounting for approximately 50% of LVAD infections [4,13]. The spectrum of pathogens involved in DLIs is described in detail below (see section *Microbiological profile of ABSSSI and LVAD DLI*).

Clinical management of DLIs consists of a 2–4-week antibiotics course combined with surgical debridement [8,14,15]. However, recurrent infections often require a prolonged course of antibiotics which evolves toward parenteral therapy when resistant organisms develop [16]. Long-lasting, suppressive antimicrobial therapy may also be required for device or pocket infections to prevent clinical relapse [5].

## CURRENT GUIDELINES

The guidelines of the Infectious Disease Council of the International Society for Heart and Lung Transplantation (ISHLT) recommend basing the treatment strategies on the identification of the responsible pathogen, the location and depth of infection (though the latter is sometimes difficult to assess without surgical exploration), and the transplant candidacy status of the patient [15]. As a first-line treatment for local superficial DLIs, the ISHLT recommends empiric therapy with oral or intravenous (i.v.) antibiotics for a minimum of 2 weeks, or until infection has resolved. DLIs of uncertain depth or deep DLIs should be treated with surgical source control (i.e., debridement and removal of infected and necrotic tissue, if necessary) as well as i.v. antibiotics, until clinical stabilization and improvement of infection (usually 6–8 weeks), followed by a long-term (oral) antibiotic suppression therapy [15]. The guidelines refrain from specifying antibiotic agents but recommend to carefully consider local and institutional epidemiology as well as antibiotic susceptibility patterns, paying special attention to methicillin-resistant *S. aureus* (MRSA) [15]. The optimal empiric therapy for DLIs as well as a standard definition for early localized infection have not yet been established [14]. In general, broad-spectrum antibiotics are initiated and adjusted to targeted antibiotic treatment upon identification of the specific pathogen [14,15].

Other recommendations, such as the Driveline Expert STagINg and carE (DESTINE) consensus, focus more on the prevention, early detection,

and stage-related management of DLIs, including surgical source control measures [3<sup>\*</sup>], without referring to MRSA, although this can be problematic in some regions or institutions [17].

## PROBLEMS WITH CURRENT GUIDELINES

In addition to the lack of specific guidance for the choice of antibiotics for treatment of DLIs, definitions and classification of LVAD infections vary across countries and studies, and the existing guidelines and recommendations are not construed equally among physicians. Differences in understanding and interpretation of the definitions and respective guidelines, especially outside the United States, may lead to misunderstanding or misclassification of the infections and impede evidence-based recommendations or comparisons. For example, in the Anglo-Saxon literature, the term ‘cellulitis’ is used as a generic term for erysipelas or for limited (or sometimes severe) soft tissue infections, while in the German terminology, the term ‘limited phlegmon’ (limited soft tissue infection/limited cellulitis) is used. National guidelines, such as the German guideline for parenteral therapy of soft tissue infections (under the auspices of the Paul-Ehrlich-Gesellschaft für Infektionstherapie e.V.) [18<sup>\*</sup>,19] have only recently tried to clarify the definitions, but misunderstandings may still occur.

An additional source of confusion arises from the term ‘acute bacterial skin and skin structure infection’ (ABSSSI, see details below), which uses the extent of erythema as a quantifiable criterion for evaluation of therapeutic response [20,21]. Guidelines or recommendations for treatment of wound or soft tissue infections under the definition of ABSSSIs have been published [18<sup>\*</sup>,19–22,23<sup>\*\*</sup>], but since DLIs are not explicitly included in the definition of ABSSSIs, it can be unclear to the treating physician or the regulatory authorities whether these treatment guidelines also apply to DLIs. Consequently, the use of certain antibiotics that are approved for ABSSSIs may be considered ‘off-label’ when used for treating DLIs, leading to rejection of reimbursement applications in some countries, thereby, affecting treatment strategies and patients’ outcomes.

Historically, most antimicrobials with broad activity against Gram-positive pathogens have been approved for specific indications (only). From the perspective of the infectious disease specialist, this limits the available therapeutic options. The choice of substances active against Gram-positive bacteria should mainly be driven by the rules of microbiological susceptibility testing, pharmacodynamics and pharmacokinetics, as is common

practice for so-called reserve antimicrobials that are active against Gram-negative pathogens (e.g., cefiderocol, ceftazidime/avibactam, cetolozane/tazobactam, imipenem/relebactam).

