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BRIEF REPORT

Tedizolid: a service evaluation in a large UK teaching hospital

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Abstract

Tedizolid is a new oxazolidinone antibiotic with little real-life data on use outside of skin and soft tissue infections. There is a paucity of safety evidence in courses greater than 6 days. Our centre uses tedizolid predominantly when linezolid-associated adverse events have occurred. This service evaluation describes our experience to date. We performed a retrospective service evaluation by reviewing case notes, prescription charts, and laboratory system results for each patient prescribed tedizolid at our hospital and recording patient demographics, clinical details, and outcomes. Sixty patients received tedizolid between May 2016 and November 2018. Most were treated for bone or joint infections and had stopped linezolid prior to tedizolid prescription. Mean length of tedizolid therapy was 27 days. Haematological adverse effects were infrequent. Most patients (72%) finished the course and their clinical condition improved during treatment (72%). Adverse events were common, but often not thought to be tedizolid related. Tedizolid appears to be safe in prolonged courses within this context. It may be suitable for longer-term antibiotic therapy within a complex oral and parenteral outpatient antibiotic therapy (COPAT) service. Patients who do not tolerate linezolid can be safely switched to tedizolid if appropriate.

Keywords Tedizolid · Oxazolidinone · Linezolid · Antibiotic · Stewardship

Introduction

Tedizolid is a relatively new oxazolidinone antibiotic, active against Gram-positive bacteria, and licenced in the UK for the treatment of acute skin and associated structure bacterial infections (SASBIs). Tedizolid 200 mg once daily for 6 days was shown to be as efficacious as 10 days of linezolid (600 mg twice daily) in a randomised controlled trial [1]. The potential to extend tedizolid use to other indications, however, remains unclear due to lack of data [2]. Data are also needed to demonstrate tolerance compared with linezolid in courses longer than 6 days [2]. A recent series of four patients showed that it was possible to use it successfully for 7 to 14 days [3].

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The potential for tedizolid to be used as a switch agent from linezolid in patients who have developed linezolid-associated adverse effects (LAAEs) has not been adequately investigated. Our centre has used tedizolid since 2016, mainly within the complex oral and parenteral antibiotic therapy (COPAT) service, to treat a range of infections other than SASBIs. Patients who have developed LAAEs have commonly been switched to tedizolid and prolonged therapy has been prescribed. Within our institution, tedizolid can only be prescribed by an infection consultant when oxazolidinone therapy is considered optimal with prescriptions approved by at least two infection consultants or within a multidisciplinary meeting. Linezolid has remained the first line oxazolidinone. This service evaluation describes our experiences of using tedizolid to date.

Methods

Our hospital is a 1400-bed teaching hospital with all subspecialties except transplantation. Patients prescribed linezolid/tedizolid as an outpatient are reviewed weekly in an established COPAT service that manages approximately

300 patients yearly. Consecutive patients prescribed tedizolid according to electronic pharmacy records (May 1, 2016, to December 31, 2018) were included. Hard copy and electronic medical records were reviewed. Demographic and clinical characteristics were transcribed to an Excel (for Windows) spreadsheet. Linezolid contraindicated co-medications (as per the linezolid summary of product characteristics (SPC), UK), diagnoses that resulted in tedizolid prescription, and relevant positive microbiological tests were also recorded [4].

Blood test values at the start and end of linezolid/tedizolid were taken from the sample immediately prior to starting/stopping therapy. For patients who had not had bloods within 7 days, the nearest previous blood tests were used. Haemoglobin (Hb) results were categorised as (1) Critical, Hb of < 90 g/L; (2) Observe, Hb 90–100 g/L (inclusive); and (3) Satisfactory, Hb > 100 g/L. Similarly, platelets were categorised as (1) Critical < 50 × 10^9/L; (2) Observe 50–100 × 10^9/L (inclusive); and (3) Satisfactory > 100 × 10^9/L. White cell counts were defined as (1) Low, < 4.0 × 10^9/L; (2) Normal, 4.0 × 10^9/L to 11.0 × 10^9/L (inclusive); and (3) Elevated, > 11.0 × 10^9.

