National Institute for Health and Care Excellence

Hospital-acquired pneumonia caused by methicillin-resistant Staphylococcus aureus: telavancin

Published: 15 July 2014

This is information from a NICE 'Evidence summary: new medicines', and is not NICE guidance. The complete commentary is available at http://publications.nice.org.uk/esnm44

Full evidence summary

Introduction and current guidance

Hospital-acquired pneumonia is defined as pneumonia that occurs 48 hours or more after hospital admission and is not incubating at hospital admission (NICE clinical guideline in development on pneumonia: final scope).

Early-onset (occurring within 4 days of admission) hospital-acquired pneumonia is usually caused by the same bacteria and viruses as community-acquired pneumonia and has a good prognosis. Late-onset (starting 5 days or more after admission) hospital-acquired pneumonia has a worse prognosis and is usually caused by microorganisms that are acquired from the hospital environment. Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* and other non-pseudomonal Gram-negative bacteria are the most common causes (NICE clinical guideline in development on pneumonia: final scope).

Hospital-acquired pneumonia is estimated to increase hospital stays by 7–9 days and has a mortality of between 30 and 70%. These figures include hospital-acquired pneumonia that develops in patients who are intubated in an intensive care unit. This is known as ventilator-associated pneumonia and is clinically distinct from hospital-acquired pneumonia in non-intubated patients. In a 2011 survey of 52,443 patients in 99 NHS trusts in England, the prevalence of hospital-associated pneumonia or lower respiratory tract infection was 1.5%. Pneumonia or lower respiratory tract infections were the most frequent types of

healthcare-associated infection, accounting for 22.8% of cases. Treatment is with oral or intravenous antibiotics (depending on illness severity). Supportive therapy including oxygen, fluids, prophylaxis against venous thromboembolism, analgesia and nutritional support is often necessary (NICE clinical guideline in development on pneumonia: final scope).

NICE is currently developing a clinical guideline on pneumonia, which will cover both community- and hospital-acquired pneumonia in adults (anticipated publication date December 2014).

Product overview

Drug action

Telavancin is a lipoglycopeptide antibacterial agent, the first of a new class of antibiotics. It has a dual bactericidal action that inhibits cell wall synthesis and disrupts bacterial cell membrane function (Clinigen Healthcare Limited: personal communication March 2014).

Telavancin is active against Gram-positive bacteria only. In mixed infections where Gram-negative or certain types of anaerobic bacteria are suspected, telavancin should be given with the appropriate antibacterial agent(s) (summary of product characteristics).

Licensed therapeutic indication

Telavancin was granted a marketing authorisation from the European Medicines Agency in 2011 for the 'treatment of adults with nosocomial pneumonia including ventilator-associated pneumonia, known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Telavancin should only be used in situations where it is known or suspected that other alternatives are not suitable.'

As stated in the approved indication, consideration should be given to official guidance on the appropriate use of antibacterial agents.

Course and cost

The recommended dose is 10 mg per kg every 24 hours for 7 to 21 days. Patients with a creatinine clearance of 30 to 50 ml/min should have the dose reduced to 7.5 mg per kg every 24 hours. Telavancin is contraindicated in patients with acute renal failure or patients with severe renal impairment (creatinine clearance less than 30 ml/min, including patients receiving

haemodialysis). In older people, or people who are obese the dose of telavancin should be adjusted in accordance with the person's bodyweight and renal function. No dose adjustment is needed for patients with mild or moderate hepatic impairment. However, the summary of product characteristics states that no data are available for people with severe hepatic impairment and, therefore, it recommends caution for this group of patients.

Telavancin is available in 2 strengths (250 mg and 750 mg) provided as a vial containing powder for concentrate for solution for infusion. It should be given as an intravenous infusion over a 60-minute period (Vibativ; summary of product characteristics).

The cost of the 750 mg vial is anticipated to be £645 and the cost of the 250 mg vial is anticipated to be £258 (Clinigen Healthcare Limited: personal communication March and May 2014). Based on this price the treatment cost for a patient of 75 kg treated at a dose of 10 mg per kg would range from £4515 for 7 days of treatment to £9030 for 14 days of treatment.

