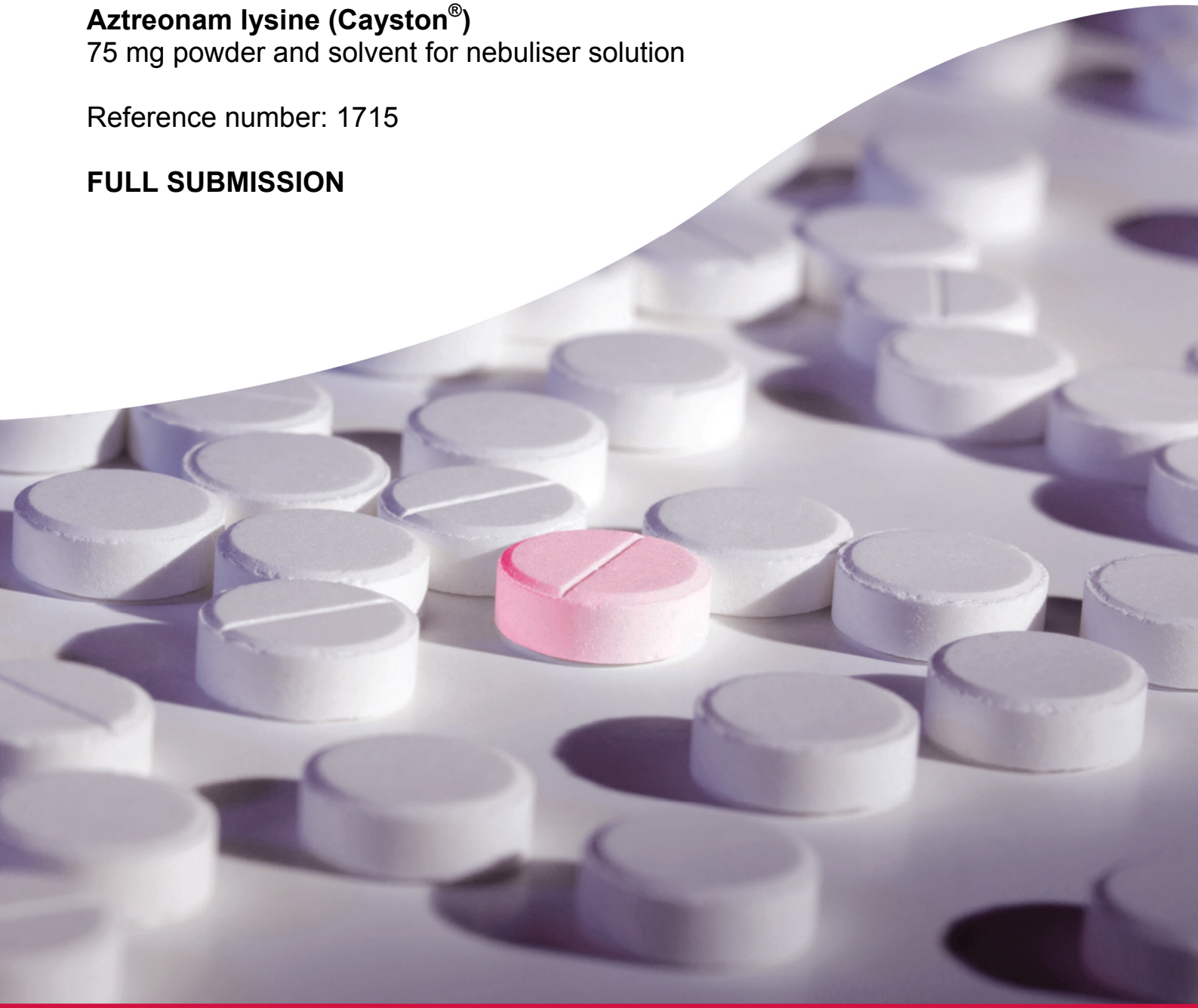
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Aztreonam lysine (Cayston®)
75 mg powder and solvent for nebuliser solution

Reference number: 1715

FULL SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics and Medicines Evaluation, Bangor University.

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This report should be cited as:
All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Aztreonam lysine (Cayston®) 75 mg powder and solvent for nebuliser solution. Reference number: 1715. February 2013.

