Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2285

# oritavancin 400mg powder for concentrate for solution for infusion (Tenkasi®)

## Menarini International Operations Luxembourg S.A.

04 September 2020 *(Issued 08 April 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 resubmission

**oritavancin (Tenkasi®)** is accepted for restricted use within NHSScotland.

**Indication under review:** treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults.

**SMC restriction:** patients with confirmed or suspected methicillin-resistant Staphylococcus aureus (MRSA) infection who are eligible for early discharge. Use should be on the advice of local microbiologists or specialists in infectious disease.

In two randomised, phase III, double-blind studies of patients with ABSSSI, oritavancin was non-inferior to a glycopeptide antibiotic for clinical cure at the end of treatment in the clinically evaluable population.

**Chairman**
**Scottish Medicines Consortium**

## Indication

Treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

## Dosing Information

1,200mg administered as a single dose by intravenous infusion over three hours.[1]

## Product availability date

04 April 2022.

## Summary of evidence on comparative efficacy

Acute bacterial skin and skin structure infections (ABSSSI) include wound infections, cellulitis and major cutaneous abscesses, and often present with redness, oedema, induration and systemic symptoms. Treatment may involve systemic antibiotics and surgical management. Oritavancin is a semi-synthetic, lipoglycopeptide antibacterial, structurally similar to vancomycin. It has activity against Gram-positive bacteria, causing rapid bacterial cell death through inhibition of cell wall biosynthesis and disruption of membrane integrity. Oritavancin has received marketing authorisation for the treatment of ABSSSI in adults.[2]

The submitting company has requested that SMC consider oritavancin when positioned for use in adult patients with ABSSSI confirmed or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and who are eligible for early discharge.

SOLO I and SOLO II were two identical, international, multicentre, randomised, double-blind, non-inferiority, phase III studies which compared the efficacy and safety of intravenous (IV) oritavancin versus IV vancomycin in patients with ABSSSI. The studies recruited adults with ABSSSI (wound infection, cellulitis, erysipelas, or major cutaneous abscess) confirmed or suspected to be caused by a Gram-positive pathogen and with evidence of systemic inflammation requiring IV treatment for at least seven days. Patients were randomised in a 1:1 ratio to IV oritavancin 1,200mg as a single dose followed by IV placebo every 12 hours for seven to ten days (SOLO I n=475; SOLO II n=503), or to IV vancomycin 1g or 15mg/kg every 12 hours for seven to ten days (SOLO I n=479; SOLO II n=502). Oritavancin was administered as an IV infusion over three hours. Vancomycin was administered as an IV infusion over three hours for the first dose; subsequent doses, which could be adjusted by an unblinded pharmacist according to standard practice, were administered over at least one hour. Patients with mixed infections were permitted to receive aztreonam and metronidazole. In the modified intention-to-treat (mITT) population, 22% (104/475) and 20% (100/503) of patients in the oritavancin groups of SOLO I and II respectively, were positive for MRSA infection-site and blood cultures, versus 21% (100/479) and 20% (101/502) of patients in the vancomycin groups.[2-4]

The protocol-defined primary composite outcome was the cessation of spreading or reduction in baseline lesion size, absence of fever, and absence of need for administration of a rescue antibiotic 48 to 72 hours after administration of study drug (early clinical evaluation). Clinical cure (determined by the study investigator) 7 to 14 days after the end of treatment (post-therapy evaluation) was the primary outcome considered by the European Medicines Agency (EMA). Non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) for the difference between oritavancin and vancomycin was higher than −10%. Primary and secondary efficacy analyses were performed in the mITT population, which included all patients who underwent randomisation and received the allocated study drug. Efficacy analyses were confirmed in the clinically evaluable (CE) population, which included all patients in the mITT population who met the inclusion criteria, received a full course of study drug for a minimum of 7 days, and had an assessment for clinical cure at the post-therapy evaluation. The microbiological ITT (MicroITT) population included all patients in the mITT population with a Gram-positive pathogen detected at baseline, and was used for secondary efficacy analyses.[2-4]

Non-inferiority was demonstrated for the protocol-defined primary composite outcome and the EMA primary outcome (clinical cure) for both studies in the mITT and clinically evaluable populations.[3, 4] Results are presented in table 1.

