

Re-submission

aztreonam lysine, 75mg, powder and solvent for nebuliser solution (Cayston[®]) SMC No. (753/12)

Gilead Sciences Limited

05 December 2014

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a re-submission considered under the orphan process

aztreonam lysine (Cayston[®]) is accepted for restricted use within NHS Scotland.

Indication under review: Suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged six years and older.

SMC restriction: When inhaled colistimethate sodium and inhaled tobramycin are not tolerated or not providing satisfactory therapeutic benefit (measured as $\geq 2\%$ decline in forced expiratory volume in 1 second [FEV₁]).

Aztreonam lysine has demonstrated superiority in improving lung function and respiratory symptoms in one active-controlled study and two 28-day placebo-controlled studies in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection.

This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost effectiveness of aztreonam lysine. It is contingent upon the continuing availability of the Patient Access Scheme in NHS Scotland or a list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Overleaf is the detailed advice on this product.

Chairman, Scottish Medicines Consortium

Indication

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.

Dosing Information

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 of aztreonam lysine.

For patients taking multiple inhaled therapies, the recommended order of administration is as follows:

1. bronchodilator

2. mucolytics

3. and lastly, aztreonam lysine.

Adults

The recommended dose for adults is 75mg three times per 24 hours for 28 days.

Doses should be taken at least 4 hours apart.

Aztreonam lysine may be taken in repeated cycles of 28 days on therapy followed by 28 days off aztreonam lysine therapy.

Paediatric population

Aztreonam lysine is indicated in children aged 6 years and older.

In clinical studies with aztreonam lysine patients younger than 6 years of age were excluded. The safety and efficacy of aztreonam lysine in children younger than 6 years of age has not been established. The dosing in children aged 6 years and older is the same as for adults. Dosage is not based on weight or adjusted for age.

Aztreonam lysine is only for inhalation use. Aztreonam lysine should only be used with the Altera Nebuliser Handset and Altera Aerosol Head connected to an eBase Controller or an eFlow rapid Control Unit.

Product availability date

01 April 2010. Aztreonam lysine meets SMC orphan criteria.

Summary of evidence on comparative efficacy

Aztreonam lysine exhibits activity against gram-negative aerobic pathogens, including *Pseudomonas aeruginosa*.¹ It binds to penicillin-binding proteins of susceptible bacteria, which leads to inhibition of bacterial cell wall synthesis, followed by filamentation and cell lysis. Aztreonam lysine has been formulated with the amino acid lysine, which is well tolerated in the airways, and may itself confer an element of mucolytic activity.

The submitting company has requested that SMC considers this product when positioned for use when inhaled colistimethate sodium and inhaled tobramycin are not tolerated or are not providing satisfactory therapeutic benefit (measured as $\geq 2\%$ decline in forced expiratory volume in 1 second [FEV₁]).

A phase III, open-label, randomised multi-centre non-inferiority study evaluated the safety and efficacy of inhaled aztreonam lysine compared with inhaled tobramycin in 268 cystic fibrosis patients with *Pseudomonas aeruginosa*. Patients were 6 years or older, with stable pulmonary disease, chronic *Pseudomonas aeruginosa* infection and a baseline predicted FEV₁ of 75% or less. Patients were stratified according to disease severity and inhaled tobramycin use in the 12 months prior to study entry and randomised in a 1:1 ratio to receive inhaled aztreonam lysine 75mg three times a day or tobramycin 300mg twice daily via a nebuliser system for three cycles (28 days on, 28 days off). The mean age was 26 years, 78% of patients were aged 18 years or older.^{2,3}

The co-primary endpoints, measured in the intention to treat population, were relative change from baseline in FEV₁ % predicted at day 28 and mean actual change from baseline in FEV₁ % predicted across three treatment cycles. The mean relative changes in FEV₁ % predicted from baseline to day 28 were 8.4% (standard error [SE] 1.7) and 0.6% (SE 1.8) for the aztreonam lysine and tobramycin treated groups respectively, mean difference 7.8% (95% CI 3.9% to 11.7%, p≤0.001). The adjusted mean actual change from baseline in FEV₁ % predicted across three treatment cycles (superiority analysis) was 2.0% (SE 0.7) and -0.7% (SE 0.7) for aztreonam lysine and tobramycin treated patients respectively, p=0.0023.^{2,3}