AWMSG Secretariat Assessment Report
Aztreonam lysine (Cayston®)
75 mg powder and solvent for nebuliser solution

This assessment report is based on evidence submitted by Gilead Sciences Ltd on 29 October 2012[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Aztreonam lysine (Cayston®) is indicated for the suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged six years and older. Consideration should be given to official guidance on the appropriate use of antibacterial agents[2].
Dosing	The recommended dose of aztreonam lysine nebuliser solution for adults and children aged six years and older is 75 mg three times per 24 hours, at least four hours apart, for 28 days. Aztreonam lysine may be taken in repeated cycles of 28 days on therapy followed by 28 days off therapy. Patients should use a bronchodilator before each dose of aztreonam lysine; short acting bronchodilators can be taken between 15 minutes and 4 hours and long acting bronchodilators can be taken between 30 minutes and 12 hours prior to each dose. Refer to the Summary of Product Characteristics (SPC) for further information[2].
Marketing authorisation date	Licensed for use in adult patients on 21 September 2009[2] and use in patients aged six years and older on 23 July 2012[3].

2.0 DECISION CONTEXT

2.1 Background

Cystic fibrosis (CF) is the most common recessively inherited genetic condition[4], affecting 9,385 people in the UK in 2010, of which 44.5% were aged less than 16 years[5]. The disorder is a result of mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR)[4]. Disruption of CFTR function results in thickened secretions in various organs, including the lungs, where the abnormally viscous mucus interferes with the clearance of microorganisms from the airways[4]. This makes CF patients susceptible to pulmonary infections caused by a range of bacterial pathogens[6]. The most common pathogen causing chronic infection in people with CF is *Pseudomonas aeruginosa*, which affected 37.5% of UK CF patients in 2010[5,7]. Chronic *P. aeruginosa* infection is associated with increased morbidity and mortality in CF patients[7].

The Cystic Fibrosis Trust 2009 guidelines recommend the use of regular nebulised antibiotics to reduce the rate of deterioration of respiratory function in CF patients that are chronically infected with *P. aeruginosa*[8]. Nebulised colistimethate sodium is recommended as the initial treatment; if colistimethate sodium is not tolerated or does not produce satisfactory clinical progress, tobramycin nebuliser solution (TNS) should be used[8].

Aztreonam lysine nebuliser solution (AZLI, Cayston®) is a monobactam antibiotic that binds to penicillin-binding proteins of susceptible bacteria, leading to inhibition of bacterial cell wall synthesis, resulting in cell lysis[2,6].

2.2 Comparators

The comparators requested by the All Wales Therapeutics and Toxicology Centre (AWTTC) were:

- TNS (Bramitob® and Tobi®)
- Tobramycin dry powder for inhalation (Tobi® Podhaler®)
- Colistimethate sodium powder for nebuliser solution (Promixin®)
- Colistimethate sodium injection for nebulisation (Colomycin®)

The company submission includes a comparison of the clinical and cost-effectiveness of AZLI and TNS (Tobi®)[1].

2.3 Guidance and related advice

- Cystic Fibrosis Trust. Standards for the clinical care of children and adults with cystic fibrosis in the UK (2011)[4].
- Cystic Fibrosis Trust. Antibiotic treatment for cystic fibrosis. Report of the UK Cystic Fibrosis Trust Antibiotic Working Group (2009)[8].

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

The company submission includes data from one active comparator-controlled, phase III trial, GS-US-205-0110[1]. Several placebo-controlled supportive studies and a follow-on study that evaluated two AZLI doses were also included[9–13]; however, these do not inform the comparison of AZLI with tobramycin and colistimethate sodium and are therefore not discussed further.

3.1 Study GS-US-205-0110

This phase III, multi-centre, open-label, randomised, parallel-group, active comparator-controlled study evaluated the safety and efficacy of AZLI versus TNS (Tobi®) in CF patients with airway *P. aeruginosa*[14,15]. Patients (aged ≥ six years) were randomised (1:1) to receive AZLI 75 mg three times daily or TNS 300 mg twice daily; a short acting bronchodilator was administered before every AZLI or TNS dose. Three cycles of treatment were administered, comprised of 28 days on therapy followed by 28 days off therapy. This was followed by an optional, open-label, 24-week, extension phase of three AZLI treatment cycles[14].