Evidence review

This evidence summary is based on a pooled analysis of 2 identically designed randomised controlled trials (RCTs) (Rubinstein et al. 2011). The 2 studies were conducted in patients with hospital-acquired pneumonia suspected to be due to Gram-positive pathogens. The studies compared intravenous (IV) telavancin (10 mg per kg every 24 hours) with IV vancomycin (1 g every 12 hours) for 7 to 21 days for the primary outcome of clinical response at follow-up or test-of-cure visit. The studies were designed to show that telavancin was non-inferior to vancomycin. A post-hoc analysis of Rubinstein et al. (2011), which excluded people with severe renal impairment and pre-existing acute renal failure at baseline (Torres et al. 2014), is briefly discussed in the clinical effectiveness section. A second post-hoc analysis (Corey et al. 2014), which investigated 28-day survival, is also briefly discussed in the safety section.

Rubinstein et al. (2011)

- Design: pooled analysis of 2 phase III identically designed randomised double-blind, comparator-controlled, parallel group studies. The method of allocation described suggests that this was concealed. The studies were conducted at 274 study sites in 38 countries.

- Population: 1503 patients (the all-treated population) aged 18 years and over (mean age 62.5 years; about one-third female) with pneumonia acquired after 48 hours in an inpatient acute or chronic care facility or that developed within 7 days of being discharged; 28.5% of

participants had ventilator-associated pneumonia. Participants were required to have at least 2 of the following signs and symptoms: cough, purulent sputum, auscultatory findings, dyspnoea, tachypnoea or hypoxaemia; or to have had an organism isolated from the respiratory tract or blood that was identified as being consistent with a respiratory pathogen. In addition, participants had to have at least 2 of the following signs and symptoms: fever (classed as a temperature greater than 38°C) or hypothermia (rectal or core temperature less than 35°C); respiratory rate greater than 30 breaths per minute; pulse rate 120 beats per minute or greater; altered mental status; need for mechanical ventilation; total peripheral white blood cell count greater than 10,000 cells per mm^3, greater than 15% immature neutrophils or total white blood cell count less than 4500 cells per mm^3. All participants were required to have new or progressive infiltrates, consolidation, with or without pleural effusion, on chest radiograph (or computed tomography) and an adequate respiratory specimen for Gram-stain and culture. Participants who were excluded included those who had received systemic antibiotic therapy for Gram-positive pneumonia for more than 24 hours before randomisation (unless there was documented clinical failure after 3 days of treatment or if the pathogen was resistant in vitro to previous treatment), those for whom only Gram-negative bacteria was seen on the Gram-stain or culture, or those who had a pulmonary disease such as lung cancer or tuberculosis that could interfere with evaluation of treatment response. More than half the patients were in intensive care units at baseline. There were a total of 480 clinically evaluable participants who had a Gram-positive pathogen isolated from baseline respiratory specimens or blood cultures; 293 (61%) of these participants had MRSA (with or without concomitant pathogens).

- Intervention and comparison: participants were randomised 1:1 to IV telavancin 10 mg per kg every 24 hours or IV vancomycin 1 g every 12 hours for 7 to 21 days. The dose of telavancin was adjusted in participants with a creatinine clearance of 50 ml/min or less. The vancomycin dose could be monitored and adjusted but this had to be done in a way that would not compromise blinding (details not provided). For participants with pneumonia due to suspected or proven methicillin-susceptible *Staphylococcus aureus* (MSSA), a switch to an antistaphylococcal penicillin from vancomycin was allowed. For participants with mixed Gram-positive and Gram-negative infection, concomitant treatment with aztreonam or piperacillin-tazobactam was allowed.

- Outcomes: the primary efficacy outcome of each study was clinical response at follow-up or test-of-cure visit. The follow-up or test-of-cure assessment was conducted 7 to 14 days after the end of treatment. (Treatment response was defined as 'cured', 'failed' or 'indeterminate'. See table 1 for definitions). Failure at end of treatment was carried forward to the follow-up

assessment. The primary efficacy end point was tested for non-inferiority of telavancin
compared with vancomycin in both the all-treated (n=1503) and clinically evaluable (n=654)
populations using a pre-specified non-inferiority margin of 20%. A pre-specified secondary
outcome assessed superiority of telavancin compared with vancomycin for cure rates in a
pooled analysis of participants from the 2 studies with microbiological confirmation of MRSA.
Adverse events, vital signs, electrocardiograms and laboratory parameters were also
evaluated.