**Table 1: Results of protocol-defined primary composite outcome and EMA primary outcome analyses for SOLO I and II** [3, 4]

| Population | Oritavancin | | Vancomycin | | % Difference (95% CI) | |
|---|---|---|---|---|---|---|
| | **SOLO I** | **SOLO II** | **SOLO I** | **SOLO II** | **SOLO I** | **SOLO II** |
| **% of patients achieving the protocol-defined primary composite outcome at early clinical evaluation (n/N)** | | | | | | |
| **mITT** | 82% (391/475) | 80% (403/503) | 79% (378/479) | 83% (416/502) | 3.4% (-1.6 to 8.4) | -2.7% (-7.5 to 2.0) |
| **CE** | 87% (344/394) | 84% (357/427) | 86% (342/397) | 88% (358/408) | 1.2% (-3.6 to 5.9) | -4.1% (-8.9 to 6.0) |
| **% of patients achieving the EMA primary outcome: clinical cure at post-therapy evaluation (n/N)** | | | | | | |
| **mITT** | 80% (378/475) | 83% (416/503) | 80% (383/479) | 80% (404/502) | -0.4% (-5.5 to 4.7) | 2.2% (-2.6 to 7.0) |
| **CE** | 91% (357/394) | 93% (398/427) | 89% (352/397) | 95% (387/408) | 1.9% (-2.3 to 6.2) | -1.6% (-4.9 to 1.6) |

mITT=modified intention-to-treat population; CE=clinically evaluable population; EMA=European Medicines Agency; CI=confidence interval

A ≥20% reduction in lesion size, 48 to 72 hours after administration of study drug, was assessed as a secondary outcome, and non-inferiority was demonstrated for both studies in the mITT population. In SOLO I, this outcome was achieved by 87% (413/475) and 83% (397/479) of patients in the oritavancin and vancomycin groups, respectively (percentage difference 4.1% [95% CI: -0.5 to 8.6]). In SOLO II, the outcome was achieved by 86% (432/503) and 85% (428/502) of patients, percentage difference 0.6% (95% CI: -3.7 to 5.0). Results were confirmed in the clinically evaluable populations for both studies.[3, 4]

In the MRSA subgroup (relevant to the company's positioning), similar efficacy was demonstrated in the oritavancin and vancomycin groups in the MicroITT populations for the protocol-defined primary composite and secondary outcomes, and the EMA primary outcome, in both studies. Results are presented in table 2.[3, 4]

**Table 2: Results of primary and secondary outcome analyses in the MRSA subgroups of SOLO I and II** [3, 4]

| Population (subgroup) | Oritavancin | | Vancomycin | | % Difference (95% CI) | |
|---|---|---|---|---|---|---|
| | SOLO I | SOLO II | SOLO I | SOLO II | SOLO I | SOLO II |
| **% of patients achieving the protocol-defined primary composite outcome (n/N)** | | | | | | |
| MicroITT (MRSA) | 81% (84/104) | 82% (82/100) | 80% (80/100) | 81% (82/101) | 0.8% (-10.1 to 11.7) | 0.8% (-9.9 to 11.5) |
| **% of patients achieving the EMA primary outcome: clinical cure (n/N)** | | | | | | |
| MicroITT (MRSA) | 83% (86/104) | 84% (84/100) | 83% (83/100) | 85% (86/101) | -0.3% (-10.7 to 10.0) | -1.1% (-11.1 to 8.8) |
| **% of patients achieving the secondary outcome: ≥20% lesion size reduction (n/N)** | | | | | | |
| MicroITT (MRSA) | 90% (94/104) | 96% (96/100) | 84% (84/100) | 90% (91/101) | 6.4% (-2.8 to 15.5) | 5.9% (-1.1 to 12.9) |

MRSA=meticillin-resistant *Staphylococcus aureus;* EMA=European Medicines Agency; CI=confidence interval; MicroITT=microbiological intention-to-treat population

