Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2453

delafloxacin 450mg tablets and 300mg powder for concentrate for solution for infusion (Quofenix®)

A. Menarini Farmaceutica Internazionale SRL

10 June 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

delafloxacin (Quofenix ®) is accepted for restricted use within NHSScotland.

Indication under review: treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the initial treatment of this infection.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

SMC restriction: Patients with suspected or confirmed polymicrobial infection following treatment failure or when standard antibacterial therapies are not suitable. Delafloxacin should be used on the advice of local microbiologists or specialists in infectious disease.

In two randomised, phase III, double-blind studies in patients with ABSSSI, delafloxacin was non-inferior to a glycopeptide antibacterial plus a monocyclic beta-lactam antibiotic for clinical cure at the follow-up visit in the intention to treat population.

Chairman
Scottish Medicines Consortium

Indication

Treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the initial treatment of this infection.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.[1, 2]

Dosing Information

The recommended dose is 450mg orally every 12 hours (with or without food), or 300mg by intravenous (IV) infusion every 12 hours administered over 60 minutes (switch from IV to oral delafloxacin is possible at the discretion of the physician). The total duration of treatment is 5 to 14 days. [1, 2]

Product availability date

July 2020

Summary of evidence on comparative efficacy

Delafloxacin is a fluoroquinolone antibacterial for systemic use with broad-spectrum activity including Gram-positive and Gram-negative bacteria; it inhibits bacterial topoisomerase IV and DNA gyrase (topoisomerase II), enzymes required for bacterial DNA replication, transcription, repair, and recombination.[1-3]

The submitting company requested that SMC considered delafloxacin for use in adult patients with suspected or confirmed polymicrobial ABSSSI following treatment failure or when standard antibacterial therapies are not suitable. Occurrences where standard antibacterial therapies are not suitable include intolerances (such as penicillin allergies), drug-drug interactions or side effects.

The evidence comes from two multicentre, randomised, double-blind, active-controlled, phase III studies, RX-3341-302 and RX-3341-303.

The studies recruited adults with an ABSSSI (cellulitis or erysipelas, wound infection, major cutaneous abscess or burn infection) with a minimum surface area of 75cm^2 of erythema and at least two signs of systemic infection. [3-5]

In study RX-3341-302, patients were randomised equally to receive delafloxacin (300mg IV infusion every 12 hours) (N=331) or vancomycin (15mg/kg IV infusion every 12 hours) plus aztreonam (2g IV every 12 hours) (N=329) for 5 to 14 days. In study RX-3341-303, patients were randomised equally to receive delafloxacin (300mg, IV infusion every 12 hours for 3 days followed by 450mg orally every 12 hours) (N=423) or vancomycin (15mg/kg IV infusion or according to local

standard of care) plus aztreonam (1g or 2g, IV every 12 hours) (N=427) for 5 to 14 days. In both studies, aztreonam or the matching placebo treatment were stopped if baseline cultures were confirmed negative for Gram-negative pathogens.[3-5]

Randomisation was stratified according to type of ABSSSI infection and designed so that no more than 25% of patients were treated for a major cutaneous abscess, and no more than 35% (Study RX-3341-302) or 30% (Study RX-3341-303) were treated for wound infections. In addition, patients who had received one dose of a single, potentially effective, short-acting antimicrobial drug or regimen in the 14 days before study entry were limited to no more than 25% of total randomly assigned patients. In study RX-3341-303, randomisation was also stratified by baseline body mass index (BMI; <30kg/m^2 and ≥30kg/m^2). Patients with a BMI ≥30kg/m^2 comprised at least 40% but no more than 50% of the enrolled population.[3]

The European Medicines Agency (EMA)-defined primary efficacy outcome was investigator-assessed response at the follow-up visit (day 14 + 1 from randomisation), which was defined as clinical cure (no remaining signs or symptoms), improved, failure or indeterminate. Non-inferiority was tested for clinical cure. The primary efficacy analysis was performed in the intent-to-treat (ITT) population that included all randomised patients and in the clinically evaluable (CE) population (that included patients in the ITT analysis set who had a non-missing assessment, who received ≥80% of their assigned treatment, had the required clinical assessments within the appropriate window, did not receive any concomitant, systemic antibacterial therapy with activity against the causative pathogens and had no protocol deviations that would have affected efficacy assessments through the time period) using a non-inferiority margin of 10%.[3-5]