The study enrolled patients with FEV_1% predicted* ≤ 75% at screening and who had received previous treatment with aerosolised antibiotics without demonstration of drug intolerance. Of the 268 patients in the intent-to-treat (ITT) population, 38.4% had received inhaled colistimethate sodium in the previous year, while 85.1% had received inhaled tobramycin for ≥ 84 days in the past year[14].

The co-primary endpoints were relative change from baseline in FEV_1% predicted at day 28 (noninferiority analysis) and actual change from baseline in FEV_1% predicted across three treatment cycles (superiority analysis). These endpoints were also analysed in the subgroup of patients who received inhaled tobramycin for ≥ 84 days in the 12 months prior to randomisation[14,15].

Mean relative changes in FEV_1% predicted at day 28 were 8.35% in the AZLI-treated group and 0.55% in the TNS group; treatment difference was 7.80% (95% confidence

* The forced expiratory volume in one second (FEV_1) expressed as a percentage of a predicted value, calculated using a reference population[16].

interval [CI]: 3.86%, 11.73%; p < 0.001); this met the prespecified noninferiority margin (95% CI lower boundary > -4%)[14]. The primary superiority endpoint of mean actual change in FEV_1% predicted across three treatment cycles was also met (2.05% AZLI versus -0.66% TNS; treatment difference 2.70%; 95% CI: 0.98, 4.43; p = 0.0023)[2,14]. Results for the co-primary endpoints are presented in Table 1.

Subgroup analysis of patients with prior use (≥ 84 days in the previous year) of inhaled tobramycin showed similar beneficial effects in the primary endpoints (see Table 1)[1,15]. In the subset of patients classed as tobramycin-naive (< 84 days treatment of inhaled tobramycin in the previous year; n = 40), improvement in FEV_1% predicted at day 28 was numerically higher in the TNS treatment group than in those that received AZLI (2.45% AZLI versus 4.65% TNS; p = 0.482)[15].

Analysis of additional secondary endpoints showed that mean change from baseline cystic fibrosis questionnaire-revised (CFQ-R) respiratory symptoms scale (RSS) was significantly larger for AZLI-treated patients than the TNS group across three treatment courses (6.30 versus 2.17 respectively; p = 0.019). At week 24, AZLI-treated patients also had significantly fewer respiratory hospitalisations (40 versus 58 for the AZLI and TNS treatment group respectively; p = 0.044) and respiratory events requiring additional antipseudomonal antibiotics (84 versus 121 for the AZLI and TNS treatment group respectively; p = 0.004). During the extension phase, patients that had received AZLI during the active comparator phase (n = 68) continued to demonstrate improvements in FEV_1% predicted with each AZLI treatment cycle; those that had been in the TNS group (n = 65) demonstrated comparable improvements with AZLI treatment[14].

Table 1. Results for key endpoints from Study GS-US-205-0110[1,2,14]

Endpoints	AZLI (n = 136)	TNS (n = 132)	AZLI−TNS treatment difference
Primary endpoint			
Adjusted mean relative change in FEV_1% predicted at day 28 (SE)	8.35 (1.70)	0.55 (1.77)	7.80 (95% CI: 3.86, 11.73) p = 0.001
Adjusted mean actual change in FEV_1% predicted across three treatment cycles (SE)	2.05 (0.69)	-0.66 (0.72)	2.70 (95% CI: 0.98, 4.43) p = 0.0023
Secondary endpoints			
Adjusted mean relative change in FEV_1% predicted at day 28 in patients with prior use (≥ 84 days) of inhaled tobramycin	10.04	0.54	9.50 p < 0.0001
Adjusted mean actual change in FEV_1% predicted across three treatment cycles in patients with prior use (≥ 84 days) of inhaled tobramycin	3.26	-0.21	3.47 p = 0.0002

AZLI: aztreonam lysine for inhalation solution; CI: confidence interval; FEV_1%: forced expiratory volume in one second expressed as a percentage of a predicted value; SE: standard error; TNS: tobramycin nebuliser solution.