Two randomised, double blind, placebo-controlled phase III studies (AIR-CF1 and AIR-CF2) were performed to evaluate the short-term efficacy and safety of inhaled aztreonam lysine. Eligibility criteria for both studies included patients 6 years and older with cystic fibrosis, moderate to severe lung disease (FEV₁ % predicted ≥25 to ≤75) and *Pseudomonas aeruginosa* infection. Patients in AIR-CF1 had received less previous treatment for *Pseudomonas aeruginosa* than in AIR-CF2. In AIR-CF1, the mean age was 27 to 31 years and 77% of patients were aged 18 years or older. In AIR-CF2, the mean age was 25 to 28 years and 78% of patients were aged 18 years or older.^{4,5}

In AIR-CF1, 164 patients were stratified by disease severity and randomised equally to receive inhaled aztreonam lysine 75mg or placebo three times a day. The primary endpoint was change in patient reported respiratory symptoms using the cystic fibrosis questionnaire-revised (CFQ-R) respiratory score. The minimum clinically important difference was considered to be 5 points. The day 28 treatment difference between aztreonam lysine and placebo patients was 10 points in favour of aztreonam lysine (95% CI 4 to 15, p<0.001).⁴

AIR-CF2 randomised 211 patients equally to receive inhaled aztreonam lysine 75mg two or three times a day or placebo for 28 days. All patients received 28 days of tobramycin prior to commencing the randomised portion of the study. The primary outcome was time to need additional inhaled or intravenous antipseudomonal antibiotics to treat symptoms of pulmonary exacerbation. This was 21 days longer for the pooled aztreonam lysine group compared with placebo, 92 versus 71 days, p=0.007. The median time to antibiotic need in the aztreonam lysine twice daily group was more than 92 days (p=0.002 compared with placebo) and 87 days (p=0.182 compared with placebo) in the aztreonam lysine three times a day group.⁵

To support the licence extension to include paediatric patients, a retrospective analysis of 179 children aged 6 to 12 years (n=49) and adolescents aged 13 to 17 years (n=130) was submitted to the European Medicines Agency (EMA). Results demonstrated that there was a similar trend in treatment effect for paediatric and adult patients; however, the studies were not powered to demonstrate a statistical significant difference in the paediatric subgroups.⁶

Summary of evidence on comparative safety

The most common adverse events occurring during the first three cycles of the active-controlled study were cough (71% versus 79%), productive cough (52% versus 60%), pyrexia (32% versus 30%) oropharyngeal pain (26% versus 28%), dyspnoea (24% versus 27%) and haemoptysis (23% versus 16%) for aztreonam lysine and tobramycin treated patients respectively.

Severe adverse events were reported by 16% of patients in the aztreonam lysine group and 8.3% of patients in the tobramycin group, most commonly cough.²

The adverse event profile for aztreonam lysine in paediatric patients was similar to that in adults. Respiratory adverse events were more likely in adult patients and pyrexia was more common in paediatric patients. The incidence of haemoptysis, particularly in children, was raised by the EMA as a concern; however, this may be due to disease and not aztreonam lysine treatment.⁶

Summary of clinical effectiveness issues

The antibiotic aztreonam arginine is available in the UK but is not licensed for use in cystic fibrosis. The aztreonam lysine formulation has been specifically developed for use in cystic fibrosis and has been designated an orphan drug by the EMA. In patients with cystic fibrosis, chronic infection with *Pseudomonas aeruginosa* leads to a faster decline in lung function and higher requirements for treatment.⁷

The submitting company has requested that SMC considers this product when positioned for use when inhaled colistimethate sodium and inhaled tobramycin are not tolerated or are not providing satisfactory therapeutic benefit (measured as $\geq 2\%$ decline in FEV1). There is an unmet need as there are no other inhaled treatment options for these patients.

The clinical studies used a variety of surrogate markers as primary endpoints; some have not been fully validated and no survival benefit has been demonstrated. The placebo-controlled phase III studies were of 28 day treatment duration and the active-controlled study was 24 weeks. Long term comparative data are lacking. An 18-month follow-up study to the two phase III placebo-controlled studies was uncontrolled so the results are difficult to interpret and no conclusions can be drawn regarding long-term benefit. In the active-controlled study, patients had previously received tobramycin so the open-label design may have biased the results.

As the patients treated in the clinical studies do not match the company's proposed positioning, the company presented information from the Cayston Treatment Evaluator, an online database created to evaluate the use of aztreonam lysine.

