atezolizumab 840mg and 1,200mg concentrate for solution for infusion (Tecentriq®)

Roche Products Ltd

08 October 2021

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

atezolizumab (Tecentriq®) is accepted for use within NHSScotland.

Indication under review: As monotherapy for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumours have a PD-L1 expression ≥50% tumour cells (TC) or ≥10% tumour-infiltrating immune cells (IC) and who do not have epidermal growth factor receptor (EGFR) mutant or anaplastic lymphoma kinase (ALK)-positive NSCLC.

In a phase III study, treatment with atezolizumab improved overall survival when compared with chemotherapy in the relevant subgroup of patients with previously untreated metastatic NSCLC (PD-L1 expression ≥50% TC or ≥10% IC).

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Vice Chairman
Scottish Medicines Consortium

Indication

As monotherapy for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumours have a PD-L1 expression ≥50% tumour cells (TC) or ≥10% tumour-infiltrating immune cells (IC) and who do not have epidermal growth factor receptor (EGFR) mutant or anaplastic lymphoma kinase (ALK)-positive NSCLC.[1, 2]

Dosing Information

The recommended dose of atezolizumab is 1,200mg administered intravenously (IV) every 3 weeks. Alternatively, the atezolizumab monotherapy dose can be 840mg IV every two weeks or 1,680mg IV administered every four weeks. The initial dose of atezolizumab must be administered over 60 minutes. If the first infusion is well tolerated, all subsequent infusions may be administered over 30 minutes.

It is recommended that patients are treated with atezolizumab until disease progression or unmanageable toxicity.

Patients with first-line NSCLC should be selected for treatment based on the tumour expression of PD-L1 confirmed by a validated test.

Atezolizumab must be initiated and supervised by physicians experienced in the treatment of cancer. See Summary of product characteristics (SPC) for further information.[1, 2]

Product availability date

May 2021

Atezolizumab meets SMC end of life criteria.

Summary of evidence on comparative efficacy

Atezolizumab is a humanised monoclonal antibody that binds to programmed death-ligand 1 (PD-L1) and blocks its interactions with the programmed death-1 (PD-1) and B7.1 receptors on tumour cells and/or tumour-infiltrating immune cells. This prevents PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the anti-tumour immune response without inducing antibody-dependent cellular cytotoxicity.[1, 2]

The key evidence supporting the efficacy and safety of atezolizumab comes from IMpower110, an international, randomised, open-label, phase III study. This study recruited adults with histologically or cytologically confirmed, measurable, stage IV non-squamous or squamous NSCLC, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and no prior treatment for their stage IV NSCLC. Patients were eligible if they had PD-L1 expression ≥1% TC or ≥1% IC (based on SP142 assay) with no known sensitising mutation in the EGFR gene or ALK fusion oncogene.[3]

Patients were randomised equally to receive atezolizumab, at a dose of 1,200mg administered by IV infusion every 21 days or platinum-based chemotherapy. For patients with non-squamous disease, chemotherapy consisted of cisplatin (75mg/m^2) or carboplatin (area under the concentration−time curve [AUC], 6) in addition to pemetrexed (500mg/m^2) IV on Day 1 of each 21-day cycle for four or six cycles, followed by maintenance therapy with pemetrexed (500mg/m^2) IV on day 1 of each cycle. For patients with squamous disease, it included cisplatin (75mg/m^2) plus gemcitabine (1,250mg/m^2) or carboplatin (AUC, 5) plus gemcitabine (1,000mg/m^2) IV on day 1 of each 21-day cycle for four or six cycles with gemcitabine also given on day 8 of each 21-day cycle, followed by best supportive care. Patients who were treated with atezolizumab and who demonstrated evidence of clinical benefit were permitted to continue atezolizumab after evidence of disease progression based on RECIST v1.1 criteria. Atezolizumab treatment continued as long as patients were experiencing clinical benefit as assessed by the investigator or until unacceptable toxicity or death. Chemotherapy treatment continued until disease progression, unacceptable toxicity, or death.[3] Randomisation was stratified according to sex (male versus female), ECOG performance status (0 versus 1), histology (non-squamous versus squamous), and PD-L1 tumour expression status (PD-L1 expression on ≥1% of TC and any IC versus PD-L1 on <1% of TC and PD-L1 expression on ≥1% of IC).[3]

The primary outcome was overall survival, which was defined as the time between date of randomisation and death due to any cause.[4, 5] The marketing authorisation for atezolizumab is only for patients whose tumours have PD-L1 expression ≥50% TC or ≥10% IC and the primary analysis of the IMpower110 study was in this subpopulation; thus only the results for this subpopulation (37% of full study population) are presented.