Table 1 Summary of pooled analysis Rubinstein et al. (2011)

	Telavancin IV 10 mg per kg every 24 hours	Vancomycin IV 1 g every 12 hours	Analysis
Randomised	n=767	n=765	
Efficacy: all-treated population[a]	n=749	n=754	
Cure rates at follow-up assessment[b]	58.9% (441/ 749)	59.5% (449/ 754)	Treatment difference −0.7%; 95% CI −5.6 to 4.3% (non-inferior)
Efficacy: clinically evaluable population[c]	n=312	n=342	
Cure rates at follow-up assessment[b]	82.4% (257/ 312)	80.7% (276/ 342)	Treatment difference 1.7%; 95% CI −4.3 to 7.7% (non-inferior)
Selected secondary outcomes:			
Cure rates at follow-up assessment in participants with confirmed MRSA[d]	74.8% (104/ 139)	74.7% (115/ 154)	Treatment difference 0.4%; 95% CI −9.5 to 10.4% (telavancin not shown to be superior to vancomycin)[e]
Safety[f]	n=751	n=752	
Death	20% (150/ 751)	18.6% (140/ 752)	Treatment difference −1.4%; 95% CI −2.6 to 5.3%

Serious adverse events	31% (234/751)	26% (197/752)	No statistical analysis presented
Discontinued study medication because of treatment-emergent adverse event	8% (60/751)	5% (40/752)	No statistical analysis presented
Treatment-emergent renal impairment[g]	10% (74/751)	8% (57/752)	No statistical analysis presented

Abbreviations: CI, confidence interval; IV, intravenous.

[a] All-treated population: all randomised participants who received at least 1 dose of study medication.

[b] Cure was defined as improvement or lack of progression of baseline radiographic findings at end of treatment and resolution of signs and symptoms of pneumonia at follow-up assessment. Follow-up assessment was conducted 7 to 14 days after the end of treatment. Failure was defined as persistence or progression of signs and symptoms of pneumonia at follow-up or progression of radiological signs at end of treatment; termination of study medications because of lack of efficacy and initiation within 2 calendar days of a different potentially effective antistaphylococcal medication; death on or after day 3 attributable to the primary infection or relapse of infection after termination of study medication. Indeterminate response was defined as the inability to determine outcome.

[c] Clinically evaluable population: participants in the all-treated population who were protocol-adherent or who died on or after study day 3, if death was attributable to hospital-acquired pneumonia.

[d] There were 480 microbiologically evaluable participants (telavancin n=243 and vancomycin n=237). The microbiologically evaluable population consisted of clinically evaluable participants who had a Gram-positive pathogen isolated from baseline respiratory specimens or blood cultures; 293 participants had MRSA (with or without concomitant pathogens).

[e] A pre-specified secondary outcome assessed superiority of telavancin compared with vancomycin for cure rates in a pooled analysis of participants from the 2 studies with microbiological confirmation of MRSA.

[f] Safety population included all participants who received at least 1 dose of study medication. Two participants were randomised to receive vancomycin but actually received telavancin. These 2 participants were included in the vancomycin group for the efficacy analysis (all-treated population) but were included in the telavancin group for the safety analysis. The vancomycin group also includes 20 patients who received antistaphyloccal penicillin instead of vancomycin.

[g] Includes renal impairment, renal insufficiency, acute renal failure, chronic renal failure and creatinine level increase.

Clinical effectiveness

For the 2 individual studies and the pooled analysis telavancin was shown to be non-inferior to vancomycin for cure rates at follow-up assessment 7 to 14 days after the end of treatment. In the pooled all-treated population (n=1503) cure rates were 58.9% (441/749) with telavancin compared with 59.5% (449/754) with vancomycin. In the pooled clinically evaluable population (n=654) cure rates were 82.4% (257/312) with telavancin compared with 80.7% (276/342) with vancomycin. The most common reason for failure at follow-up was treatment failure at end of treatment.