3.2 Comparative safety

The Committee for Medicinal Products for Human Use (CHMP) has previously reviewed the observed adverse event (AE) profile based on two phase III placebo-controlled studies (CP-AI-005 and CP-AI-007) and concluded that the profile was consistent with the signs and symptoms of CF lung disease, while the incidence of most AEs was similar to that of placebo[6]. CHMP further noted that the AEs considered attributable to AZLI treatment were primarily self-limiting, local effects associated with inhalation of the medication with few AZLI-associated serious adverse events (SAEs)[6].

The overall incidence of AEs during study GS-US-205-0110 was comparable between the treatment groups (130/136 [95.6%] in AZLI treated-patients versus 128/132 [97.0%] in TNS-treated patients); these were considered treatment-related in 22.8% and 12.9% patients in the AZLI and TNS groups respectively ($p = 0.039$)[14,15]. Three patients experienced treatment-related SAEs, all of which had received AZLI; two patients experienced wheezing, while one reported productive cough, dyspnoea, haemoptysis and discoloured sputum. Discontinuation due to AEs occurred in ten patients (nine had received AZLI versus one TNS-treated patient) and this was most commonly due to cough or haemoptysis. Two patients died due to complications of CF during the extension phase; both deaths were considered unrelated to treatment[14,15].

The most frequently reported AEs were cough (96 [70.6%] AZLI versus 104 [78.8%] TNS) and productive cough (70 [51.5%] versus 79 [59.8%] respectively). Haemoptysis occurred more frequently in AZLI-treated patients as compared to the TNS treatment group (31 [22.8%] versus 21 [15.9%])[14]. Haemoptysis is a common symptom in CF due to damaged airways[15]; however, it could potentially be exacerbated due to cough or bronchospasms associated with inhaled therapies such as AZLI[17]. This is reflected in the SPC, which states that administration of AZLI in CF patients with active haemoptysis should be undertaken only if the benefits of treatment are considered to outweigh the risks of inducing further haemorrhage[2].

3.3 AWTTC critique

- The company submission includes a study comparing the effectiveness of AZLI with that of TNS; data regarding other comparators requested by AWTTC has not been provided[1].
- The company has highlighted that AZLI will be targeted as a third-line treatment, in patients who cannot tolerate colistimethate sodium and TNS therapy or for whom these inhaled antibiotics are not providing satisfactory therapeutic benefit[1]. However, the population enrolled in study GS-US-205-0110 appears not to reflect the use of AZLI and TNS in the company-stated position as a third-line treatment[14].
- It should also be noted that in study GS-US-205-0110 85.1% of patients had received inhaled tobramycin for ≥ 84 days in the past year[14] . In those patients classed as tobramycin-naive (received inhaled tobramycin < 84 days in the past year; n = 40), no statistically significant differences in FEV_1% predicted were observed in patients who received AZLI compared to those in the TNS group[15].
- While discussing the use of AZLI in paediatric patients, CHMP noted that only small numbers of paediatric patients were included in the studies (during study GS-US-205-0110, 28 patients < 18 years received AZLI, while 31 received TNS). However, CHMP stated that studies demonstrated similar efficacy trends in paediatric patients as for adults and concluded that AZLI continues to be a generally well-tolerated and effective inhaled antipseudomonal antibiotic therapy in both patient groups over multiple treatment courses[17].
- During study GS-US-205-0110, an emerging trend was noted of increased resistance of *P. aeruginosa* isolates to aztreonam, more frequent isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) and appearance of cross-resistance to beta-lactam antibiotics[15,17]. Despite the potential negative effect of these trends, CHMP concluded that the increase in aztreonam minimum inhibitory concentration (MIC) and appearance of cross-resistance in AZLI-treated patients did not result in a decrease of the favourable efficacy of AZLI during the 48-week study. However, it is uncertain whether this may impact future treatment strategies in these patients, and this is reflected in the SPC, Risk Management Plan (RMP) and Paediatric Investigation Plan (PIP)[15,17].
- In a guideline regarding the clinical development of treatments for CF, CHMP advised that study duration of six months is recommended for the demonstration of efficacy on respiratory function, with a predefined 12-month follow-up for safety[18]. Study GS-US-205-0110 included a 24-week randomised

phase and a 24-week extension, providing 48 weeks of follow-up overall[14]. However, no comparative evidence of the safety or efficacy of AZLI beyond this time is available.