The longest continuous course of tedizolid for each patient was used for this evaluation. Documented adverse effects/events were recorded regardless of causality. Outcomes at the end of therapy were categorised as improved, no change, or worsened. Improved was defined as clearly documented evidence of clinical improvement in the patient's case records. No change was if there was no clinical improvement or deterioration. Worsened was if there was a documented deterioration in the patient's condition.

Statistical analyses were performed using Excel (for Windows). Descriptive statistics, with means, medians, and 95% confidence interval (CI), as appropriate, are presented. By United Kingdom (UK) National Research Ethics Service definitions, this study did not require formal ethical assessment as it was defined as a service evaluation, but it was approved by the hospital's clinical governance and audit committee (reference 2018.256) prior to commencement. All data were recorded and held according to UK data protection laws.

Results

Sixty-eight patients were identified with eight excluded; four because clinical notes were unavailable, two because tedizolid was never received, and in two it was unclear if they had received tedizolid. Baseline demographics are presented in Table 1. All patients had at least one comorbidity with a mean/median of 3 comorbidities; 7 (12%, $N = 60$) patients had 6 or more comorbidities.

Twenty patients (33%) had more than one diagnosis leading to tedizolid prescription. Microbiology is shown in the Appendix; two patients, who had Gram-negative bacteria isolated from relevant clinical specimens, received tedizolid despite having no Gram-positive bacteria detected.

Forty-nine (82%) patients received linezolid immediately prior to tedizolid for a mean of 18 days (median = 15 days). Table 2 shows the reasons for linezolid cessation. Eleven patients did not receive linezolid beforehand; 10 were prescribed tedizolid because they were taking linezolid contraindicated

Table 1 Demographics, co-morbidities, and underlying diagnoses

Demographics	Number and patients OR mean/median
Male	29 (48%)
Female	31 (52%)
Age	62 years/64 years
Co-morbidities	
Metabolic/endocrine	32 (53%)
Cardiovascular	29 (48%)
Musculoskeletal	25 (42%)
Neurological/neurosurgical	15 (25%)
Respiratory	14 (23%)
Vascular	12 (20%)
Gastroenterological/surgical	10 (17%)
Psychiatric	9 (15%)
Haematological	9 (15%)
Oncological	9 (15%)
Dermatological	7 (12%)
Renal	6 (10%)
Ophthalmological	4 (7%)
Urological	3 (5%)
Rheumatological	3 (5%)
Ear nose and throat	2 (3%)
Drug use/alcohol dependence	2 (3%)
Gynaecological	1 (2%)
Diagnosis	
Foot infection	15 (25%)
Prosthetic joint infection	15 (25%)
Osteomyelitis	12 (20%)
Bacteraemia	7 (12%)
Surgical site infection	7 (12%)
Discitis	6 (10%)
Cellulitis	5 (8%)
Other soft tissue infection	6 (10%)
Infected metal work	3 (5%)
Infected muscle flap	3 (5%)
Septic arthritis	2 (3%)
Abscess	3 (5%)
Intercurrent bacterial infection	1 (2%)
Line infection	1 (2%)
Endocarditis	1 (2%)
Infected thrombus	1 (2%)

Table 2 Reasons for stopping linezolid therapy

Reasons for stopping	Number of patients	% of patients on linezolid
Nausea	26	53%
Anorexia	15	31%
Loose stools	6	12%
Mouth ulcers/soreness	6	12%
Thrombocytopenia	6	12%
Anaemia	5	10%
Visual disturbance	4	8%
Fatigue	4	8%
Angular stomatitis	2	4%
Paraesthesia	2	4%
Taste change	2	4%
Leukopenia	2	4%
Tendonitis	1	2%
Oral candidiasis	1	2%
Malaise	1	2%
Dizziness	1	2%
Planned switch	1	2%
Folliculitis	1	2%
Weakness	1	2%
Patient stopped	1	2%
Unclear	2	4%
Multiple Reasons	24	49%
Single reason	23	47%
Unclear reason	2	4%

co-medications and one by mistake. Tedizolid was prescribed with other antibiotics in 33 patients (55%); most commonly ciprofloxacin in 20 patients (33%) [see Appendix].