## CURRENT DEFINITIONS

Skin and soft tissue infections (SSTIs) include a variety of bacterial infections of the skin and subcutaneous tissue, muscle, and fascia and range from mild to serious life-threatening infections [18<sup>\*</sup>,22,24,25]. Older age, immunosenescence or immunocompromising conditions, obesity, trauma, and comorbidities such as diabetes mellitus or cardiopulmonary or hepatorenal disease are the main risk factors for SSTIs [26] and a substantial proportion of SSTIs is associated with hospitalization and significant morbidity [18<sup>\*</sup>,22,24–28]. SSTIs are usually classified according to the causative pathogen with its associated toxins or enzymes, and their clinical presentation and severity [26]. SSTIs have been further classified into simple (uncomplicated) or complicated (can be necrotizing or nonnecrotizing) infections, with the distinction depending on several factors, including comorbidities. Simple infections are restricted to the skin and underlying superficial soft tissues, and typically respond well to outpatient management. Complicated infections extend into the underlying deep tissues and may be associated with systemic inflammatory response syndrome or sepsis, and ischemic necrosis in rare cases [29].

ABSSSI is a term introduced by the Food and Drug Administration (FDA) to assist the drug development industry in designing clinical trials for the treatment of skin infections. ABSSSIs constitute a subset of SSTIs that is usually treated with parenteral antibiotics [20]. According to the FDA definition, ABSSSIs include cellulitis/erysipelas, wound infection, and major cutaneous abscess, and have a minimum lesion surface area of approximately 75 cm<sup>2</sup> [21]. Although not explicitly mentioned in the FDA guidance, subsequent guidelines have clarified the term ‘wound infection’ as infection resulting from minor injuries that break the skin, or from other causes such as animal bites or foreign objects such as gunshot and knife wounds [20]. This quantitative parameter was primarily intended to enable quantification of the response to therapy. In trial designs, a sufficiently large lesion size would allow a more reliable, quantitative estimate of treatment effects in patients having a surgical incision and drainage for a minor cutaneous abscess [21].

However, ‘ABSSSI’ is an artificial term that was introduced to improve standardization of clinical studies and is a valid inclusion criterion for clinical trials, but in clinical practice, size is not a relevant

diagnostic criterion. It was not meant as a term for a particular diagnosis and does not, for example, distinguish between *Streptococcus pyogenes*-induced erysipelas and *S. aureus*-caused cellulitis which require different narrow-spectrum antibiotics [18<sup>a</sup>,19]. When the term ‘ABSSSI’ is used in drug approval dossiers (since it is the term used in inclusion criteria of the respective clinical studies), one must consider which clinically defined soft tissue infections would fall under this term. Thus, we believe there is a need to clarify and harmonize the different definitions.

Considering that LVAD DLIs are soft tissue infections or wound infections around a percutaneous wire (i.e., a foreign body leading to a break of the skin which may lead to the entry of bacteria with potential for systemic infection), they should be classified as ABSSSIs, even though neither the existing guidelines, nor the ABSSSI definition for drug approvals, explicitly list DLIs.

### MICROBIOLOGICAL PROFILE OF ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTION AND LEFT VENTRICULAR ASSIST DEVICE DRIVELINE INFECTIONS

*S. aureus* (including MRSA) and coagulase-negative staphylococci (CoNS) are the most common pathogens associated with ABSSSIs, followed by *Pseudomonas aeruginosa* and *S. pyogenes*. Less common

bacteria include other *Streptococcus* species, other Gram-negative bacteria such as *Enterobacterales*, and fungal pathogens [20,27].

In LVAD infections, staphylococci are the most frequently isolated bacteria, but other bacteria and fungi have also been reported (Table 1). Polymicrobial infections may account for more than 50% of LVAD infections [4,12,14]. These infections often occur due to superinfection of an existing DLI while the patient is still being treated for the initial pathogen. In such infections, the most common secondary pathogen is *P. aeruginosa* [14,30].

DLIs and ABSSSIs are similar with regards to the spectrum of pathogens that cause the infections: both are mainly associated with Gram-positive species which colonize the skin, such as *S. aureus* and CoNS, while Gram-negative infections are less common, and fungal infections are observed occasionally. These similarities provide evidence to justify classifying DLIs as ABSSSIs.