Non-inferiority was demonstrated for the outcome of clinical cure in study RX-3341-302 in the ITT and CE populations and in study RX-3341-303 in the ITT population but not in the CE population (lower limit of the 95% confidence interval of the difference was below -10%). The results are presented in Table 1.[3-5]

Table 1: EMA primary outcome results from RX-3341-302 and RX-3341-303 [3-5]

Population	delafloxacin		vancomycin + aztreonam		% difference (95% CI)	
	RX-3341-302	RX-3341-303	RX-3341-302	RX-3341-303	RX-3341-302	RX-3341-303
% of patients achieving investigator-assessed clinical cure at the follow-up visit (n/N)						
ITT	52% (172/331)	58% (244/423)	50% (166/329)	60% (255/427)	1.5% (−6.1 to 9.1)	−2.0% (−8.6 to 4.6)
CE	59% (142/240)	62% (220/353)	58% (142/244)	68% (224/329)	1.0% (−7.8 to 9.7)	−5.8% (−12.9 to 1.4)

ITT, intent-to-treat population; CE, clinically evaluable population; EMA, European Medicines Agency; CI, confidence interval

Secondary outcomes included investigator-assessed clinical success (cure or improved and no further antibiotic needed) at the follow-up visit. Across treatment groups in both studies, clinical success rates were comparable (varying between 82% and 87% across groups in the ITT population).[4, 5]

Another secondary outcome of interest was microbiological eradication response (documented or presumed eradicated infection) in the microbiologically evaluable (ME) population at the follow-up visit. In both studies, high (≥98%) microbiological eradication response rates were seen in the delafloxacin group and the vancomycin plus aztreonam group. Relevant to the proposed positioning, subgroup results were presented for microbiological eradication response by infection types (monomicrobial and polymicrobial) and baseline target pathogens. Delafloxacin microbiological eradication response rates were high and generally similar across infection types and baseline target pathogens, including for the subgroups with polymicrobial Gram-positive bacteria (98% [40/41]) and with mixed polymicrobial caused by Gram-positive and Gram-negative pathogens (100% [26/26]).[4-6]

Patients' subjective assessment of pain was recorded on a numerical rating scale ranging from 0 (no pain) to 10 (pain as bad as imaginable) at baseline, during treatment, and at end of therapy (EOT), follow-up visit, and late follow-up visit. In both studies, at the different time points, patient reported pain scores and reductions in pain were similar between the delafloxacin and vancomycin plus aztreonam groups.[4, 5]

Supportive evidence came from RX-3341-202, a multicentre, randomised, double-blind, active controlled, phase II study in adults with ABSSSI (with lesion size ≥75cm^2) and at least one systemic sign of infection. In total, 256 adults were randomised equally to receive, for 5 to 14 days, delafloxacin (IV 300mg every 12h), linezolid (IV 600mg every 12h), or vancomycin (IV 15mg/kg every 12h). Patients whose microbiological cultures grew Gram-negative bacteria could have aztreonam added to their treatment regimen at the investigator's discretion. Investigator-assessed clinical cure rates at the follow-up visit (ITT population) were higher in the delafloxacin group (70%) compared with the linezolid group (65%) and the vancomycin group (54%).[3]

A Bayesian network meta-analysis (NMA) was conducted to compare the efficacy and safety of delafloxacin and a number of antibacterial comparators (ampicillin + sulbactam or amoxicillin / clavulanic acid [co-amoxiclav], ceftaroline fosamil, ceftobiprole, dalbavancin, daptomycin, fusidic acid, iclaprim, linezolid, vancomycin, oxacillin + dicloxacillin, omadacycline, standard therapy [an antistaphylococcal penicillin or vancomycin], tedizolid, telavancin, tigecycline, vancomycin + aztreonam, and vancomycin + linezolid). The NMA included 37 studies of adult patients with ABSSSIs, complicated skin and soft tissue infections (cSSTIs), complicated skin and skin structure infections (cSSSIs) or severe cellulitis with infections of Gram-positive/negative or mixed aetiology. The outcomes assessed in the NMA were composite clinical response, early clinical response, microbiological response, nausea and diarrhoea. Delafloxacin performed better than a few comparators (fusidic acid, iclaprim, vancomycin, and ceftobiprole) for composite clinical response and for the remaining comparisons, delafloxacin and comparators showed similar results (as 95% credible intervals spanned one). In terms of safety, there were some comparisons that favoured delafloxacin and others that favoured some of the comparators, however the 95% credible intervals of the odds ratios generally crossed one indicating no difference. The submitting company concluded that the NMA results are consistent with demonstrating non-inferiority in the effectiveness of ABSSSI treatment across the comparators considered. They noted that no studies