Both studies had a pre-specified non-inferiority margin of 20%. The European public assessment report for telavancin highlighted that it is difficult to accept a margin of this magnitude. However, it was acknowledged that the actual lower 95% confidence intervals around the difference in cure rates were within −10% for both studies for the all-treated and clinically evaluable populations.

There were 480 microbiologically evaluable participants, of which 293 had MRSA isolated (with or without concomitant pathogens). Telavancin was not shown to be superior to vancomycin for the pooled analysis of cure rates for participants with confirmed MRSA. In participants with confirmed MRSA, cure rates were 74.8% (104/139) with telavancin compared with 74.7% (115/154) with vancomycin (treatment difference 0.4%; 95% CI −9.5 to 10.4%).

A post-hoc analysis of Rubinstein et al. (2011) excluded people with severe renal impairment (creatinine clearance less than 30 ml/min) and pre-existing acute renal failure at baseline (Torres et al. 2014). In this post-hoc analysis the primary efficacy end point was clinical response at follow-up assessment in the all-treated (n=1266) and clinically evaluable (n=579) populations. Clinical cure rates in the all-treated and clinically evaluable populations were similar for telavancin and vancomycin and similar to the rates reported by Rubinstein et al. (2011). In the all-treated population, cure rates were 62.6% (391/625) with telavancin compared with 61.2% (392/641) with vancomycin. In the clinically evaluable population, cure rates were 82.5% (231/280) with telavancin compared with 81.3% (243/299) with vancomycin (treatment difference 1.3%; 95% CI −5.0 to 7.6%).

Safety and tolerability

For the pooled analysis, death rates were similar between the 2 groups (20% with telavancin compared with 18.6% with vancomycin). In the first study, 21.5% (80/372) in the telavancin group died compared with 16.6% (62/374) in the vancomycin group (95% CI for the difference −0.7 to

10.6%); and in the second study, 18.5% (70/379) in the telavancin group died compared with 20.6% (78/378) in the vancomycin group (95% CI for the difference −7.8 to 3.5%).

For the pooled analysis the overall rate of treatment-emergent adverse events was the same for the 2 groups (82% [616/751] with telavancin compared with 82% [613/752] with vancomycin). The rate of serious adverse events and treatment-emergent adverse events leading to discontinuation were higher with telavancin (31% [234/751] and 8% [60/751] respectively) compared with vancomycin (26% [197/752] and 5% [40/752] respectively). However, no statistical analysis was presented. The most frequent serious adverse events were septic shock (4% in both groups), respiratory failure (3% in both groups) and multi-organ failure (3% in the telavancin group compared with 2% in the vancomycin group). The most frequently reported adverse event leading to study discontinuation was acute renal failure in the telavancin group (1.2%) and septic shock in the vancomycin group (0.7%). Participants with potentially clinically significant increases in serum creatinine were more common in the telavancin group than the vancomycin group (16% compared with 10%). This included people who had abnormal serum creatinine levels at baseline. Treatment-emergent renal impairment (see table 1 for definition) occurred in 10% (74/751) of the telavancin group compared with 8% (57/752) of the vancomycin group.

A post-hoc analysis of Rubinstein et al. (2011) (Corey et al. 2014) investigated 28-day all-cause mortality in a subgroup (n=1289) of the all-treated population. Overall 28-day survival rates were similar in the telavancin group (76%) and vancomycin group (77%). However, survival rates were lower in the telavancin group for patients with moderate to severe or severe renal impairment. For patients with a creatinine clearance less than 50 ml/min, 28-day survival rates were 59% in the telavancin group and 70% in the vancomycin group (no statistical analysis presented). For patients with a creatinine clearance less than 30 ml/min, 28-day survival rates were 47% in the telavancin group and 61% in the vancomycin group (no statistical analysis presented).