There are no comparative data available with other treatments currently used in Scottish clinical practice (for example IV teicoplanin, IV daptomycin, IV dalbavancin or oral linezolid). Therefore, the submitting company presented Bayesian network meta-analyses (NMAs) that included 39 studies and compared treatments for a range of clinical and safety outcomes in adult patients with ABSSSI, complicated SSSI (cSSSI) and complicated skin and soft tissue infection (cSSTI). The NMAs allowed a comparison of oritavancin versus various comparators including IV daptomycin, IV dalbavancin and oral linezolid. In addition, clinical response, early response and microbiological response were also assessed in the subgroup of patients with MRSA. The submitting company concluded that the NMAs demonstrated non-inferiority of oritavancin, compared with available treatments, for the majority of efficacy and safety outcomes and that there were no results demonstrating a significant difference between oritavancin and any other alternative treatment in composite clinical response in the full or MRSA populations.

## Summary of evidence on comparative safety

Due to the long half-life of oritavancin, patients were followed up for safety assessment for a period of 60 days in the SOLO I and II studies.

In the oritavancin and vancomycin treatment groups of SOLO I, adverse events were reported in 60% (284/473) and 64% (307/481) of patients, respectively, and were considered to be treatment-related in 23% (108/473) and 31% (151/481) of patients. Serious adverse events were reported in 7.4% (35/473) and 7.3% (35/481) of patients and were treatment-related in three patients (0.6%) in both groups. Treatment discontinuation due to adverse events occurred in 3.8% (18/473) of

patients in the oritavancin group and in 5.8% (28/481) in the vancomycin group. The most commonly reported adverse events in the oritavancin group were nausea (11% [52/473], versus 8.9% [43/481] in the vancomycin group), headache (7.2% [34/473] versus 7.9% [38/481]), vomiting (4.9% [23/473] versus 3.7% [18/481]), and diarrhoea (4.9% [23/473] versus 3.5% [17/481]). A greater proportion of patients in the oritavancin group (2.7% [13/473]) reported limb abscess compared with the vancomycin group (1.0% [5/481]). Osteomyelitis was reported in one patient in each treatment group (0.2% [1/473] and 0.2% [1/481]).[3]

Similar results were observed in SOLO II. A greater proportion of patients in the oritavancin group (2.8% [14/503]) reported limb abscess compared with the vancomycin group (1.6% [8/502]), and osteomyelitis was reported in five patients (0.9%) in the oritavancin group and in zero patients in the vancomycin group.[4]

The European Public Assessment Report (EPAR) noted that, with a few exceptions, there were no marked differences between oritavancin and vancomycin in terms of safety. Particular safety concerns with regards to excess reports of abscesses and osteomyelitis with oritavancin are to be followed up by the EMA, and precautions related to these adverse events are reflected in the Summary of Product Characteristics (SPC).[1, 2]

## Summary of clinical effectiveness issues

Oritavancin is licensed for the treatment of ABSSSI in adults. SMC has accepted ceftaroline, tigecycline, daptomycin, tedizolid and dalbavancin in ABSSSI for restricted use on the advice of microbiologists or specialists in infectious diseases. The restrictions are mainly for second-line use or to use in MRSA infections.

The submitting company has requested that SMC consider oritavancin when positioned for use as a therapy in adult patients with ABSSSI confirmed or suspected to be caused by MRSA who are eligible for early discharge. The submitting company considers that, in this setting, patients will have initially received treatment with flucloxacillin or vancomycin. Clinical experts consulted by SMC considered that vancomycin is currently used as first line treatment for patients with ABSSSI caused by MRSA who are unlikely to be discharged shortly after admission and that IV teicoplanin, IV daptomycin, IV dalbavancin or oral linezolid would most likely be used in the subgroup of patients with MRSA at time of early discharge (IV antibiotics administered as outpatient parenteral antibiotic therapy [OPAT]).