had been identified to include the triple combination therapies (daptomycin + ciprofloxacin + metronidazole, linezolid + ciprofloxacin + metronidazole, and vancomycin + ciprofloxacin + metronidazole) in the NMA. Thus, they assumed that the clinical benefit and adverse events (AEs) of each triple combination therapy were equivalent to that obtained from the NMA for the Gram-positive treatment components of this combination therapy. In addition, they noted that comparisons in the relevant subgroup of patients with polymicrobial infections were not feasible and assumed that the clinical efficacy and safety of each intervention in this relevant subgroup were equivalent to that obtained from the NMA for the broad patient population. While the only specific result that was used in the economic base case was from the comparison of delafloxacin with vancomycin in terms of early clinical response (used to represent the early response for flucloxacillin, which could not be included in the NMA due to lack of randomised controlled trials), the overall conclusions of the NMA were used to support a cost-minimisation analysis.

Summary of evidence on comparative safety

Overall, IV and oral delafloxacin were considered well tolerated and the safety profile of delafloxacin was considered comparable to that of other fluoroquinolones. However, because an improved safety profile could not be demonstrated for delafloxacin relative to other fluoroquinolones (which are linked to potentially disabling and long lasting adverse effects such as tendon ruptures or neuropathies and indicated in second or later line), a first-line indication was not recommended.[3]

In pooled data from the RX-3341-302 and RX-3341-303 studies, any treatment-emergent AE was reported by 45% (334/741) of patients in the delafloxacin group and 48% (358/751) in the vancomycin plus aztreonam group and these were considered treatment-related in 22% and 26% respectively. In the delafloxacin and vancomycin plus aztreonam group respectively, patients reporting a severe AE were 3.5% versus 2.8%, patients with a reported serious AE were 3.6% versus 3.5%, and patients with any AE leading to premature study drug discontinuation were 1.8% versus 3.5%.[3]

In pooled data from the RX-3341-302 and RX-3341-303 studies, the most frequently reported treatment-emergent AEs of any grade with an incidence >5% in any group were in the delafloxacin group versus the vancomycin plus aztreonam group, respectively: nausea (7.6% versus 6.3%), diarrhoea (7.8% versus 3.2%), infusion site extravasation (5.5% versus 7.2%), infection (5.9% versus 5.1%), and headache (3.2% versus 5.5%).[3]

Summary of clinical effectiveness issues

Acute bacterial skin and skin structure infections (ABSSSI) are commonly occurring infections in both hospitals and community settings and remain a significant source of morbidity. These infections are most commonly caused by Gram-positive pathogens, of which the most frequently isolated ones are *Staphylococcus aureus* including methicillin-resistant (MRSA) and methicillin-

susceptible (MSSA). To treat ABSSSIs, a number of antibacterial options are available and the benefit of systemic antibacterial therapy accompanied by surgical intervention as necessary is established. Initially, ABSSSI is usually treated empirically because culture results are not immediately available and patients benefit from rapid treatment initiation. Infections due to MRSA are complex to manage and drug-resistant bacteria are playing an increasing role as causative pathogens. When MRSA is identified as a single pathogen, a number of treatment options are available (including vancomycin, daptomycin, linezolid, tigecycline, tedizolid, oritavancin, dalbavancin, and ceftaroline). ABSSSIs may also be caused by Gram-negative pathogens and can often be polymicrobial in patients with comorbidities and in those previously treated with antibiotics. However, most approved antibacterial options for ABSSSI are only active against Gram-positive pathogens. Options that can be used against Gram-negative pathogens include ceftaroline and tigecycline. If both MRSA and Gram-negative organisms are isolated, options that can be added to MRSA active agents to provide Gram-negative coverage include cephalosporins and aminoglycosides. Fluoroquinolones may also be indicated for cSSSIs/ABSSSIs, as second/last line indication, but they are associated with limitations including a high MRSA resistance rate and safety concerns.[3] SMC has accepted ceftaroline, tigecycline, daptomycin, tedizolid and dalbavancin for restricted use in ABSSSI on the advice of microbiologists or specialists in infectious diseases. The restrictions are mainly for second-line use or to use in MRSA infections. If the infection worsens despite antibiotic therapy, guidelines recommend considering microbiological testing if not already done, reviewing the antibiotic choice when microbiological results are available, and, if the infection is not improving, changing antibiotic, using narrow-spectrum antibiotics where possible.[7]