A retrospective review of this database to assess the effectiveness of aztreonam lysine in routine practice in nine treatment centres in the UK and Ireland was recently presented at the European Cystic Fibrosis Conference and included 113 patients. Most (53%) patients were female and the mean (standard deviation) age was 33 (9.6) years. Data from one year prior to aztreonam lysine treatment and up to one year post aztreonam lysine treatment were compared. The median (interquartile range [IQR]) FEV₁% predicted was 39.6% (29.2% to 48.5%) in the six to 12 months and 36.2% (25.1% to 45.4%) in the zero to six months pre-aztreonam lysine periods. In the zero to six months period after commencing aztreonam lysine, the median (IQR) FEV₁ % predicted was 37.3% (27.5% to 44.5%), and in the six to 12 month period after commencing aztreonam lysine it was 37.3% (27.3% to 46.3%).⁸

This evidence is limited in that this is a retrospective database review, and patients were not randomized, so the data may be prone to bias.

Aztreonam lysine is administered over two to three minutes and would provide a treatment option for patients who require an inhaled antipseudomonal antibiotic and cannot tolerate colistimethate or tobramycin or are no longer benefiting from either of these medicines.

Other data were also assessed but remain commercially confidential.*

Summary of patient and clinician engagement

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of aztreonam lysine inhalation as an orphan medicine, in the context of treatments currently available in NHS Scotland.

The key points expressed by the group were:

- Currently there are no other options available for the small number of patients who cannot tolerate or have deteriorated on current treatments.
- The importance of maintaining and improving FEV1 cannot be underestimated in terms of improving both health outcomes and quality of life.
- Patients have noted a positive impact on their quality of life with reports of increased appetite, improved exercise tolerance and a fuller social life providing benefits for patients and their families.
- Patients emphasised the significant benefit of being able to take the medication away from home.
- The PACE group was strongly supportive of this medicine, noting that it may provide a range of benefits including the potential to bridge to transplant for some patients.

Summary of comparative health economic evidence

The submitting company presented a cost analysis over a one-year time horizon comparing the cost of treatment prior to aztreonam lysine to the cost of treatment one year post-aztreonam lysine treatment, in cystic fibrosis patients who were unable to tolerate or were not obtaining satisfactory therapeutic benefit with inhaled collistimethate sodium and/or inhaled tobramycin. Prior to treatment with aztreonam lysine, patients were on a variety of drug regimens including collistimethane sodium and/or tobramycin, or no regimen.

The clinical data used in the analysis came from the Cayston Treatment Evaluator (CTE), a retrospective database which collected data from 53 patients across nine cystic fibrosis centres in Ireland and the UK. The database was used to estimate the efficacy of treatment regimens pre- and post-aztreonam lysine, and recorded data on several outcomes including mean exacerbations per year, mean days in hospital per year and mean days on antibiotics per year. Based on the analysis, aztreonam lysine achieved an annual mean reduction for all outcomes. It should be noted that a subgroup analysis was also conducted in 31 patients who were not obtaining satisfactory therapeutic benefit with an inhaled tobramycin based regimen.

A range of medicines costs was included in the analysis, including drug acquisition costs and the cost of intravenous antibiotics. Drug acquisition costs were calculated by multiplying the proportion of patients pre- or post-aztreonam lysine by the cost of the treatment. Resource use consisted primarily of exacerbation care costs including inpatient, home care and follow-up costs. Inpatient resource use was estimated from the CTE data. The company also assumed that each exacerbation would require one outpatient follow up. A Patient Access Scheme (PAS) is in place in NHS Scotland for tobramycin solution for inhalation and was incorporated into the analysis as the relevant price of the medicine.

In the base case analysis, aztreonam lysine resulted in an incremental cost of £5,277 versus the preaztreonam lysine treatment regimens, based on total costs of £27,197 and £32,474 for pre- and postaztreonam lysine treatment regimes respectively. Although aztreonam lysine was associated with cost savings as a result of lower exacerbation costs, the treatment was more expensive because of higher drug costs. Simple one-way and two-way sensitivity analysis were provided and results were most sensitive to the number of home care visits assumed for each exacerbation.

A PAS was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount was given on the list price of the medicine. SMC would wish to present the with-PAS results that informed the decision but the company has indicated that this must remain commercial in confidence. Therefore, only the without-PAS cost-effectiveness estimates can be presented.