Outcomes

Most patients (72%) had clearly documented improvement whilst taking tedizolid. Eighteen per cent had no change in their clinical condition and required surgery or alternative antibiotic therapy and 10% deteriorated [see Appendix].

Adverse effects and events

Tedizolid was prescribed for a mean of 27 days (95% CI 22–32, median 21, range 106); 19 mean days (95% CI 9–28, median 15) in those who had not received linezolid prior and 29 mean days (95% CI 23–34, median 22) in those who had. Blood results at the start/end of linezolid/tedizolid are shown in Table 3. The mean difference in platelets at the start and end of therapy was − 131 × 10^9/L (95% CI 166 to − 36) for linezolid and + 5.4 × 10^9/L for tedizolid (95% CI 23 to 33).

Table 4 shows tedizolid associated adverse effects and events, course length and clinical outcomes at stopping therapy. Most patients (72%) completed the planned course of tedizolid; 82% in those who had not received linezolid prior and 73% in those who had. Course length in those who stopped early was a mean of 23 days (95% CI 14–31, median 18, range 62), versus 28 days (95% CI 22–34, median 21, range 105) in those who completed. Many patients (31, 52%) had a possible adverse effect whilst taking tedizolid, most commonly nausea in 9 (15%) patients. See Table 4 and Appendix for further details of adverse effects and events.

Discussion

Whilst this is a small descriptive study, there are currently limited published data on the tolerance and efficacy of tedizolid with prolonged use and for indications other than SASBIs. To our knowledge, our study represents the largest to date, and may be of use to clinicians considering tedizolid for their patients or their institutions antimicrobial formulary.

With a mean course length of 27 days, and most patients completing the planned course (72%), in a cohort of patients within which a high proportion had stopped linezolid due to adverse effects immediately prior to tedizolid, it would appear that tedizolid was well tolerated despite approximately one in two patients suffering an apparent adverse effect (see Appendix). Nausea, fatigue, and loose stools were the most common adverse effects likely to be due to tedizolid, consistent with existing literature [5].

Most patients had complex, often polymicrobial, infections, particularly diabetic foot and bone/joint; required prolonged antimicrobial therapy; and had multiple co-morbidities. Within this context, it is very challenging to accurately attribute the contribution of tedizolid to clinical outcomes, but most patients had clearly documented clinical improvement. Our findings may therefore suggest a wider role for tedizolid than current, supporting recent in vitro data indicating activity against a wide variety of Gram-positive isolates [6]. One must be mindful that prior antibiotic therapy, however, may have been the predominant influencer of clinical outcomes.

Tedizolid penetration in diabetic foot infections was investigated in vivo by Stainton et al. who found levels in soft tissue extracellular fluid of the lower limb adequate for a “high probability of bacterial kill” [7]. This supports our findings that tedizolid may be useful in managing diabetic foot infections. In bone and joint

Table 3 Blood parameters at the beginning and end of Linezolid and tedizolid therapy, and the unadjusted changes