RX-3341-302 (which assessed delafloxacin IV) and RX-3341-303 (which assessed delafloxacin IV followed by oral delafloxacin) demonstrated that delafloxacin was non-inferior to vancomycin plus aztreonam in patients with ABSSSI in the ITT population of both studies and in the CE population only in RX-3341-302. The EMA considered it acceptable to view the CE population as secondary; and overall non-inferiority of IV as well as IV followed by oral delafloxacin versus vancomycin plus aztreonam was concluded.[3]

The EMA noted that the clinical cure rates in the key studies (around 50% and 60% in the ITT) were somewhat lower than that seen in some other ABSSSI studies; and they noted that this could be explained by the early assessment time point and strict definition of clinical cure (complete resolution of all baseline signs and symptoms of ABSSSI at the follow-up visit) used in delafloxacin studies, while in other studies a broader definition was chosen. **[3]** The clinical success rates, based on a broader definition that included cure but also improvement and no further antibiotic needed, were higher in delafloxacin key studies (around 80% to 90% in the ITT population).

The submitting company requested that SMC considered delafloxacin for use in patients with suspected or confirmed polymicrobial infection in adult patients with an ABSSSI following treatment failure or when standard antibacterial therapies are not suitable. Occurrences where standard antibacterial therapies are not suitable includes intolerances, such as penicillin allergies, drug-drug interactions or side effects.

However, the studies' populations were wider than the proposed positioning; only a limited number of patients in both studies had a microbiological diagnosis at baseline (less than one-third) and very few appeared to have suffered from a polymicrobial infection (less than one fifth of patients with microbiological diagnosis at baseline had a mixed polymicrobial infection). The submitting company presented microbiological eradication response results that suggested efficacy was similar across infection types and across pathogens, including in patients with polymicrobial infection; however, none of the key studies were powered to detect non-inferiority in the subgroup of patients with polymicrobial infection, relevant to the proposed positioning. In addition, no results were available for patients that had experienced treatment failure or for patients for whom standard antibacterial therapies were considered not suitable. Overall, uncertainty remains about the generalisability of study results to the Scottish population that might receive delafloxacin treatment in practice.

In both key studies, the comparator was vancomycin plus aztreonam (aztreonam was added to treat Gram-negative infection and was stopped if baseline cultures were confirmed negative for Gram-negative pathogens). The EMA noted that although vancomycin may not have been the optimal choice of comparator in the treatment of MSSA and streptococci infection and that linezolid would have been more appropriate, it was considered acceptable as it would target a high proportion of MRSA.[3]

The submitting company considered that vancomycin plus aztreonam was a relevant comparator. However, its relevance in the proposed positioning in Scottish clinical practice remains uncertain. The submitting company also defined the following antibacterial triple combinations as relevant comparators in the proposed positioning: daptomycin + ciprofloxacin + metronidazole, linezolid + ciprofloxacin + metronidazole, and vancomycin + ciprofloxacin + metronidazole. Clinical experts consulted by SMC noted other options may also be used in the proposed positioning in Scotland and may be relevant comparators (such as combination therapies that include gentamicin, doxycycline or co-trimoxazole). In practice, antibiotic choice for a particular patient may be influenced by various factors including the microbiology results, the previous failed antibiotic, the patient's comorbidities and drug-drug interactions, which create challenges in defining the most relevant comparators.

The submitting company conducted an NMA with several antibacterial therapies that had a number of limitations. The population was broader than the proposed positioning, and some uncertainty remains about the assumption of clinical equivalence for each treatment in the polymicrobial subgroup and in the broad patient population. There was a high level of clinical and methodological heterogeneity across the included studies, including in terms of disease type, outcome assessment time points, and patients' baseline characteristics. Many comparators were included in the NMA including some that do not appear to be relevant to Scottish clinical practice. In addition, it was not possible to include triple combination therapies and the validity of the assumption of equivalence between these and the gram-positive (monotherapy) component of these combination therapies is uncertain. No other fluoroquinolones were included in the NMA. Clinical experts noted some treatment options that may also be relevant comparators but that were not included in the NMA (such as combination therapies that include gentamicin,

doxycycline or co-trimoxazole). Wide credible intervals were reported for some of the comparisons, indicating uncertainty in the results. Finally, although there were generally no clear differences across treatments, non-inferiority cannot be concluded without formal testing.