A number of weaknesses were noted with the analysis:

- The base case analysis revealed that the introduction of aztreonam lysine resulted in an incremental cost of £5,277 versus pre-aztreonam lysine regimens without the PAS. In the subgroup of 31 patients i.e. those who were not obtaining satisfactory therapeutic benefit with an inhaled tobramycin regimen, the incremental cost increased to £7,198 without the PAS. Although aztreonam lysine resulted in a higher proportion of savings from a reduction in exacerbations versus pre aztreonam lysine regimens, these savings were insufficient to offset the higher drug acquisition cost.
- The clinical evidence supporting the economics is uncertain. The company used retrospective data to ascertain treatment efficacy. Retrospective analysis is generally considered to be a weak evidence base as patients are not randomised. Therefore, it is uncertain if the difference in treatment outcomes is due to external factors such as the natural history of the disease or concomitant medication. However, the company highlighted the challenges of conducting a randomised controlled trial in this patient group and these were noted by the Committee.
- Due to the limitations of the clinical evidence, the appropriateness of the estimated savings from reduced exacerbations is unclear. In view of this, the company provided a scenario which assumed a 50% reduction in exacerbation costs. Based on this analysis, aztreonam lysine resulted in an incremental cost of £8,422 (without PAS). Based on the subgroup analysis, the incremental cost increases to £8,935 (without PAS). Given the limitations with the clinical data, it would have been helpful to also see the results of the analysis assuming no difference in exacerbation rates between the treatment arms. The company was asked to provide this but deemed this analysis to be unrealistic.
- The cost analysis provided by the company departs from the SMC guidance to manufacturers. It is normal practice for companies to submit a base case cost utility analysis (when a treatment is more effective and more expensive) in order to estimate a plausible incremental cost effectiveness ratio.
- There is considerable uncertainty surrounding the plausibility of the QALY gain estimates in both the threshold analysis and the hypothetical patient scenarios. The company used QALY gains from previous SMC submissions (ivacaftor and rafaximin) as a means of validation;

however, due to fundamental differences within the individual submissions, these analyses were not considered robust.

The Committee considered the benefits of aztreonam lysine inhalation in the context of its decision modifiers that can be applied when there is increased uncertainty due to the orphan status of the medicine and concluded that the criteria for absence of other therapeutic options and bridging to another definitive therapy (such as lung transplant) was met.

After considering all the available evidence, the output from the PACE process, and after application of the appropriate modifiers, the Committee accepted aztreonam lysine for restricted use in NHS Scotland.

Other data were also assessed but remain commercially confidential.*

Summary of patient and public involvement

The following information reflects the views of the specific patient groups.

- Submissions were received from the Cystic Fibrosis Trust, a registered charity and the Ivacaftor Patient Interest Group, an unincorporated organisation.
- Cystic Fibrosis Trust has received funding from several pharmaceutical companies in the past 2 years, including from the submitting company. The Ivacaftor Patient Interest Group has received no funding in the past 2 years.
- Cystic Fibrosis (CF) is an incurable, life-threatening, life-shortening and life-limiting inherited disease that affects the lungs and digestive system. It can also affect the bones, joints, liver and sweat glands, and can cause infertility and CF related diabetes.
- CF has an enormous impact on day-to-day living for patients, carers and family. Burdensome and time-consuming medication and physiotherapy regimens are required which results in huge emotional and physical strain on all involved. The ability to study, work, have a social life or take part in everyday activities is severely restricted with many experiencing low self esteem, isolation and depression.
- Advantages of aztreonam lysine inhalation include ease of administration, possible increased lung function and increased daily living activities. Aztreonam lysine inhalation provides additional patient choice and can improve quality of life for patients and families.

Additional information: guidelines and protocols

The National Institute of Health and Care Excellence conducted a multiple technology appraisal (TA276) reviewing colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis in March 2013.⁹

Tobramycin dry powder for inhalation (DPI) is recommended as an option for treating chronic pulmonary infection caused by *Pseudomonas aeruginosa* in people with cystic fibrosis only if:

• nebulised tobramycin is considered an appropriate treatment, that is, when colistimethate sodium is contraindicated, is not tolerated or has not produced an adequate clinical response and

• the manufacturer provides tobramycin DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.

Colistimethate sodium DPI is recommended as an option for treating chronic pulmonary infection caused by *P. aeruginosa* in people with cystic fibrosis only if:

- they would clinically benefit from continued colistimethate sodium but do not tolerate it in its nebulised form and thus tobramycin therapy would otherwise be considered **and**
- the manufacturer provides colistimethate sodium DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.

Healthcare Improvement Scotland has advised that these recommendations are valid for NHS Scotland.