### LEFT VENTRICULAR ASSIST DEVICE DRIVELINE INFECTION AS ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTION, IMPLICATIONS FOR PATIENTS AND TREATMENT OPTIONS

Although LVAD is a temporary option for patients awaiting a heart transplant, it is increasingly being

**Table 1.** Overview of commonly identified pathogens associated with left ventricular assist device infections

Pathogen	Reported proportion of infections (%)	References
Gram-positive bacteria		
<i>Staphylococcus aureus</i>	0–56	[6,9,12,31,32]
Methicillin-susceptible	8–43	[7 <sup>a</sup> ,9,12,31,32]
Methicillin-resistant	0–30	[7 <sup>a</sup> ,8,12,31,33]
Coagulase-negative staphylococci	2–56	[6,7 <sup>a</sup> ,8,9,12,31,32]
<i>Enterococcus</i> spp.	0.9–29	[6,7 <sup>a</sup> ,8,12,31,32]
<i>Corynebacterium</i> spp.	0–20	[7 <sup>a</sup> ,12,31,32]
<i>Streptococcus</i> spp.	0–6	[7 <sup>a</sup> ,32]
Gram-negative bacteria		
<i>Pseudomonas aeruginosa</i>	2–28	[6,7 <sup>a</sup> ,8,9,12,31,32]
<i>Serratia</i> spp.	2–9	[7 <sup>a</sup> ,8,32]
<i>Klebsiella pneumoniae</i>	2–13	[7 <sup>a</sup> ,8,12,31,32]
<i>Enterobacter</i> spp.	0–5	[7 <sup>a</sup> ,32]
<i>Escherichia coli</i>	0–11	[7 <sup>a</sup> ,8,12,32]
<i>Acinetobacter baumannii</i>	1.8	[7 <sup>a</sup> ]
Fungi		
<i>Candida</i> spp.	0–45	[6,8,12,32]
<i>Aspergillus</i> spp.	28	[12]

used as a destination therapy for patients who are ineligible for transplant [31,34]. Many of the latter patients also require end-of-life care, and severe complications leading to repeated hospitalizations put these patients at higher risk of acquiring nosocomial infections, including those by multiresistant bacteria such as MRSA; therefore, in settings where removal of an infected device (or parts thereof) is not feasible, life-long antimicrobial therapy is often needed [35].

Guidelines for treatment of ABSSSIs and SSTIs [20,23<sup>11</sup>] are similar to the guidelines for treatment of DLIs, but – in contrast to the guidelines for DLIs – also include recommendations for specific antibiotics to be used. Recently approved novel antibiotics (such as dalbavancin, oritavancin, and delafloxacin) add to the available treatment options for ABSSSIs [27,36]. Considering the similarities between DLI and ABSSSI with regards to the pathogens involved, these antibiotics could also be beneficial for patients with DLIs [37,38].

Treatment should be tailored to the susceptibility profile after the pathogen has been identified. Based on the current guidelines, the literature, and the personal experience of the authors, a list of recommended antibiotics, focusing on the most common Gram-positive pathogens, was compiled. Details on dosage, frequency, administration, pharmacodynamics, and interactions can be found in Table 2. A proposal for the treatment of superficial and deep-seated LVAD infections is shown in Fig. 1.

## TREATMENT IN AN OUTPATIENT SETTING

To avoid or limit repeated hospitalizations and reduce length of stay, so-called outpatient parenteral antimicrobial therapy (OPAT) should also be considered in patients with DLIs. OPAT is used to treat cardiovascular and surgical wound infections, as well as SSTIs due to *S. aureus* (including MRSA) and CoNS, when having a predictable course and a low probability of progression [49,50]. The optimal antibiotics for OPAT are those with a long half-life that can be administered 1–2 times daily, or less frequently. Several i.v. antimicrobial agents that could be used in OPAT are available [50].

OPAT can be used for LVAD patients in acute care and for patients in a palliative care setting who may require life-long treatment to control the infection. The use of OPAT in these patients would likely be associated with improved patients' comfort, cost savings as well as treatment compliance [51].