Summary of comparative health economic evidence

The company submitted a cost-minimisation analysis comparing delafloxacin to four different combination therapies. The comparators were daptomycin + ciprofloxacin + metronidazole, linezolid + ciprofloxacin + metronidazole, vancomycin + aztreonam and vancomycin + ciprofloxacin + metronidazole. Patients in the economic analysis reflected a sub-population of the licensed indication - suspected or confirmed polymicrobial (PM) infection in adult patients with an ABSSSI following treatment failure or when standard antibacterial therapies are not suitable.

The company developed a decision tree model with a 30-day time horizon. Within each branch, a hypothetical patient cohort was split between a PM-subgroup whose baseline culture results were available and a subgroup whose driving pathogen was unconfirmed. All patients entering the model were assumed to have a PM ABSSSI and initiate empiric, first-line flucloxacillin therapy for their infection at day 0, as an inpatient. After day 2, patients' baseline culture results are presented, with an assumed 30% of patients having a confirmed-PM infection and the remaining 70% of patients having a suspected-PM infection.

All patients with confirmed-PM infection switch to second-line therapy with delafloxacin or comparator after day 2. Patients were assessed for treatment success following receipt of full course of second-line treatment. Non-responders were assumed to be re-hospitalised to receive third- line treatment.

For patients with suspected-PM infection, early responders to flucloxacillin continued on this first-line regimen and were either successfully cured or received a subsequent treatment (same as third- line treatment for confirmed-PM infections). Patients with suspected-PM infection without early response to flucloxacillin in the first 2 days, were switched to delafloxacin or a comparator as second-line treatment.

The clinical response rate for delafloxacin was estimated based on the weighted average of the primary endpoint: treatment success rates reported in the delafloxacin phase II and III trials (RX-3341-201, RX-3341-202, RX-3341-302, RX-3341-303). The weighted average treatment success rate was 84.17%. The same clinical cure rate was also applied to all comparators in the economic model, as the NMA demonstrated no clear differences between delafloxacin and the comparators.

Acquisition and administration costs for delafloxacin and all comparators were included in the analysis, as were the costs associated with inpatient hospital stay, drug monitoring, out-patient parenteral antimicrobial therapy, subsequent treatment and health professional visits.

In the base case analysis, delafloxacin was associated with -£591, -£272, -£279 and -£1,379 lower costs, versus daptomycin + ciprofloxacin + metronidazole, linezolid + ciprofloxacin + metronidazole, vancomycin + aztreonam and vancomycin + ciprofloxacin + metronidazole, respectively. As such, delafloxacin is a cost-saving intervention.

The company provided sensitivity and scenario analysis. The model was most sensitive to treatment success rate, length of inpatient stay, total treatment duration and healthcare costs. However, delafloxacin remained cost saving across all parameters relative to all four comparators across most scenarios. The key driver of cost savings with delafloxacin is the potential for reducing the length of inpatient hospital stays due to the availability of both intravenous and oral formulations.

There were a number of limitations with the analysis which include the following:

- The lack of direct comparative evidence introduces uncertainty regarding the clinical equivalence of delafloxacin to comparator treatments. The NMA supporting this claim suffers from high levels of heterogeneity.
- Uncertainty about the external validity of clinical evidence. The clinical studies included a patient population much broader than that of the proposed positioning and the pivotal trials powered to detect non-inferiority in the subgroup of patients with PM infections.
- There is some uncertainty about delafloxacin treatment duration and length of inpatient stay. The base case analysis includes a treatment duration based on data from the clinical studies, however, there is the potential for longer duration of treatment in practice since delafloxacin is likely to be used in complicated/difficult-to-treat cases. Increasing treatment duration reduces the level of cost savings versus comparators. Inpatient length of stay for delafloxacin was based on data from only one phase II study and this was a key driver of cost savings. Scenario analysis showed that increasing the inpatient stay beyond 5 days combined with increased treatment duration can substantially impact cost savings – particularly versus vancomycin + aztreonam and linezolid + ciprofloxacin+ metronidazole.
- It is unclear whether the comparator treatments included in the analysis are the most relevant and widely used for treating the proposed sub-population. SMC clinical experts noted other treatments which are likely to be used in Scotland.