Efficacy results at data cut-off 10 September 2018 and updated exploratory analysis results at data cut-off 4 February 2020 for patients with ≥50% PD-L1 expressing TCs or ≥10% IC are detailed in Table 1 below.

Table 1: Primary and relevant secondary outcomes of IMpower110 study for the subpopulation with PD-L1 ≥50% TC or ≥10% IC.[4, 5, 6]

	Atezolizumab (n=107)	**Chemotherapy** (n=98)	**Atezolizumab** (n=107)	**Chemotherapy** (n=98)
Data cut-off date	Interim analysis 10 September 2018		Exploratory analysis 4 February 2020	
Overall survival				
Median duration of follow-up, months	15.7		31	
Number of deaths	44	57	64	64
Median overall survival, months	20.2	13.1	20.2	14.7
HR (95% CI)	0.59 (0.40 to 0.89)		0.764 (0.54 to 1.09)	
p-value	0.01		-	
KM estimate at 12 months	65%	51%	66%	52%
KM estimate at 24 months	46%	25%	47%	34%

PFS assessed by investigator (RECIST v1.1 criteria)				
Patients with event, n	67	79	82	87
Median PFS, months	8.1	5.0	8.2	5.0
Stratified HR (95% CI)	0.63 (0.45 to 0.88)		0.59 (0.43 to 0.81)	
KM estimate at 12 months	37%	22%	39%	19%
Response outcomes (RECIST v1.1 criteria)				
ORR, %	38%	29%	40%	29%
Median DOR, months	NE	6.7	38.9	8.3

Abbreviations: CI, confidence interval; DOR, duration of response; HR: hazard ratio; KM, Kaplan Meier; NE, not estimable; ORR, objective response rate; PFS, progression free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumours Version 1.1.

Exploratory analyses using different immunohistochemical assays for PD-L1 status were consistent with the primary analyses.[4]

Two Bayesian network meta-analyses (NMAs) were conducted, one used hazard ratio (HR) data and the other used individual patients survival time to compare the efficacy and safety of atezolizumab (data from the PD-L1 ≥50% TC or ≥10% IC subgroup of IMpower110)[5, 6] versus pembrolizumab (data from KEYNOTE-024[7] and from the TPS ≥50% subgroup of KEYNOTE-042[8]) in adult patients with stage IV squamous or non-squamous NSCLC who have not received prior chemotherapy and have confirmed tumour PD-L1 expression. Efficacy outcomes assessed included overall survival, progression-free survival (PFS) and objective response rate (ORR). Safety outcomes included any treatment-related adverse event (TRAE), any treatment-related serious adverse event (TRSAE), any treatment-related adverse event grade 3 or above and withdrawal due to adverse event (AE). The submitting company concluded that despite the observed increase in HR between the 2018 and 2020 IMpower110 data cuts, results indicate no evidence of a difference between atezolizumab and pembrolizumab in terms of either overall survival or PFS. In addition, no differences between treatments were generally noted in terms of ORR and safety outcomes.

Summary of evidence on comparative safety

Overall, the safety profile of atezolizumab monotherapy was considered acceptable and no new safety issues were identified.[4]

In the IMpower110 study at data cut-off 4 February 2020, the median duration of treatment in the atezolizumab group was 5.3 months and in the chemotherapy group was 2.1 to 3.5 months. In the atezolizumab and chemotherapy groups respectively, patients reporting a treatment-related grade 3 or higher AE were 14% versus 45%, patients with a treatment-related serious AE were 9.4% versus 16%, patients with a dose modification/interruption due to treatment emergent AEs were 32% versus 44%, and the proportion of AEs that led to treatment withdrawal were 7.3% versus 17%.[4]

At the September 2018 data cut-off, the most common AE with an incidence >20% in the atezolizumab group versus the chemotherapy group included gastrointestinal disorders (32% versus 51%); blood and lymphatic system (18% versus 61%); general disorders and administration site disorders (34% versus 39%), respiratory, thoracic and mediastinal disorders reflective of the condition (21% versus 16%).[4]

Clinically meaningful differences in AE profiles that were observed between the treatment groups were typically chemotherapy-related, such as nausea, vomiting, decreased platelets and neutrophil count versus immunotherapy-related hypothyroidism observed frequently with atezolizumab.[4]