The implementation of OPAT is associated with several challenges. While delivery of parenteral antimicrobials in an outpatient setting is available in many European countries, some of them lack

structured OPAT teams or services [37,52<sup>12</sup>], and patients may have difficulties in receiving their treatment regularly, especially on weekends or during holiday periods. In contrast, countries such as Italy, the United Kingdom, or the United States, have widely implemented this approach for treatment of various SSTIs [49,51,52<sup>12</sup>,53]. In addition, not all patients may be good candidates for OPAT, since the patient and his/her caregivers must be able to physically and mentally cope with the OPAT. In some cases, social and/or health-system barriers can further complicate the successful use of OPAT [50,54] and without appropriate recommendations the exact indications for treatment can be unclear to the treating physicians.

A growing amount of evidence supports novel antibiotics such as dalbavancin or oritavancin as an effective, long-term therapy for various 'off-label' indications, including osteomyelitis and endocarditis [55–58,59<sup>13</sup>,60]. Due to their long half-life, these antibiotics appear to be promising options not only for LVAD patients with acute DLIs, but especially for long-term chronic suppression therapy consisting of once-weekly or twice-weekly infusions. Oral treatment is associated with pharmacokinetic limitations. For instance, it has been shown for dicloxacillin in the oral treatment of infective endocarditis that the target antibiotic level of dicloxacillin was attained in only 17% of the patients (LIT POET study) [61<sup>14</sup>].

## PHARMACO-ECONOMIC ASPECTS OF TREATMENT FOR PATIENTS WITH DLIs

Hospital readmissions are frequently reported for LVAD recipients (over 50%) and are associated with significant healthcare costs in this patient population [62]. The most common causes of rehospitalization after implantation of LVAD include infection, device malfunction, cardiac events, strokes, and bleeding events [62]. Up to 60% of unplanned hospital readmissions are related to DLIs [14,63–67], with a reported median direct hospital cost of approximately \$7500 per readmission during an 11-month follow-up [62].

Effective treatment of DLIs in an outpatient setting should contribute to decreasing the rates of hospital readmission due to DLIs and the associated financial burden. It may therefore be beneficial to also consider the ABSSSI guidelines for treatment of DLIs, particularly regarding the use of OPAT.

## CONCLUSIONS AND FUTURE DIRECTIONS

In this paper, we have focused on the current definitions and treatment guidelines for ABSSSI

**Table 2. Recommended antibiotics for patients with left ventricular assist device driveline infections with Gram-positive pathogens**