SOLO I and II demonstrated that, for the primary and secondary outcomes, a single dose of IV oritavancin was non-inferior to twice-daily dosing of IV vancomycin in patients with ABSSSI due to Gram-positive pathogens, and similar efficacy was demonstrated in the MRSA subgroups. However, vancomycin is not considered a relevant comparator for the positioning proposed by the company. Additionally, only 21% (204/978) of patients in the oritavancin groups of SOLO I and II were positive for MRSA (relevant to the proposed positioning), and the studies were not powered

to detect non-inferiority in this subgroup. Patients were excluded from the studies if they received prior treatment with systemic or topical antibacterials with activity against Gram-positive pathogens within the previous 14 days so the treatment pathway does not correlate with the proposed positioning in patients previously treated with flucloxacillin and vancomycin. There was no direct evidence to compare oritavancin with IV teicoplanin, IV daptomycin, IV dalbavancin or oral linezolid, and no quality of life information was presented.

The submitting company presented NMAs that compared the efficacy of oritavancin versus active comparators (including IV daptomycin, IV dalbavancin and oral linezolid) including in the MRSA subgroup. It was not possible to include teicoplanin in the network since no studies including teicoplanin for the treatment of complicated infections were found in the systematic literature review. The NMA results were not directly used in the economic model, however they were used to support the assumption of equivalence amongst treatments used in the proposed positioning and, therefore, the use of a cost-minimisation analysis. The NMAs consisted of eight networks to compare the efficacy of antimicrobials for treating adults with ABSSSI and other SSSI. The NMA was limited by considerable heterogeneity across studies regarding patients' characteristics, population, study design and setting. The wide 95% credible intervals in some comparisons indicated a high level of uncertainty, which can be explained by the small number of studies informing the networks and the heterogeneity across included studies. While the NMAs' conclusions are uncertain, they provide some reassurance of similar clinical effectiveness versus alternatives.

The EPAR for oritavancin noted that there was limited experience of oritavancin in immunocompromised patients and in those with bacteraemia, peripheral vascular disease, neutropenia, or aged over 65 years old; the limitations are reflected in the SPC.[1]

Clinical experts consulted by SMC considered that the introduction of oritavancin would provide an additional treatment option for ABSSSI confirmed or suspected to be caused by MRSA.

## Summary of comparative health economic evidence

The company submitted a cost-minimisation analysis comparing oritavancin to four different comparators namely dalbavancin, teicoplanin, daptomycin and linezolid for the treatment of adult patients with ABSSSI, confirmed or suspected to be caused by MRSA, who are eligible for early discharge from hospital (inpatient) and have initially received treatment with flucloxacillin or vancomycin. Clinical expert input received by SMC suggests that dalbavancin appears to be the comparator most likely to be displaced in Scotland.

The company used a decision analytic model to assess the cost-effectiveness of oritavancin versus the comparators. The time horizon used in the analysis was 30 days. In terms of model structure, all patients entered the model with initiation of empiric therapy for ABSSSI with flucloxacillin or vancomycin at day 0 as an inpatient. On day 3, patients found to have confirmed or suspected

MRSA switched to MRSA specific treatment with vancomycin. On day 4, all patients were found to be suitable for early discharge were discharged and continued therapy as an outpatient with either oritavancin or another of the comparators for next six days. Following discharge, patients received outpatient monitoring dependent on the administration route of their therapy. On day 10, assessment of clinical cure took place and patients who were cured were discharged from outpatient monitoring, with no requirement for further follow-up. Patients who were not cured were considered to experience 'treatment failure 'and were initiated a 10-day course of rescue therapy (IV linezolid) in hospital. Between assessment of clinical cure and the completion of the model time horizon, patients were at risk of rehospitalisation due to recurrence of their initial infection which did not vary according to whether clinical cure was determined or not. Re-hospitalised patients were treated for a further 10 days with IV linezolid.

The clinical effectiveness parameters for oritavancin were estimated from two phase III clinical studies (SOLO I and SOLO II). The results from these two studies were pooled across studies and treatment arms to estimate a clinical cure rate for oritavancin at post therapy evaluation (PTE) visit, which is between 7-14 days after the end of treatment. Clinical cure was defined as complete or nearly complete resolution of baseline signs and symptoms of the primary infection such that no further treatment with antibiotics is needed. The same clinical cure rate was also applied to all comparators in the economic model as the NMA demonstrated similar effectiveness of oritavancin across all comparators for the majority of efficacy and safety outcomes in the full population and efficacy outcomes in the MRSA population. The specific data from the NMA were not used directly in the economic model, but the results and overall conclusions of the NMA were still used to support the assumption of similar equivalence between the therapies given at earlier discharge for ABSSSI in Scotland, as necessary for the use of a cost-minimisation approach.