Summary of clinical effectiveness issues

Lung cancer is estimated to be responsible for nearly one in five cancer deaths globally. Around 85% of lung cancers are NSCLC (subdivided into non-squamous carcinoma and squamous cell carcinoma) and the majority of patients are diagnosed at an advanced stage, which is associated with extremely poor survival (untreated median overall survival of 4 months).[4] Recently updated guidelines recommend pembrolizumab as the standard first-line in patients with PD-L1 expression ≥50% who do not otherwise have contraindications to use of immunotherapy.[9, 10]

At the interim analysis of IMpower110, in the relevant PD-L1 ≥50% TC or ≥10% IC subpopulation, treatment with atezolizumab was associated with a statistically significant improvement in overall survival with a median gain of 7.1 months over chemotherapy. At the exploratory analysis (with a follow-up of approximately 31 months; when 62% of patients had died) it was associated with a numerical improvement of 5.5 months over chemotherapy. With longer follow-up, the median overall survival in the chemotherapy group became longer and the HR 95% CI crossed 1, but the European Medicines Agency (EMA) still considered the benefit clinically meaningful. The marketing authorisation applicant noted that the change was maybe due to the subsequent use of immunotherapy in the chemotherapy group. A third of patients in the chemotherapy group subsequently received immunotherapy (as of data cut-off February 2020, 35% of patients in the chemotherapy group had received a subsequent immunotherapy versus 3.7% in the atezolizumab group); subsequent treatments may have affected the later data cut off but may not fully explain the change in observed treatment effect. Therefore, there is uncertainty in atezolizumab effect over time.[4, 11]

Of note, the Kaplan Meier overall survival curves crossed after approximately 4 months, suggesting that initially treatment with chemotherapy may be superior to atezolizumab, with the shape of the curve indicating more early deaths with atezolizumab. The higher number of deaths seen within 2.5 months after randomisation in the atezolizumab group may potentially be due to a delayed onset of atezolizumab effect and is reflected in the SPC, although the EMA also noted that no risk factors could be identified.[4]

Secondary outcomes were supportive, including PFS and ORR/DOR.[4] However, several limitations hinder the interpretation of secondary/exploratory outcomes in IMpower110. The study was limited by its open-label design, which may have introduced bias for certain outcomes such as safety and quality of life outcomes. Another design limitation was the lack of blinded, independent review of PFS and response outcomes, introducing the possibility of assessment bias; an independent review may have improved the robustness of the results. In addition, secondary endpoints were not controlled for multiplicity.

The relevant subgroup supporting the indication under review, which comprised of patients with PD-L1 expression on ≥50% of TC or on ≥10% of IC, consisted of 205 patients. All patients had an ECOG PS 0 or 1, which limits generalisability to patients with poorer performance status. In addition, limited data are available for patients ≥75 years old.

There are no direct comparative data with the most relevant comparator, pembrolizumab. Thus, the submitting company performed NMAs comparing atezolizumab with pembrolizumab. There were some limitations with the NMAs' results. There was heterogeneity in the populations included in the NMAs for overall survival. The analyses were conducted using subgroups of patients drawn from IMpower110 and KEYNOTE-042 studies (though relevant to the licensed indication). There were differences in the duration of follow-up between the studies. The 95% CIs for all outcomes in the base case and sensitivity analyses cross one, with some being quite wide. PFS and ORR, where assessed by the investigators in IMpower110 and by a blinded independent central review in the KEYNOTE studies. The submitting company assumed that results measured by investigators were comparable to results assessed by BIRC. The company submission did not include SUCRA scores, probability best, or mean rank for the analyses. Overall, despite these limitations, the conclusion of no evidence of a difference between atezolizumab and pembrolizumab seems reasonable.

Companion diagnostic required: contact local laboratory for information.

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis of atezolizumab compared to pembrolizumab for the indication of adults with metastatic NSCLC whose tumours have a PD-L1 expression ≥50% TC or ≥10% IC, defined as the PD-L1 high population, and who do not have EGFR mutant or ALK-positive NSCLC. SMC clinical experts confirmed that single agent pembrolizumab is the relevant comparator.