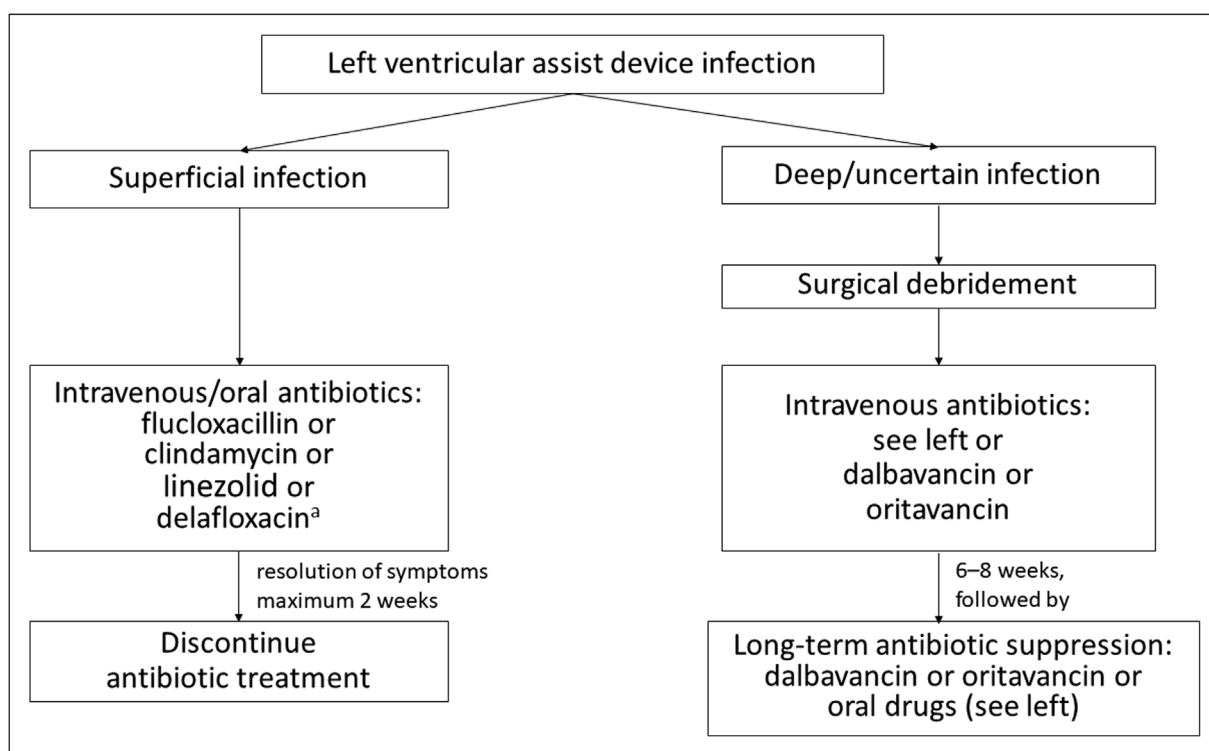
Antimicrobial agent	Spectrum	Dosage	Route	Skin and soft tissue permeability (% of serum concentration)			Frequent interactions	Comments	References
				OPAT-ready (Y/N)	Antibiofilm activity (Y/N)	Antibiofilm activity (Y/N)			
<b>β-Lactam antibiotics</b>									
Cefazolin	<i>Staphylococcus aureus</i> CoNS	i.v.: 2000–4000 mg every 8h Oral: 1000 mg every 6–8h	i.v./oral	N	Y	None		[39]	
Ceftaroline	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <i>Streptococcus</i> spp. Enterobacterales	600–1200 mg every 8h	i.v.	N	Y?	None	Regular monitoring of leukocyte levels required	[40,41]	
Ceftiprole	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <i>Streptococcus</i> spp. Enterobacterales <i>Pseudomonas aeruginosa</i>	500–1000 mg every 8h	i.v.	N		None			
Flucloxacillin	<i>S. aureus</i> CoNS (only MSSE)	i.v.: 2000–4000 mg every 8h Oral: 1000 mg every 8h	i.v./oral		N	None	Regular monitoring of liver function parameters required		
<b>Lincosamides and Oxazolidinones</b>									
Clindamycin	<i>Streptococcus</i> spp. <i>Staphylococcus</i> spp. Anaerobic bacteria	600–900 mg every 8h	i.v./oral		N	95%	None	Increased risk of <i>Clostridioides difficile</i> infection [20,40,42]	
Linezolid	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <i>Streptococcus</i> spp. Enterococcus spp.	600 mg every 8–12h	i.v./oral			105%	Seldom: Monoamine oxidase inhibitors and selective inhibitors of serotonin reuptake	Regular monitoring of hemoglobin and thrombocytes required [20,40,42]	
Tedizolid	<i>S. aureus</i> (incl. MRSA) CoNS <i>Streptococcus</i> spp. Enterococcus spp.	200 mg every 24h	i.v./oral		?	110–120%		In case of ABSSSI, therapy duration >7 days required [20,40,43]	
<b>Lipoglycopeptides</b>									
Dalbavancin	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <sup>a</sup> Enterococcus spp. (incl. VanB VRE and vanC-expressing enterococci) <sup>a</sup> <i>Streptococcus</i> spp.	1500 mg (single dose, or 1000 mg followed by 500 mg after 1 week)	i.v. infusion during 30 min	Y	Y	80–85%	None	Alternative dosing: 1500 mg followed by 1000 mg every 15 days [20,36,40,44–47]	
Oritavancin	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <i>Streptococcus pyogenes</i> Enterococcus spp. (incl. VRE, all resistant strains)	1200 mg followed by 800 mg after 1 week	i.v. infusion during 3 h	Y	Y		Interaction with phospholipid dependent coagulation tests	Active against all vancomycin-resistant enterococci [20,40]	
Teicoplanin	<i>S. aureus</i> (incl. MRSA) <i>Streptococcus</i> spp. Enterococcus spp.	2 × 15 mg/kg every 12h for 1–3 days, then 1 × 15 mg/kg 3 × /week	i.v.	Y	N		None	Therapeutic drug monitoring necessary: trough level 40–60 µg/ml [20,40,42]	
Vancomycin	<i>S. aureus</i> (incl. MRSA) CoNS <i>Streptococcus</i> spp. Enterococcus spp.	15–20 mg/kg every 8–12h	i.v.	N	N	8–10%		Monitoring necessary: trough level 15–20 µg/ml [20,40,42]	