Bloods at starting therapy	Number of patients (%) Mean [95% CI]	Number of patients (%) Mean [95% CI]
Haemoglobin at critical level < 90 g/L	7 (14%)	7 (12%)
Haemoglobin 90–100 g/L	11 (22%)	10 (17%)
Haemoglobin > 100 g/L	31 (63%)	44 (72%)
Haemoglobin g/L	110 [102 to 112]	110 [106 to 115]
White cell count × 10^9/L	8.6 [7.8 to 9.4]	8.0 [6.9 to 9.2]
Platelets ×10^9/L	353 [312 to 395]	257 [220 to 293]
White cell count at low level < 4.0 × 10^9/L	3 (6%)	5 (8%)
White cell count 4.0–11.0 × 10^9/L	37 (76%)	49 (82%)
White cell count > 11.0 × 10^9	9 (18%)	6 (10%)
Platelets at critical Level < 50 × 10^9/L	1 (2%)	0
Platelets 50–100 × 10^9/L	0 (0%)	6 (10%)
Platelets > 100 × 10^9/L	48 (98%)	53 (88%) (1 patient did not have platelets tested)
Bloods at cessation of therapy		
Haemoglobin at critical level < 90 g/L	8 (16%)	5 (8%)
Haemoglobin 90–100 g/L	9 (18%)	8 (13%)
Haemoglobin > 100 g/L	32 (65%)	47 (78%)
Haemoglobin g/L	107 [102 to 112]	115 [111 to 120]
White cell count × 10^9/L	6.8 [6.2 to 7.5]	7.6 [6.9 to 8.3]
Platelets × 10^9/L	222 [191 to 254]	262 [236 to 257]
White cell count at low level < 4.0 × 10^9/L	4 (8%)	3 (5%)
White cell count 4.0–11.0 × 10^9/L	44 (90%)	50 (83%)
White cell count > 11.0 × 10^9	1 (2%)	3 (5%)
Platelets at critical level < 50 × 10^9/L	0 (0%)	0 (0%)
Platelets 50–100 × 10^9/L	8 (16%)	1 (2%)
Platelets > 100 × 10^9/L	41 (84%)	58 (97%) (1 patient did not have platelets tested)
Unadjusted change in % (Cessation–starting)		
Haemoglobin at critical level < 90 g/L	2%	− 4%
Haemoglobin 90–100 g/L	− 4%	− 4%
Haemoglobin > 100 g/L	2%	6%
White cell count at low level < 4.0 × 10^9/L	2%	− 3%
White cell count 4.0–11.0 × 10^9/L	14%	2%
White cell count > 11.0 × 10^9	− 16%	2%
Platelets at critical level < 50 × 10^9/L	− 2%	0%
Platelets 50–100 × 10^9/L	16%	− 8%
Platelets > 100 × 10^9/L	− 14%	9%
Mean differences [95% CI]		
Haemoglobin g/L	− 3 [− 7 to 1]	5 [2 to 8]
White cell count × 109/L	− 1.8 [− 2.4 to − 1.2]	− 0.5 [− 1.4 to 0.51]
Platelets × 109/L	− 131 [− 166 to − 96]	5 [− 23 to 33]

Table 4 Number of patients stopping tedizolid therapy early and the reasons why, and the final outcomes on stopping tedizolid

	Number of patients	% of total patients
Tedizolid given to planned completion		
Yes	43	72%
No	15	25%
Unclear	2	3%
Reason tedizolid stopped early		% of patients who stopped early
Not improving/worsening	4	27%
Fatigue	3	20%
Vomiting	2	13%
Anorexia	1	7%
Tendonitis	1	7%
Anaemia	1	7%
Error	1	7%
Changed by another hospital during an unrelated admission	1	7%
Joint/muscle pains	1	7%
Patient choice	1	7%
Potential adverse effects of tedizolid		% of total patients
Nausea	9	15%
Fatigue	7	12%
Loose stool	5	8%
Dry/sore mouth/cracked lips	3	5%
Acute kidney injury	2	3%
SOB	2	3%
Anorexia	2	3%
Dizziness	2	3%
Itchy feet	1	2%
Thrombocytopenia	1	2%
Malaise	1	2%
Tendonitis	1	2%
Muscle ache	1	2%
Numbness	1	2%
Seizure	1	2%
Pain	1	2%
Weakness	1	2%
Superinfection	1	2%
Sweating	1	2%
Visual change	1	2%
Abdominal pain	1	2%
Cough	1	2%
Falls	1	2%
Anaemia	1	2%
Paraesthesia	1	2%
Palpitations	1	2%
Outcome at stopping tedizolid		
Improved	43	72%
No change	11	18%
Worsened	6	10%

infections, however, Abad et al. found that whilst tedizolid can prevent biofilm formation, it is inactive against "biofilm-embedded *S. aureus*" [8]. In our cohort, 9 patients with prosthetic joint infections (PJI) were prescribed tedizolid monotherapy; 6 of these showed clear improvement, whilst 3 showed no change. Overall, of 15 patients with PJI 10 improved whilst taking tedizolid.