The economic analysis used a standard partitioned survival model with three health states: progression free, progressed and death. The model had a weekly cycle and a lifetime horizon of 20 years, with a starting age of 63.7 years based on patient characteristics from the IMpower110 study (IMpower110 PD-L1 ≥50% TC or ≥10% IC subpopulation). Atezolizumab and pembrolizumab were assumed to be administered every three weeks. The clinical data used in the economic analysis for atezolizumab was the PD-L1 ≥50% TC or ≥10% IC subpopulation at 4th February 2020

cut-off (N=107 in the atezolizumab arm) from the phase III, randomised, open-label IMpower110 study. For the comparison with pembrolizumab the results of a NMA was used to generate hazard ratios for PFS and overall survival versus the reference arm atezolizumab. The hazard ratios for pembrolizumab were applied to the reference arm PFS and overall survival estimates assuming proportional hazards for extrapolation. Choice of function for extrapolation was performed by fitting the Generalized Gamma and Weibull curves to the atezolizumab reference arm for PFS and overall survival respectively, with functions chosen based on visual and statistical fit as well as clinical plausibility. Alternative parametric functions were applied in scenario analysis.

Treatment duration for atezolizumab was based on time to treatment discontinuation (TTD) data from IMpower110, applying parametric distributions fitted to TTD Kaplan-Meier (KM) curves. Treatment with pembrolizumab is expected to be stopped after two years of continuous treatment, or if loss of benefit or unacceptable toxicity occurs prior to this. In the model for the base case, the submitting company adopted the approach of fitting parametric functions to KEYNOTE-042 PFS and TTD KM data to obtain a HR to be applied to the PFS curve in the model to generate an adjusted TTD curve for pembrolizumab, as this was considered to be the most conservative approach. Alternative methods of applying TTD were considered in scenario analysis including applying a weighted average of fitted TTD curves from KEYNOTE-042 and KEYNOTE-024, or using pembrolizumab PFS data as a proxy for TTD but imposing a 2-year stopping rule.

Utility values were applied by health state based on EQ-5D-3L data collected in the IMpower110 study, estimated using UK tariffs. The base case applied utility values estimated for the whole ITT wild-type population. Alternative utility values from the IMpower110 PD-L1 ≥50% TC or ≥10% IC sub-population were explored in scenario analysis. Alternative methods of applying utility values such as time to death were also explored.

Grade ≥3 treatment-related adverse events with an incidence of ≥2% in the atezolizumab arm of the IMpower110 trial are included in the base case analysis for costs and resource use. Adverse event disutilities were assumed to be captured within the IMpower110 quality of life data so were not included separately in the base case.

Costs included medicine acquisition and administration costs, monitoring costs, health state and supportive care costs, subsequent therapies, adverse event management and end of life have all been in included in the economic analysis.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a simple discount was offered on the list price of atezolizumab. A confidential price discount is also in place in Scotland for comparator pembrolizumab.

The company also presented a cost-minimisation analysis (CMA) based on the results of the NMA, as well as clinical expert opinion, showing no evidence of a difference in outcomes between atezolizumab and pembrolizumab. Assuming both atezolizumab and pembrolizumab are administered every 3 weeks, atezolizumab was estimated to be cost-saving at PAS price.

The results presented do not take account of the PAS for pembrolizumab but these were considered in the results used for decision-making. SMC is unable to present the results provided by the company which used an estimate of the PAS price for pembrolizumab due to commercial confidentiality and competition law issues.

In the cost-utility analysis presented for atezolizumab versus pembrolizumab when applying the atezolizumab PAS price it was estimated that atezolizumab is less costly and less effective than pembrolizumab; lying in the south-west quadrant of a cost-effectiveness plane. Hence, in this analysis the submitting company presented the net monetary benefit (NMB) of atezolizumab versus pembrolizumab as well as incremental cost-effectiveness ratios (ICERs). The main driver of incremental costs was treatment costs, with the direction of cost-effectiveness dependent on the PAS prices applied. Cost savings were also accrued relating to supportive care in progressive disease, subsequent therapies and terminal care cost.

Table 2: Base case cost-utility analysis results for atezolizumab (PAS price) versus pembrolizumab (list price)

Analysis	Incremental LYG	ICER (cost/ QALY)
Atezolizumab versus pembrolizumab - with PAS for atezolizumab (versus pembrolizumab at list price)		
Atezolizumab	-0.14	£580,523*
Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life years gained; PAS, patient access scheme; QALYs, quality-adjusted life years; * SW quadrant ICER indicating atezolizumab is cost saving but also less effective.		

A subgroup analysis of patients using the 22C3 assay to determine TPS ≥50% was also presented, as this assay is expected to be widely used in Scotland. This analysis estimated atezolizumab to be more effective than pembrolizumab.

Table 3: Subgroup analysis

Analysis	Incremental LYG	ICER (cost/ QALY)
22C3 subgroup: Atezolizumab versus pembrolizumab - - with PAS for atezolizumab (versus pembrolizumab at list price)		
Atezolizumab	0.01	Dominant*
Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life years gained; PAS, patient access scheme; QALYs, quality-adjusted life years; *atezolizumab is cost saving and more effective		

In one way sensitivity analysis, the ICERs were not sensitive to variations in discount rates, utility values and administration costs. Additional scenario analyses were explored varying extrapolation, atezolizumab treatment effect, time horizon and utility values.