- The recommended AZLI treatment frequency is three times daily[2], while TNS is administered twice daily[19], which may have implications for patient/carer preference. However, while AZLI should be administered by inhalation over a 2–3 minute period, TNS is recommended to be administered over 15 minutes[2,19,20]. Further, vial usage during study GS-US-205-0110 was above 90% for both products[15], indicating that compliance during the trial was not affected. Additionally, patient satisfaction, as measured by CFQ-R RSS scores, was higher with AZLI treatment than TNS[17].
- In certain patients treated with TNS there is a requirement for renal and auditory monitoring, which is not a requirement in the AZLI SPC[2,19,20].
- AZLI is an antibiotic of a different class from tobramycin and colistimethate sodium, with a distinct mechanism of action[2,19,21], and so could provide an alternative treatment option for CF patients with chronic *P. aeruginosa* infection.

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company submission describes a cost utility analysis (CUA) of three times daily AZLI compared against twice daily TNS for suppressive therapy of chronic pulmonary infections due to *P. aeruginosa* in patients with CF aged 6 years and older[1]. AWTTC also requested comparison of AZLI against tobramycin dry powder for inhalation, and against nebulised colistimethate sodium; however, no such comparisons have been provided. The company has clarified that AZLI will be targeted at third-line use, in a subset of the licensed patient population who cannot tolerate colistimethate sodium and TNS or for whom these inhaled antibiotics are not providing satisfactory therapeutic benefit.

A Markov model is presented with health states defined by levels of FEV_1% predicted as a predictor of disease severity, where FEV_1 is reported to be a predictor of morbidity and mortality in CF patients[22,23]. Patients can move between the model health states or die from CF-related causes. Patients with FEV_1% predicted below 30% can undergo lung transplant, facing an increased risk of perioperative mortality. The cycle length used is 28 days to reflect the recommended treatment regimen, where patients follow 28-day "on-off" treatment cycles for the length of the model. A lifetime horizon was adopted for the analysis, with a maximum age of 77 years.

Efficacy estimates used in the model are based on the results of the active comparator study GS-US-205-0110[14], which compared AZLI versus TNS in patients who were largely tobramycin-experienced, and the open-label extension phase. Patients enrolled in this trial therefore do not reflect those targeted for third-line use of AZLI. Extrapolation beyond the trial period (6 months for TNS and 12 months for AZLI) has been performed using data from the last observed treatment cycles, which are assumed to apply for the remaining life time.

Drug costs are based on British National Formulary (BNF) prices[24], with a reduced price for AZLI in line with an agreed Wales Patient Access Scheme (WPAS). Costs of hospitalisations, lung transplant and other routine resource use are based on National Schedule of Reference costs 2010–2011[25]. Utility values used in the model are based on a UK study that used the EQ-5D health outcome measure[26]. Utility decrements due to exacerbation and utility of patients undergoing lung transplant are based on two published studies[26,27]. Costs and benefits beyond one year are discounted at 3.5%.

Deterministic and probabilistic sensitivity analyses are used to assess parameter uncertainty. Threshold analyses of the most influential input parameters are also presented. Scenario analysis, in which SF-36 health survey data mapped to EQ-5D were used to estimate utilities for the model health states, is also presented.

4.1.2 Results

In all the reported analyses, a reduced price for AZLI is used in accordance with an agreed WPAS. All results are commercially in confidence (CIC).

Results of the base case analysis are CIC. AZLI is estimated to be both more costly and more effective compared to TNS.

Several scenario analyses were reported; this information is CIC.