There remains a debate about the tolerance of tedizolid versus linezolid. Pooled analyses of randomised trials (ESTABLISH-1 and ESTABLISH-2) showed fewer episodes of thrombocytopenia and gastrointestinal adverse effects with tedizolid, although tedizolid was prescribed for a shorter duration [9]. A review of FDA reported data indicated similar risks of thrombocytopenia with both medications [10]. Our evaluation suggests that patients who do not tolerate linezolid can switch to tedizolid and subsequently often tolerate prolonged therapy; haemoglobin and platelet counts did not deteriorate during prolonged tedizolid. Indeed, in our limited data

set, average platelet counts and the number of patients with a platelet count in the "observe" category improved with tedizolid, but not linezolid. There is existing literature that suggests that switching to tedizolid in cases of linezolid related myelotoxicity can result in improved blood counts [11]. The apparently high occurrence of adverse effects associated with concomitant use of ciprofloxacin (see Appendix) is of interest and in keeping with recent concerns regarding its use and our clinical experience with linezolid plus ciprofloxacin combination.

In summary, our evaluation suggests that the prolonged use of tedizolid when clinically indicated is safe. Tedizolid may also be a useful switch agent for patients with LAAEs when ongoing oxazolidinone therapy is felt to be clinically important. Further evaluation in larger cohorts of patients is required.

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Authors' contributions Dr. J A York and Dr. G Barlow contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Dr. J A York. The first draft of the manuscript was written by Dr. J A York and Dr. G Barlow, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. Advice, guidance, and support were given throughout by Dr. G Barlow.

Availability of data and material All data held according to Data Protection Law.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval Not required as Service Evaluation (as per UK National Research Ethics Service), Approved by Trust Clinical Governance and Audit Committee (2018.256).

Consent to participate Not required as Service Evaluation.

Consent for publication Not required as Service Evaluation.

Transparency No conflict of interest to declare by any author.

Appendix

Patient characteristics

Twenty-two patients (37%) were taking either a monoamine oxidase inhibitor or another drug contraindicated during linezolid therapy according to the UK SPC.

Linezolid before tedizolid

Of the 49 patients who received linezolid prior to tedizolid, almost all (47, 96%) received linezolid via the oral route prior to tedizolid prescription, whilst two patients received intravenous and then oral linezolid.

Combination antibiotic therapy

Those on combination antibiotic therapy (Appendix Table 5) tended to have shorter courses of tedizolid; mean length = 24 days (median 18 days) with combination versus mean length = 30 days (median 27 days) with monotherapy. Furthermore, those on combination therapy tended to be less likely to finish their course with 61% of those on combination therapy finishing the planned course versus 85% of those on monotherapy.

Table 5 Antibiotics used alongside tedizolid

Antibiotic	Number and percent *N* (%) of patients
Ciprofloxacin	20 (33%)
Metronidazole	5 (8%)
Moxifloxacin	4 (7%)
Aztreonam	1 (2%)
Ceftazidime	1 (2%)
Clarithromycin	1(2%)
Clindamycin	1 (2%)
Co-trimoxazole	1(2%)
Doxycycline	1(2%)
Flucloxacillin	1(2%)
Levofloxacin	1(2%)
Meropenem	1(2%)
Piperacillin-Tazobactam	1(2%)
Temocillin	1(2%)
Trimethoprim	1(2%)
Single (i.e. dual therapy)	28 (47%)
Multiple	5 (8%)
Tedizolid only	27 (45%)