The economic analysis was associated with a number of limitations and uncertainties:

- The clinical evidence for atezolizumab consists of clinical study data from IMpower110 versus chemotherapy so there is an absence of direct head-to-head data comparing atezolizumab against pembrolizumab. Based on the NMA the submitting company concluded there is no clear evidence of a difference between atezolizumab and pembrolizumab in terms of overall survival or progression free survival, hence the CMA represents an appropriate base for

assessment of the cost-effectiveness of atezolizumab vs pembrolizumab. There is uncertainty in the atezolizumab overall survival data due to limited median duration of follow-up so data requires long-term extrapolation over the model time horizon. This is associated with uncertainty on the treatment effect of overall survival though this has been explored in scenario analysis by capping the atezolizumab treatment effect and through exploring alternative extrapolations for overall survival, as well as progression free survival.

- Time on treatment for pembrolizumab is uncertain as it is expected to be stopped after two years of continuous treatment, or until loss of benefit or unacceptable toxicity. This has been applied in the model based on KEYNOTE-042 PFS data to obtain adjusted time to treatment discontinuation.
- A sub-group analysis using alternative assay 22C3 for detection of PD-L1 was conducted within the enrolled SP142-selected patients with PD-L1 expression on ≥1% of TC or IC, as it was suggested that this assay was most used in Scottish clinical practice based on clinical expert feedback. Whilst this analysis is a plausible alternative scenario to reflect Scottish clinical practice the scenario is associated with limitations due to IMpower110 22C3 patients being double screened based on assay criteria initially using the SP142 assay followed by the 22C3 assay.

Despite the limitations outlined above, the economic case was demonstrated.

Summary of patient and carer involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from the Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. Roy Castle Lung Cancer Foundation is a registered charity and the Scottish Lung Cancer Nurses Forum is an unincorporated organisation.

- Roy Castle Lung Cancer Foundation has received 12.5% pharmaceutical company funding in the past two years, including from the submitting company. Scottish Lung Cancer Nurses Forum has received 100% pharmaceutical company funding in the past two years, including from the submitting company.

- Advanced NSCLC is a life-threatening disease with little change in survival in the last 40 years. Cure is not an option for this patient group. Patients with advanced or metastatic lung cancer are often debilitated with multiple distressing symptoms. Improving quality of life, symptom management and even small extensions in duration of life are of considerable importance to the individual and their family.

- Options for this targeted group are very limited. The availability of new targets and therapy choices is of key importance. Some patients will receive a platinum based chemotherapy regimen as a first-line treatment; however this is associated with debilitating side effects, which can affect quality of life.

- Atezolizumab represents an additional first line therapy option for this patient group. It would be welcomed by patients as an effective treatment option. It also offers flexible administration. Patients expect to have a treatment which can have better outcomes than chemotherapy, which is easier to tolerate, administer and requires less time spent in hospital than chemotherapy. This may lead to improvement in quality of life for this group of patients. There is potential that this treatment will contribute to research and developments within lung cancer that could lead to the disease becoming more treatable and manageable as a long-term condition.

Additional information: guidelines and protocols

European Society for Medical Oncology (ESMO)[9] published in September 2020 the clinical practice guidelines: 'Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up'. In regards to the indication under review, these guidelines consider pembrolizumab as the standard first-line option in patients with PD-L1 expression ≥50% who do not otherwise have contraindications to use of immunotherapy. In addition, atezolizumab is mentioned as a promising first-line treatment option in patients. However, at the time of publication it had not received approval from the European Medicines Agency.

The National Institute for Health and Care Excellence (NICE)[10] published in 2019 'Lung cancer: diagnosis and management' (NICE guideline 122).

The Scottish Intercollegiate Guidelines Network (SIGN)[12] published in 2014 the "Management of lung cancer", a national clinical guideline. These guidelines pre-date the authorisation of immunotherapy agent pembrolizumab.

Additional information: comparators

Pembrolizumab

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per 3-week cycle (£)
Atezolizumab	**1,200mg administered IV every 3 weeks**	**3,808**

Costs from BNF online on 10 August 2021. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 279 patients eligible for treatment with atezolizumab in year 1 and 281 patients in year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 14 September 2021.

**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*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are

therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine 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 NHSScotland 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 NHSScotland 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.