4.1.3 AWTTC critique

The clinical trial data used in the model was derived from patients randomised to AZLI or TNS, most of whom were tobramycin-experienced. The trial population therefore appears not to reflect the use of AZLI and TNS in the company-stated position as a third-line treatment in patients who cannot tolerate colistimethate sodium and tobramycin therapy or for whom these inhaled antibiotics are not providing satisfactory therapeutic benefit. In addition, no long-term data exist to support the assumptions made regarding the persistence of treatment benefit beyond 12 months. Scenario analyses demonstrate the sensitivity of the cost-effectiveness estimates to this assumption, and to the method chosen for extrapolating data in the long-term. Collectively, it is therefore unclear whether the base case analysis reflects the cost-effectiveness of AZLI in the target population in practice, and the cost-effectiveness estimates that are provided appear subject to considerable uncertainty.

Strengths of the economic evidence:

- Direct comparative data for AZLI versus TNS are used to inform the model.
- A wide range of sensitivity, threshold and scenario analyses are provided to characterise the model parameter uncertainty.

Limitations of the economic evidence:

- In line with the AZLI licensed indication, AWTTC requested comparison against TNS, tobramycin dry powder for inhalation, Promixin® powder for nebuliser solution and Colomycin® injection for nebulisation as the most appropriate comparators. However, the evidence provided by the company relates only to TNS.
- The model assumes sustained efficacy of AZLI over patients' life-time. There are no long-term data to support this assumption. The AZLI SPC notes a decrease in *P. aeruginosa* susceptibility to AZLI and other beta-lactam antibiotics observed during clinical studies[2]. Although this reduction in susceptibility was not predictive of clinical outcome during the (short-term) trial period, it is unclear if this would be the case with longer term use. Scenario analyses 1 and 2 in Table 3 demonstrate the sensitivity of the model to assumptions of continued benefit, and the ICER (CIC) generated in a scenario analysis using a shorter time horizon of 36 months, suggests a reliance of the model estimates on QALY gains accrued later in life.
- The company has adopted the most favourable method of extrapolating the short-term trial data to the long-term for the base case analysis, and an alternative plausible method generates a substantially greater estimate of the ICER (Scenario 3 in Table 3).
- FEV_1% predicted, a surrogate outcome measure in the comparative trial, is used to predict mortality based on a published study[22]. No details of a systematic review to identify this or alternative data with which to model mortality have been presented, although the model appears relatively

insensitive to the baseline risk of mortality in patients with FEV1 predicted <30%.

- The active comparator study enrolled patients with $FEV_1 \leq 75\%$ predicted at screening who had received previous treatment with aerosolised antibiotics without demonstrating drug intolerance[14]. It is uncertain whether the economic evaluation, driven by the results of this trial, adequately reflects the cost-effectiveness of AZLI if used as the company-suggested third line treatment following colistimethate sodium and TNS.
- Based on expert opinion, patients in severe health states are assumed in the model to receive colistimethate sodium during the 28-day "off-period" of TNS or AZLI treatment. However, colistimethate sodium was not used in this way for severe patients in the active comparator trial. Excluding the cost of colistimethate sodium from the model increases the base case ICER marginally (cost per QALY gained is CIC). Costs of bronchodilators, required before use of nebulised AZLI and TNS are also excluded from the analysis which, given the three times daily regimen for AZLI versus twice daily regimen for TNS, could marginally increase the ICER further.
- AE costs and tobramycin-associated renal and auditory monitoring costs are not included in the model[24]. However, the company reported that there was no difference in AEs between the two drugs in the active comparator study and as such, it is unlikely that the inclusion of AE costs would change the results.

4.2 Review of published evidence on cost-effectiveness

Standard literature searches conducted by AWTTC have identified two published abstracts assessing the cost-effectiveness of AZLI within its current licensed indication in the USA. The first study was a cost-effectiveness analysis of AZLI compared to TNS[28]. It used individual patient level efficacy data (increase in FEV_1% predicted) from two placebo-controlled trials and included only the acquisition cost of drugs. It concluded that in 93% of simulations, TNS was less costly and more effective compared to AZLI (i.e. dominated AZLI) while in the remaining simulations AZLI was both more costly and more effective. The study author was affiliated to the manufacturer of tobramycin.