Acquisition and administration costs for oritavancin and all comparators were included in the analysis, as were the costs associated with inpatient (hospital stay), medicines monitoring, OPAT costs and health professional visit costs were included. Oritavancin was costed as a single dose treatment; dalbavancin was given either as a single dose of 1,500 mg, to 25% of patients, or a single dose of 1,000 mg followed by a dose of 500 mg a week later, to 75% of patients.

The cost-minimisation analysis reported that the cost per patient for treating ABSSSI from empiric treatment through to clinical cure with oritavancin was £5,066. The cost of dalbavancin was £5,352 whereas the cost of teicoplanin, daptomycin and linezolid were £4,652, £4,973 and £4,068 respectively as shown in table 3 below. On the basis of these findings, oritavancin was cost-minimising compared to dalbavancin but not against the other comparators (which are administered as multiple doses).

**Table 3: Base case analysis results**

| | Oritavancin | Dalbavancin | Teicoplanin | Daptomycin | Linezolid |
|---|---|---|---|---|---|
| **Medication costs (£)** | 1,798 | 1,974 | 349 | 670 | 832 |
| **Inpatient costs (£)** | 3,236 | 3,236 | 3,236 | 3,236 | 3,236 |
| **OPAT costs (£)** | - | 133 | 1,067 | 1,067 | - |
| **Outpatient costs (£)** | 32 | 8 | - | - | - |
| Total (£) | 5,066 | 5,352 | 4,652 | 4,973 | 4,068 |
| **Treatment days** | 7 | 8 | 12 | 12 | 12 |
| **Inpatient days** | 6 | 6 | 6 | 6 | 6 |
| Cost per treatment day avoided | - | Oritavancin is dominant | 83 | 19 | 200 |
| Incremental cost per patient comparator versus oritavancin | - | £286 | -£414 | -£93 | -£998 |

OPAT= outpatient parenteral antibiotic therapy

One way sensitivity analysis varying parameters +/- 30%, used to provide sufficient variation for uncertainties in the parameter estimates in the model, demonstrated the impact of varying individual parameters on the incremental costs of oritavancin relative to the four comparators in the model in turn. Overall the figures showed that the model was most sensitive to clinical cure rate for oritavancin and the cost of treatment with oritavancin. For example, the results versus dalbavancin ranged from a cost saving of -£1,308 to an incremental cost of £1,290 when the range of clinical cure rate for oritavancin was varied. Versus dalbavancin, the one way analysis results were also sensitive to the cost of treatment associated with dalbavancin. Scenario analysis was also provided on request to vary the proportion of patients assumed to be treated with a single dose of dalbavancin as shown in table 4. This indicated that the estimated cost savings of -£286 (in the base case) from using oritavancin instead of dalbavancin reduced as proportion of patients assumed to be treated with a single dose of dalbavancin increased, but oritavancin remained cost-minimising.

**Table 4: Total costs associated with dalbavancin treatment according to proportion of patients treated in a single dose**

| Proportion of patients treated in a single dose | Total costs of treatment with dalbavancin |
|---|---|
| 25% (base case) | £5,352 |
| 50% | £5,315 |
| 75% | £5,279 |
| 100% | £5,242 |

Weaknesses in the economic analysis were as follows:

- The main weakness in the analysis results from the lack of direct comparative data for oritavancin against the relevant comparators in the proposed positioning, such as daptomycin, teicoplanin, dalbavancin and linezolid. This gives rise to uncertainty around the estimate of clinical cure rates at PTE which has been applied across all comparators. This limitation is further heightened since the trials (SOLO I & SOLO II) from which clinical cure rates have been estimated were not powered to test the non-inferiority of oritavancin by pathogen subgroups, including the MRSA subgroup. Sensitivity analysis highlighted the sensitivity around this parameter as it has the maximum influence on base case incremental costs.
- Resource use frequencies used in the analysis were primarily based on clinical expert opinion, but don't seem to influence the results significantly.

Despite the issues stated above, the economic case was considered to be demonstrated, particularly compared to dalbavancin as the likely predominant comparator.