The European public assessment report for telavancin concluded that the safety profile of telavancin was inferior to that of vancomycin and that this conclusion applies even after removing patients with pre-existing severe renal impairment from the analyses. The original marketing authorisation that was applied for also included a proposed indication for complicated skin and soft tissue infections. However, the Committee for Medicinal Products for Human Use (CHMP) considered that the benefit/risk balance for this indication was negative and use for this indication was not approved. Despite telavancin having a non-favourable benefit/risk balance in the overall patient population, the CHMP acknowledged that for patients with nosocomial pneumonia due to

Gram-positive pathogens, who cannot receive commonly used antibacterial agents (for example, because of hypersensitivity or MRSA), there are limited treatment options for this life-threatening infection. The CHMP, therefore, considered that the benefit/risk balance of telavancin was favourable for treating nosocomial pneumonia, including ventilator-associated pneumonia, known or suspected to be caused by MRSA, exclusively in situations where it is known or suspected that other alternatives are not suitable. However, they recommended a number of risk minimisation measures that are reflected in the summary of product characteristics (SPC). The CHMP also recommended that a healthcare professional educational pack should be distributed to all clinicians expected to prescribe or use telavancin.

Telavancin has a risk of nephrotoxicity and increases the risk of mortality in patients with pre-existing acute renal failure. Acute renal failure is listed as a common (between 1 in 10 and 1 in 100) adverse reaction in the SPC. It also states that telavancin is contraindicated in patients with acute renal failure and in patients with severe renal impairment (creatinine clearance less than 30 ml/min, including patients undergoing haemodialysis). Caution should be used when prescribing telavancin to patients receiving concomitant nephrotoxic medicines, those with pre-existing renal disease or with a co-morbidity known to predispose to kidney dysfunction (for example, diabetes mellitus, congestive heart failure or hypertension). Renal function (serum creatinine and urinary output for oliguria/anuria) should be monitored daily for at least the first 3 to 5 days of treatment and every 48 to 72 hours thereafter in all patients receiving telavancin. The initial dose and dose adjustments during treatment should be based on calculated or measured creatinine clearance. Patients with a creatinine clearance of 30 to 50 ml/min should have the dose reduced to 7.5 mg per kg every 24 hours. If renal function markedly decreases during treatment, the benefit of continuing telavancin should be assessed (SPC).

The SPC states that there is a risk of QTc prolongation with telavancin. Therefore, it should be used with caution in patients taking drugs known to prolong the QTc interval or in patients with congenital long QT syndrome, known prolongation of the QTc interval, uncompensated heart failure, or severe left ventricular hypertrophy.

In addition, the SPC states that telavancin is contraindicated in pregnancy. There is a potential risk of teratogenicity; there are no human studies but animal studies have shown reproductive toxicity (including teratogenic effects). The SPC therefore states that the pregnancy status of women of childbearing potential has to be established before treatment is given.

The manufacturer of telavancin (Clinigen Healthcare Limited) sent a direct healthcare professional communication letter in June 2014 highlighting important safety concerns associated with the use of telavancin. The letter which is available on the MHRA website highlights the risks of nephrotoxicity, QTc prolongation, reproductive toxicity and off-label use and outlines how to manage these safety concerns in order to minimise the risk to the patient.

As with other glycopeptides, ototoxicity (deafness and tinnitus) has been reported in patients treated with telavancin. Patients who develop signs and symptoms of impaired hearing or disorders of the inner ear during treatment with telavancin should be carefully evaluated and monitored.

The SPC also warns that there is a risk of infusion-related reactions including red man syndrome-like reactions. It also includes warnings and precautions for other adverse events associated with antibiotic use, such as hypersensitivity reactions and antibiotic-associated colitis and pseudomembranous colitis. Telavancin may also interfere with some coagulation laboratory tests and urine protein tests.

The most common adverse reactions (occurring in more than 1% of patients) reported in the SPC are fungal infection, insomnia, dysgeusia, headache, dizziness, nausea, constipation, diarrhoea, vomiting, increased alanine aminotransferase increased and aspartate aminotransferase, pruritus, rash, acute renal failure, increased blood creatinine, urine abnormality (foamy urine), fatigue and chills.

Evidence strengths and limitations

Rubinstein et al. (2011) was a large study which included 293 clinically evaluable patients with confirmed MRSA (with or without concomitant pathogens).