The second study aimed to compare the utilisation of health care resources and their costs between CF patients using AZLI and those using TNS[29]. Data on hospitalisations were based on the results from the GS-US-205-0110 study of AZLI versus TNS. The results showed that AZLI incurred the highest drug acquisition cost. The abstract does not provide the complete study results relating to efficacy. One of the study authors is affiliated to the manufacturer of AZLI.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

Based on Welsh data from Llandough Adult CF centre, Cardiff and Vale University Health Board, the company reports that 456 patients, of whom 274 are adults, are currently treated for CF in Wales. Approximately 139 of the adult patients have chronic *P. aeruginosa* infection. The yearly incidence of CF is estimated to be 15 patients (number of patients expected to receive AZLI in each of the next five years is CIC)[1].

5.1.2 Results

The company anticipates an incremental cost resulting from using AZLI in place of current treatment. The incremental costs are summarised in Table 4 below. Results are based on a discounted price agreed under WPAS.

Table 4. Company-reported costs associated with the use of AZLI

All company-reported costs are CIC.

5.1.3 AWTTC critique

- The company used data from Llandough Adult CF centre to estimate the prevalence of CF in Wales, with estimates of the number of patients to receive AZLI in each of the next five years based on expert opinion. The company notes the difficulties in estimating the number of treated patients, as this will depend on response to treatment.
- The analysis provided focused on the difference in the comparators' prices. No other costs were considered in the analysis (e.g. differences in the costs of concomitant medications, routine resource use, hospitalisations).
- Collectively, the budget impact analysis provided by the company is subject to considerable uncertainty.

5.2 Table of comparative unit costs

Table 5 below provides example comparative costs for treatments of chronic *P. aeruginosa* infections in CF patients.

Table 5. Examples of costs of chronic *P. aeruginosa* infection treatments licensed for use in CF patients.

Drug	Recommended Dose	Approximate cost per year
AZLI (Cayston®) Powder for re-constitution, 75 mg	75 mg by Altera Nebuliser Handset and Altera Aerosol Head connected to an Altera Control Unit or an eFlow® rapid Control Unit, three times daily for 28 days, followed by a 28-day treatment-free period	£15,399 WPAS price CIC Price includes handset
Tobramycin (Bramitob®) Solution for inhalation (75 mg/ml), 4 ml nebuliser solution	4 ml (300 mg) inhaled via a nebuliser twice daily for 28 days, followed by a therapy-free interval of 28 days.	£7,122
Tobramycin (Tobi®) Solution for inhalation (60 mg/ml), 5 ml	5 ml (300 mg) by a Pari LC Plus® nebuliser twice daily for 28 days, followed by a therapy-free interval of 28 days.	£7,123
Tobramycin (Tobi® Podhaler®) Dry powder for inhalation, 28 mg per capsule	112 mg inhaled using Podhaler® twice daily for 28 days, followed by a therapy-free interval of 28 days.	£10,740 Price includes inhaler device
Colistimethate sodium (Colomycin®) Powder in vial, 1 and 2 million units	1–2 million units twice daily via a nebuliser.	£1,314–£2,365
Colistimethate sodium (Promixin®) Powder in vial for nebuliser solution, 1 million units	1–2 million units two or three times daily via a nebuliser	£3,358–£10,074
Costs based on MIMS[30] list prices as of 8 November 2012, excluding nebuliser unit costs. This table does not imply therapeutic equivalence of the stated drugs and doses. See all relevant SPCs for full dosing details[2,19–21,31,32].		

6.0 ADDITIONAL INFORMATION

6.1 Appropriate place for prescribing

AWTTC is of the opinion that, if recommended, aztreonam lysine (Cayston®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration. It may be appropriate for prescribing within NHS Wales for the indication under consideration with a shared care agreement.

6.2 Ongoing studies

The company submission highlighted the aztreonam lysine for pseudomonas infection eradication study (ALPINE), which is an open-label phase II trial to evaluate the safety and efficacy of AZLI 75 mg powder and solvent for nebuliser solution/AZLI solution in paediatric patients with CF and new onset lower respiratory tract culture positive for *P. aeruginosa*[1,33]. Interim results from this study are expected in the second half of 2013[1].

6.3 AWMSG review

This assessment report will be considered for review three years from the date of Ministerial ratification (as disclosed in the Final Appraisal Recommendation).

6.4 Evidence search

Date of evidence search: 19 November 2012
Date range of evidence search: No date limits were applied to database searches.

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