Despite these limitations, the economic case was deemed demonstrated.

*Other data were also assessed but remain confidential.**

Summary of patient and carer involvement

No patient group submission was received.

Additional information: guidelines and protocols

No specific guidance was identified for ABSSSIs with polymicrobial infections, however the guidelines below make the following relevant recommendations.

The National Institute for Health and Care Excellence (NICE) published the guideline 'Cellulitis and erysipelas: antimicrobial prescribing' in 2019. This guideline recommends that when choosing an antibiotic consideration should be given to symptoms severity, infection site, previous microbiological results from a swab if any, and the person's MRSA status if known. It also recommends to give oral antibiotics first-line if the patient can take oral medicines, and the severity of their condition does not require IV antibiotics. If IV antibiotics are given, it recommends to review by 48 hours and consider switching to oral antibiotics if possible. The first oral antibiotic of choice should be flucloxacillin (or co-amoxiclav if the infection is near the eyes or nose). For penicillin allergy or if flucloxacillin is unsuitable, alternative first choice antibiotics are clarithromycin, erythromycin (in pregnancy) or doxycycline. Clarithromycin with metronidazole is an alternative first choice if the infection is near the eyes or the nose for penicillin allergy or if co-amoxiclav is unsuitable. For severe infection, the guidance recommends the following alternative choice antibiotics: co-amoxiclav, cefuroxime, clindamycin or ceftriaxone (only for ambulatory care, but the guidance notes that other antibiotics may be appropriate based on microbiological results and specialist advice). Antibiotics to be added if an MRSA infection is suspected or confirmed are vancomycin, teicoplanin or linezolid (if vancomycin or teicoplanin cannot be used). The guideline recommends to consider a swab for microbiological testing if not done already. If infection is not improving/ worsening, recommendations include: to consider taking a swab for microbiological testing if the skin is broken and this has not been done already, a review of the antibiotic choice when any microbiological results are available, and a change of antibiotic using narrow-spectrum antibiotics where possible. [7]

The Surgical Infection Society (SIS) published the 'Guidelines for the treatment of complicated skin and soft tissue infections (SSTIs)' in 2009, which was updated in 2020. The guidance recommends linezolid, doxycycline or minocycline, and trimethoprim-sulfamethoxazole as first-line oral treatment options for suspected or confirmed MRSA infection. Additional oral alternatives that may be considered include tedizolid, delafloxacin and omadacycline. The guideline also recommends vancomycin, linezolid, daptomycin, ceftaroline and telavancin as first-line IV treatment options, but additional alternatives may include dalbavancin, oritavancin, omadacycline, tedizolid, delafloxacin and tigecycline. The guidance notes that narrow-spectrum antibiotics without Gram-negative coverage for complicated SSTI can be considered in areas with low levels of antibiotic resistance and patient populations not needing immediate broad-spectrum due to severity of illness or risk for polymicrobial infections.[8]

The British Society for Antimicrobial Chemotherapy (BSAC) and the British Infection Association (BIA) published in 2021, 'Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): updated guidelines from the UK', which updated the previous guideline from 2008. For severe cellulitis or soft tissue infection caused by MRSA, the guidance recommends vancomycin or teicoplanin IV but linezolid and daptomycin may be considered as alternatives. The guidance also

notes that recently licensed agents such as ceftaroline, delafloxacin, oritavancin, or telavancin may be considered. No recommendations could be made on the use of ceftobiprole, dalbavancin and tedizolid over standard therapeutic agents in the treatment of SSTI caused by MRSA.[9]

Additional information: comparators

Mono or combination antibiotic therapies (which include daptomycin, ciprofloxacin, metronidazole, linezolid, vancomycin, teicoplanin, dalbavancin, co-trimoxazole, doxycycline, co-amoxiclav, or gentamicin).

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per patient (£)
Delafloxacin	**450mg orally or 300mg IV every 12 hours for 5 to 14 days.**	**615 to 1,722**

Costs from BNF online on 01/04/2022.

Additional information: budget impact

The gross medicines budget impact was estimated to be £12k in year 1 rising to £50k in year 5. As other medicines were assumed to be displaced the net medicines budget impact was estimated to be -£2k in year 1 rising to -£6k in year 5.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 13 May 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.