For the 2 individual studies and the pooled analysis, telavancin was shown to be non-inferior to vancomycin for cure rates at follow-up assessment 7 to 14 days after the end of treatment. Both studies had a pre-specified non-inferiority margin of 20%. The European public assessment report for telavancin highlighted that it is difficult to accept a margin of this magnitude. However it was acknowledged that the actual lower 95% confidence intervals around the difference in cure rates were within −10% for both studies for the all-treated and clinically evaluable populations.

Rubinstein et al. (2011) included a pre-specified secondary outcome which assessed superiority of telavancin compared with vancomycin for cure rates in a pooled analysis of participants from

the 2 studies with microbiological confirmation of MRSA. However, telavancin was not found to
be superior to vancomycin and this was a secondary outcome of the pooled analysis, which was
not powered to show superiority of telavancin.

The mean age of the study population was around 62 years. As stated in the summary of product
characteristics, the safety and efficacy of telavancin in children and young people aged under 18
years have not been established.

A limitation of the evidence is that the studies in people with hospital-acquired pneumonia
excluded those who had certain diseases or conditions. For example, people with known or
suspected pulmonary disease such as granulomatous diseases, lung cancer, cystic fibrosis or
active tuberculosis. People with meningitis, endocarditis or osteomyelitis, refractory shock,
uncompensated heart failure or with a QTc interval greater than 500 milliseconds or abnormal
potassium or magnesium levels that could not be corrected were also excluded. The studies also
excluded people who had HIV infection with a CD4 count less than 100/mm^3 during the past
6 months, were severely neutropenic or who were anticipated to develop severe neutropenia due
to prior or planned chemotherapy (SPC). There is, therefore, a lack of information on the use
telavancin in people with these conditions. Another limitation of the evidence is that the studies
were not carried out in the UK and so the results may not be applicable to UK clinical practice.

Telavancin was compared with IV vancomycin in the 2 studies. However there are no published
studies which compare telavancin with other antibiotics for treating hospital-acquired pneumonia
known or suspected to be caused by MRSA, such as linezolid.

In Rubinstein et al. (2011), the primary efficacy end point was tested for non-inferiority of
telavancin compared with vancomycin in both the all-treated and clinically evaluable populations.
The all-treated population included all randomised patients who received at least 1 dose of study
medication (n=1503). The clinically evaluable population (participants in the all-treated
population who were protocol-adherent or who died on or after study day 3, if death was
attributable to hospital-acquired pneumonia) included just 44% of the all-treated population
(n=654). The most common reasons for exclusion from the clinically evaluable population were
indeterminate or missing response at follow-up (394 participants), receiving potentially effective
non-study systemic antibiotics (354 participants) and isolation of only Gram-negative bacteria
(292 participants).

Torres et al. (2014) was a post-hoc analysis of Rubinstein et al. (2011), which excluded people with severe renal impairment and pre-existing acute renal failure at baseline. However, results from this study should be considered as exploratory because the original study was not designed to compare telavancin with vancomycin in this subgroup of patients.

Context

Alternative treatments

Alternative treatment options for hospital-acquired pneumonia caused by MRSA include intravenous (IV) vancomycin and (IV or oral) linezolid.

Costs of alternative treatments

	Estimated cost (excluding VAT) [a]
Telavancin IV 750 mg every 24 hours (based on a dose of 10 mg per kg and a bodyweight of 75 kg)	£4515 for 7 days of treatment to £9030 for 14 days of treatment £13,545 for 21 days' treatment (duration of study)
Vancomycin IV 1 g every 12 hours [b]	£225.54 for 7 days of treatment to £451.08 for 14 days of treatment £676.62 for 21 days' treatment (duration of study)
Vancomycin IV 500 mg every 6 hours [b]	£225.40 for 7 days of treatment to £450.80 for 14 days of treatment £676.20 for 21 days' treatment (duration of study)
Linezolid IV 600 mg twice a day [b]	£623 for 7 days of treatment to £1246 for 14 days of treatment £13,545 for 21 days' treatment (duration of study)

Linezolid film-coated tablets 600 mg twice a day[b]	£623 for 7 days of treatment to £1246 for 14 days of treatment
	£1869 for 21 days' treatment (duration of study)
[a] Prices based on MIMS June 2014. [b] For prescribing information on IV vancomycin, IV linezolid and linezolid film-coated tablets please refer to the summary of product characteristics.	