**Table 2 (Continued)**

Antimicrobial agent	Spectrum	Dosage	Route	OPAT-ready (Y/N)	Skin and soft tissue permeability (% of serum concentration)	Antibiofilm activity (Y/N)	Frequent interactions	Comments	References
Quinolones									
Ciprofloxacin	<i>P. aeruginosa</i> Enterobacteriales	i.v.: 400–600 mg every 12h Oral: 500–750 mg every 8h	i.v./oral		Y	Y		Typical side effects of quinolones	
Delafloxacin	<i>S. aureus</i> (incl. MRSA) CoNS (incl. MRSE) <i>S. pyogenes</i> <i>P. aeruginosa</i>	i.v.: 300 mg over 60 min every 12h Oral: 450 mg every 12h	i.v./oral		Y	Y	No association with delayed ventricular repolarization	Some activity in ciprofloxacin-resistant <i>P. aeruginosa</i> Not a regular treatment for <i>Enterococcus</i> spp	[40]
Moxifloxacin	<i>S. aureus</i> CoNS <i>S. pyogenes</i> Enterobacteriales	400 mg every 24h	i.v./oral		Y			Typical side effects of quinolones	
Various									
Intravenous fosfomycin	<i>S. aureus</i> (incl. MRSA) <i>Enterococcus</i> spp. Enterobacteriales	i.v.: 12–24g daily in 2–4 separate infusions	i.v.		50–91%	Y	None	Must be co-administered with another antibiotic Regular monitoring of the electrolytes required	[42,48]
Rifampicin	<i>Staphylococcus</i> spp. (incl. MRSA and MRSE) <i>Streptococcus</i> spp.	300–450 mg every 12h for at least 6 weeks	i.v. infusion during 30 min/ oral		NA	Y	Interactions with many drugs such as methadone, oral hypoglycemics, hormonal contraceptives, anticoagulants, protease inhibitors, phenytoin, theophylline, cardiac glycosides	Must be co-administered with another antibiotic Maximum daily dose 900 mg	[42]

Information specified in this table is based on the mentioned references, as well as the authors' personal experience.

<sup>a</sup>Delbaavancin was shown to inhibit all VanB-type enterococci (*E. faecalis* and *E. faecium*) and 95.5% of teicoplanin-resistant CoNS isolated from hospitalized patients with a proven or suspected infection [47].  
 ABSSSI, acute bacterial skin and skin structure infection; CoNS, coagulase-negative staphylococci; i.v., intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; MSSE, methicillin-susceptible *Staphylococcus epidermidis*; OPAT, outpatient parenteral antimicrobial therapy; VRE, vancomycin-resistant enterococci.



**FIGURE 1.** Proposal for the treatment of superficial and deep/uncertain depth left ventricular assist device infections. Recommended for polymicrobial Gram-positive and Gram-negative infections.

and LVAD-associated infections. The wording and terminology used in current guidelines may be interpreted differently across institutions and countries. In our opinion, DLIs are soft tissue infections around indwelling wires that can appear as superficial, deep, or complicated forms of soft tissue infections, and are therefore encompassed by ABSSSIs.

A consequence of the confusion surrounding the definitions of DLI and ABSSSI is that, currently, certain drugs that are approved for ABSSSI and suitable for patients with DLI are considered ‘off-label’ for LVAD infection. We argue that DLIs meet the criteria for ABSSSIs, enlarging the ‘on-label’ antibiotic armamentarium for treating these severe infections. Furthermore, considering DLIs as being ABSSSIs might legally and clinically facilitate future studies of these new drugs with regards to pharmaco-economics and patient comfort.

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*Instructions to authors:* <https://journals.lww.com/co-infectiousdiseases/Pages/informationforauthors.aspx>

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### Conflicts of interest

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