The Cystic Fibrosis Foundation published an update to their consensus statement "Cystic Fibrosis Pulmonary Guidelines. Chronic Medications for Maintenance of Lung Health" in 2013. They recommend aztreonam lysine for moderate to severe disease with a high degree of certainty for a substantial net benefit. The benefit in patients with mild disease was rated as moderate. They also strongly recommend inhaled tobramycin to improve lung function and reduce exacerbations in cystic fibrosis patients, six years and older, with moderate to severe lung disease and *Pseudomonas aeruginosa*. For patients with mild lung disease the evidence was fair. They did not consider the evidence for other antibiotics (including colistimethate) to be sufficient to recommend their use.¹⁰

The European Cystic Fibrosis Society updated their consensus statement in 2012. There is still considered to be a need for additional antibiotic choices for the management of cystic fibrosis airways disease due to intolerance or lack of efficacy. The guideline discusses colistimethate, tobramycin and aztreonam lysine but does not make recommendations for the use of one in preference over another.¹¹

The 2009 report from the UK Cystic Fibrosis Trust recommends that patients with chronic *Pseudomonas aeruginosa* infection be considered for regular nebulised antipseudomonal antibiotics. Colistimethate is the drug of first choice for nebulised use since resistance rarely occurs, even after prolonged use. If colistimethate is unsuitable or unsatisfactory then tobramycin should be used. This guideline predates the licensing of aztreonam lysine.¹²

Additional information: comparators

Inhaled colistimethate sodium and tobramycin.

Cost of relevant comparators

Drug	Dose Regimen	Cost per cycle (£)	Cost per year (£)
Aztreonam lysine	75mg inhaled via a nebuliser three times a day for 28 days followed by 28 days off treatment.	2,182	13,089
Tobramycin	112mg via a Podhaler twice daily for 28 days followed by 28 days off treatment.	1,790	10,740
Tobramycin	300mg via a nebuliser twice daily for 28 days followed by 28 days off treatment.	1,187	7,122
Colistimethate sodium	1,662,500 international units (125mg) inhaled via a Turbospin inhaler twice daily	969	5,813
Colistimethate sodium	1 million to 2 million international units (80mg to 160mg) via a nebuliser two or three times daily	258 to 773	1,546 to 4,637

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVADIS on 1 September 2014 except for aztreonam lysine from MIMS online on 1 September 2014. Costs do not take any patient access schemes into consideration. Cost calculated as a 28 day cycle and six cycles given in a year for comparison; the 28 days on and off treatment is not part of the collistimethate licensed dosing schedule.

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 828 in all years, with an estimated uptake rate of 7.55% in year 1 and 32.36% in year 5.

The gross impact on the medicines budget without the PAS was estimated to be $\pounds119k$ in year 1 and $\pounds511k$ in year 5. As other drugs were assumed to be displaced, the net medicines budget impact is expected to be $\pounds82k$ in year 1 $\pounds350k$ in year 5.

Other data were also assessed but remain commercially confidential.*

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

- 1. Aztreonam lysine (Cayston®) Summary of Product Characteristics. Gilead Sciences Ltd. Electronic Medicines Compendium <u>www.medicines.org.uk</u> Last updated 20 August 2014
- 2. Assael BM, Pressler T, Bilton D, et al. Inhaled aztreonam lysine vs. inhaled tobramycin in cystic fibrosis: A comparative efficacy trial. Journal of Cystic Fibrosis 2013;12:130-40
- 3. The European Medicines Agency (EMA) European Public Assessment Report. Aztreonam lysine (Cayston®). EMEA/H/C/000996/R/15. 23 June 2011 <u>www.ema.europa.eu</u>
- 4. Retsch-Bogart GZ, Quittner AL, Gibson RL et al. Efficacy and safety of inhaled aztreonam lysine for airway pseudomonas in cystic fibrosis. Chest 2009;135:1223-32
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- 7. UK Cystic Fibrosis Registry. Annual data report 2013. July 2014. www.cysticfibrosis.org.uk
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- National Institute of Health and Care Excellence. Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis. TA276 March 2013 <u>www.nice.org.uk</u> <u>Link</u>
- 10. Mogayzel PJ, Jr., Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. American Journal of Respiratory and Critical Care Medicine. 2013;187(7):680-9
- 11. Doring G, Flume P, Heijerman H, Elborn JS, Consensus Study G. Treatment of lung infection in patients with cystic fibrosis: current and future strategies. Journal of Cystic Fibrosis. 2012;11(6):461-79
- 12. Cystic Fibrosis Trust. Antibiotic treatment for cystic fibrosis: Report of the UK cystic fibrosis trust antibiotic working group 2009. <u>www.cftrust.org.uk Link</u>

This assessment is based on data submitted by the applicant company up to and including 17 October 2014.

*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About SMC/Policy Statements/Policy Statements

Drug 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.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a drug and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG, established under the auspices of NHS National Services Scotland reviews and advises NHS Scotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

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.