## Summary of patient and carer involvement

Patient Group Submissions were not required as this submission was assessed through an amended process used during the COVID-19 pandemic.

## Additional information: guidelines and protocols

The Scottish Antimicrobial Prescribing Group (SAPG) published in 2019 'Guidance on management of proven or suspected *Staphylococcus aureus* bacteraemia (SAB) in adults'; a best practice algorithm for the management of patients with SAB. This guidance indicates that early prescription and administration of empirical IV antibiotic therapy should be initiated in all patients with SAB. If the infection is confirmed or suspected to be caused by MRSA, treatment with IV vancomycin is recommended, either as intermittent infusions or as continuous infusion for a minimum period of 2 weeks.[5]

The World Society of Emergency Surgery (WSES) and the Surgical Infection Society Europe (SIS-E) consensus conference, published in 2018 'Recommendations for the management of skin and soft-tissue infections'. For patients with suspected severe MRSA infections, this guidance recommends the following IV antibiotic treatments: vancomycin 15mg/kg every 12 hours; teicoplanin LD 12mg/kg every 12 hours for three doses, then 6 mg/kg every 12 hours; tigecycline 100mg as a single dose, then 50mg every 12 hours; linezolid 600mg every 12 hours; daptomycin 4–6 mg/kg once a day; ceftaroline 600mg every 12 hours, dalbavancin 1000mg once followed by 500mg after 1 week or 1500 mg one dose and tedizolid 200mg once a day. When clinical improvement is

documented, the goal should be to transition to the oral route as soon as possible. Otherwise, oral antibacterial options are recommended for mild infections.[6]

The British National Formulary (BNF) online prescription guidance for MRSA infections indicates that choice of treatment is guided by the sensitivity of the infecting strain. A tetracycline alone or a combination of rifampicin and fusidic acid can be used for skin and soft-tissue infections caused by MRSA; clindamycin alone is an alternative. For severe skin and soft-tissue infections associated with MRSA, a glycopeptide, such as vancomycin can be used; if a glycopeptide is not suitable, linezolid can be used on expert advice. As linezolid is not active against Gram-negative organisms, it can be used for mixed skin and soft-tissue infections only when other treatments are not available; linezolid must be given with other antibacterials if the infection also involves Gram-negative organisms. A combination of a glycopeptide and fusidic acid or a glycopeptide and rifampicin can be considered for skin and soft-tissue infections that have failed to respond to a single antibacterial. It is noted that tigecycline and daptomycin are licensed for the treatment of complicated skin and soft-tissue infections involving MRSA.[7]

The National Institute for Health and Care Excellence (NICE) published in 2019 an antimicrobial prescribing guideline for cellulitis and erysipelas. This recommends that the first oral antibiotic of choice should be flucloxacillin. For suspected or confirmed MRSA infection, vancomycin, teicoplanin or if these cannot be used, for specialist use, linezolid, are recommended. It is also noted that other antibiotics may be appropriate based on microbiological results and specialist advice.[8]

## Additional information: comparators

Vancomycin IV is used for first line treatment of MRSA, then teicoplanin, daptomycin, dalbavancin or linezolid.

## Additional information: list price of medicine under review

| Medicine | Dose Regimen | Cost per course (£) |
|---|---|---|
| Oritavancin | 1,200mg by IV infusion as a single dose | 1,500 |

*Costs from company submission. Costs calculated using the full cost of vials/ampoules assuming wastage.*

## Additional information: budget impact

The estimated number of patients eligible for treatment was 108 in each year from year 1 to year 5. Treatment uptake was estimated at 0.55% in year 1 and 5.16% in year 5. This resulted in 1 patient assumed to be treated in year 1 rising to 6 in year 5.

The company estimated that the gross medicines budget impact in year 1 was £888 rising to £8.3k in year 5. As medicines were assumed to be displaced the net medicines budget impact was assumed to be £122 in year 1 rising to £1k in year 5.

The budget impact model estimated savings due to reduced use of OPAT. The net total budget impact was savings of £90 in year 1 rising to £892 in year 5.

**References**

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This assessment is based on data submitted by the applicant company up to and including 27 July 2020.

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.*