Table 6 Microbiology

Organism	Number of patients	% of patients	% of organism types
Gram-positive			
Staphylococcus aureus	20	33%	19%
Staphylococcus epidermidis	19	32%	18%
Enterococcus faecalis	9	15%	9%
Group C/G haemolytic streptococcus	5	8%	5%
Group B haemolytic streptococcus	6	10%	6%
Streptococcus milleri	4	7%	4%
Group A haemolytic streptococcus	3	5%	3%
Staphylococcus haemolyticus	2	3%	2%
Streptococcus oralis	2	3%	2%
Streptococcus anginosus	1	2%	1%
Rothia mucilaginosa	1	2%	1%
Staphylococcus lugdunensis	1	2%	1%
Staphylococcus capitis	1	2%	1%
Corynebacterium spp.	1	2%	1%
Streptococcus intermedius	1	2%	1%
Total	76		72%
Gram Negative			
Pseudomonas spp.	10	17%	10%
Escherichia coli	3	5%	3%
Proteus spp.	3	5%	3%
Enterobacter aerogenes	2	3%	2%
Pantoea agglomerans	1	2%	1%
Alicaligenes faecalis	1	2%	1%
Morganella spp.	1	2%	1%
Stenotrophomonas maltophilia	1	2%	1%
Haemophilius parainfluenzae	1	2%	1%
Citrobacter spp.	1	2%	1%
Bacteroides fragilis	1	2%	1%
Total	25		24%
Anaerobe	4	7%	4%
Single organism	23	38%	
Polymicrobial	28	47%	
None	9	15%	

Deterioration on tedizolid

Six patients (10%) clinically deteriorated whilst prescribed tedizolid; one had a diagnosis of cerebral aspergillosis, in which tedizolid was prescribed due to concern about superadded bacterial infection; this patient subsequently died. An elderly patient with comorbidities of six organ systems, who was being treated for prosthetic joint infection, declined generally; antibiotic therapy was subsequently withdrawn prior to death. Both deaths were not considered to be tedizolid related.

Another patient stopped their analgesia (described below). Of the other three patients who clinically deteriorated whilst taking tedizolid, one had diabetic foot infection and was switched to co-trimoxazole. Another patient with diabetic foot infection (and osteomyelitis) subsequently required amputation. Finally, a patient with complex discitis, bacteraemia, splenic abscess, and endocarditis was switched back to intravenous antibiotics due to a lack of clinical improvement and increasing inflammatory markers, despite the splenic abscess decreasing in size on tedizolid.

Further adverse events

Ten patients (17%) required admission to hospital or surgery within 30 days of stopping tedizolid: three readmissions were

for surgery; one was admitted for pain control (she had stopped all of her analgesics and requested a switch to IV teicoplanin, which she had previously been on); two were readmitted with nausea and vomiting or anorexia (one of these was diagnosed with norovirus and the other had been discharged on linezolid which was felt to be the likely cause); one was admitted feeling generally unwell and was found to have a hospital-acquired pneumonia; one was admitted due to adverse effects of oral moxifloxacin and infection; two were admitted due to deterioration, one with worsening foot pain and increased discharge and the other with a worsening infection despite clinically improving on a short course of tedizolid, having been discharged from hospital on clindamycin prior to this; and one was admitted for a seizure (thought to be unrelated). No readmission was felt, therefore, to be related directly to tedizolid.

Thirteen patients (25%) required ongoing antimicrobial therapy after tedizolid (without admission or surgery): six of these had complex prosthetic joint infections where prolonged antibiotic therapy would be expected; four had diabetic foot infections which included one patient who deteriorated on tedizolid and was switched to co-trimoxazole; one patient had a complex shoulder infection for who prolonged antibiotic therapy was planned after initial tedizolid; and two patients were switched to IV teicoplanin, one with discitis, endocarditis, bacteraemia, and a splenic abscess (as discussed above) and the other is the patient who stopped their analgesia (see above and below).