Estimated impact for the NHS

Likely place in therapy

Telavancin has a very narrow approved indication. It has been granted a marketing authorisation for the 'treatment of adults with nosocomial pneumonia including ventilator-associated pneumonia, known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Telavancin should only be used in situations where it is known or suspected that other alternatives are not suitable.'

Telavancin is active against Gram-positive bacteria only. In mixed infections where Gram-negative or certain types of anaerobic bacteria are suspected, telavancin should be given with the appropriate antibacterial agent(s) (summary of product characteristics).

As stated in the approved indication consideration should be given to official guidance on the appropriate use of antibacterial agents. The antimicrobial resistance page of the Public Health England website provides guidance to the NHS on this topic.

The European public assessment report for telavancin concluded that the safety profile of telavancin was inferior to that of vancomycin. However, the Committee on Medicinal Products for Human Use (CHMP) acknowledged that for patients with nosocomial pneumonia due to Gram-positive pathogens and who cannot receive commonly used antibacterial agents (for example, because of hypersensitivity or MRSA) there are limited treatment options for this life-threatening infection. The CHMP, therefore, considered that the benefit/risk balance of telavancin was favourable for treating nosocomial pneumonia, including ventilator-associated pneumonia, known or suspected to be caused by MRSA, exclusively in situations where it is known or suspected that other alternatives are not suitable.

An application for a marketing authorisation for complicated skin and soft tissue infections was also submitted. However, the CHMP considered the benefit/risk balance for this indication to be negative. Therefore, the European public assessment report states that telavancin should not be used for this or any other indications not approved.

The manufacturer considers that telavancin is a treatment reserved for use only when other treatments such as intravenous (IV) vancomycin and linezolid (IV or oral) are inappropriate or have failed and is, therefore, a third-line treatment option for adults with hospital-acquired pneumonia known or suspected to be caused by MRSA (Clinigen Healthcare Limited: personal communication March and May 2014).

The summary of product characteristics for telavancin includes a number of warnings and precautions for use that reflect the risk minimisation measures recommended by the CHMP.

Estimated usage

The manufacturer estimates that, considering the third-line status of telavancin and the falling rate of MRSA cases in UK hospitals, the estimated number of patients that telavancin may be used for is in the range of 100 to 500 patients per year (Clinigen Healthcare Limited: personal communication March 2014).

Relevance to NICE guidance programmes

Telavancin was not considered appropriate for a NICE technology appraisal and is not currently planned into any other work programme.

NICE is currently developing a clinical guideline on pneumonia, which will cover both community- and hospital-acquired pneumonia in adults (anticipated publication date December 2014).

References

Corey G R, Kollef M H, Shorr AF et al. (2014) Telavancin for hospital-acquired pneumonia: clinical response and 28-day survival. Antimicrobial Agents and Chemotherapy 58: 2030–7

European Medicines Agency (2011) European public assessment report: Vibativ (EMEA/H/C/ 1240) [online; accessed May 2014]

National Institute for Health and Clinical Excellence (2012) Pneumonia: diagnosis and management of community- and hospital-acquired pneumonia in adults. NICE clinical guideline final scope

Rubinstein E, Lalani T, Corey GR et al. (2011) Telavancin versus vancomycin for hospital-acquired pneumonia due to gram-positive pathogens. Clinical Infectious Diseases 52: 31–40

Torres A, Rubinstein E, Corey G R et al. (2014) Analysis of Phase 3 telavancin nosocomial pneumonia data excluding patients with severe renal impairment and acute renal failure. Journal of Antimicrobial Chemotherapy 69: 1119–26

Development of this evidence summary

The integrated process statement sets out the process NICE uses to select topics for the evidence summaries: new medicines and how the summaries are developed, quality assured and approved for publication.

Expert advisers

Dr Devadas Ganesh Pillay, Consultant Microbiologist, Public Health England

Public Health England

Professor Mark H. Wilcox

Consultant / Head of Microbiology, Leeds Teaching Hospitals NHS Trust

Professor of Medical Microbiology, University of Leeds

Declarations of interest

No relevant interests declared.

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance**.

Copyright

ISBN 978-1-4731-0645-1