Two patients required blood transfusions whilst on therapy (3%) and one had severe anaemia which limited linezolid therapy but then improved on tedizolid—this was felt to be multifactorial (her Hb was 72 g/L at the start of linezolid therapy) and was not considered to be tedizolid related. The other patient was transfused due to a low Hb (68 g/L) following linezolid therapy. Three patients were taking oral iron supplements (5%) and 1 was on erythropoietin injections, with chronic kidney disease requiring haemodialysis (2%).

Early cessation of tedizolid

Of the 15 patients who stopped tedizolid early, the reason for stopping was not considered to be due to tedizolid in 6 patients. One patient, who stopped tedizolid due to fatigue, had stopped taking analgesia just prior to this and was felt to be exhausted by severe pain. Another patient stopped because they felt they had been on antibiotics for long enough. Two patients who stopped due to joint pains (one also had tendonitis) were also taking ciprofloxacin concomitantly, which was felt to be the more likely cause. One patient was mistakenly prescribed tedizolid by a junior doctor and was switched to linezolid when this was identified. Another patient stopped tedizolid after being admitted to another hospital that did not have tedizolid on their formulary. In 2 patients, it was unclear whether tedizolid was given to planned completion or not—these were recorded as unclear. In one of these, tedizolid was given for a week (confirmed by pharmacy), but at the follow-up appointment, the clinical notes simply stated, "To continue moxifloxacin". In the other case, the notes stated: "has probably had enough", but it was unclear whether this was felt to be due to adverse effects or because the infection was treated.

Details of adverse effects

Whilst many patients had a documented adverse effect that could have conceivably been due to tedizolid, in particular nausea, fatigue, and loose stools, many were not subsequently thought to be tedizolid associated. One patient with nausea, for example, required admission to hospital, but was diagnosed with norovirus infection. Another patient reported shortness of breath but was also prescribed ciprofloxacin. A patient who also complained of shortness of breath only did so at one clinic review, but not subsequently during prolonged therapy. The dry mouth and dizziness described by one patient resolved despite continuing therapy. One of two patients who developed acute kidney injury (AKI) was also prescribed multiple nephrotoxic medications, whilst in another patient, it was unclear whether AKI was related to underlying infection or antibiotic therapy. A patient with anaemia received a treatment break for 40 days during which their haemoglobin recovered from 70 to 121 g/L with oral iron. This patient then tolerated prolonged courses of tedizolid (107 and 78 days) without a clinically important decline in haemoglobin. The patient with thrombocytopenia had a platelet count of 74 × 10^9/L on stopping linezolid that remained low (75 × 10^9/L) whilst taking tedizolid without further deterioration.

Of the other documented adverse effects, one patient complained of loose stools, but the sample provided was fully formed. The same patient also stopped tedizolid due to palpitations (she was also prescribed ciprofloxacin, which was felt to be the probable cause); on restarting tedizolid, she had no further adverse effects. A patient who reported loose stools described as "loose to normal" had resolved fully at follow-up 1 week later. Another patient developed hyponatraemia (sodium = 119 mmol/L at nadir), which resulted in tedizolid cessation, but then tolerated it for 63 days without hyponatraemia. The cough that one patient complained of was thought to be a viral upper respiratory tract infection and not antibiotic related. The documented case of leukopenia (nadir 3.4×10^9/L) resolved without stopping tedizolid (to 4.5×10^9/L). One patient had a seizure on the last day of tedizolid, but this was not felt to be antibiotic related. The abdominal pain one patient developed while prescribed tedizolid was also not thought to be antibiotic related. One patient suffered from weakness and falls, thought to be due to poor oral fluid intake. Malaise reported by one patient at the beginning of tedizolid therapy improved during treatment and

was felt to be infection related. Finally, the paraesthesia reported by one patient was not felt to be clinically significant; the onset of subsequent visual disturbance in the same patient occurred 1 week after stopping tedizolid.

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