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Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2120

pertuzumab 420mg concentrate for solution for infusion (Perjeta®)

Roche Products Limited

7 December 2018

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 NHSScotland. The advice is summarised as follows:

ADVICE: following a third resubmission assessed under the orphan equivalent process

pertuzumab (Perjeta®) is accepted for use within NHSScotland.

Indication under review: In combination with trastuzumab and docetaxel, in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.

Addition of pertuzumab to current first-line treatment, trastuzumab plus docetaxel, significantly increased progression-free and overall survival for women with HER2-positive metastatic or locally recurrent unresectable breast cancer.

This SMC advice takes account of the benefit of Patient Access Schemes (PAS) that improves the cost effectiveness of pertuzumab and trastuzumab IV (Herceptin®). This advice is contingent upon the continuing availability of these PAS in NHSScotland or list prices that are equivalent or lower.

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

Chairman
Scottish Medicines Consortium

Indication

In combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.[1]

Dosing Information

840mg intravenous (IV) infusion over 60 minutes, then 420mg IV infusion over 30 to 60 minutes every three weeks until disease progression or unmanageable toxicity. An observation period of 30 to 60 minutes is recommended after each dose of pertuzumab and before commencement of any trastuzumab or docetaxel infusions.

(The recommended dose of concomitant trastuzumab is either 600mg subcutaneous injection every three weeks, or 8mg/kg IV infusion then 6mg/kg IV infusion every three weeks. The recommended dose of docetaxel is 75mg/m^2 every three weeks; this may be increased to 100mg/m^2 if the initial dose is well tolerated. The medicines should be administered sequentially. Pertuzumab and trastuzumab may be given in any order, but docetaxel should be administered after these.)

Therapy should only be initiated under the supervision of a physician experienced in the administration of anti-cancer agents. It should be administered by a healthcare professional prepared to manage anaphylaxis and in an environment where full resuscitation service is immediately available.

Patients must have HER2-positive tumour status, defined as a score of 3+ by immunohistochemistry (IHC) and / or a ratio of ≥2.0 by in situ hybridisation (ISH) assessed by a validated test. To ensure accurate and reproducible results, the testing must be performed by a specialised laboratory, which can ensure validation of the testing procedure.[1]

Product availability date

March 2013

Pertuzumab meets SMC orphan-equivalent criteria.

Summary of evidence on comparative efficacy

Pertuzumab is the first monoclonal antibody that binds to subdomain II, the dimerisation domain, of human epidermal growth factor-2 (HER2) receptor. It blocks heterodimerisation of HER2 with other HER receptors, including HER1 (epidermal growth factor receptor [EGFR]), HER3 and HER4 and it also mediates antibody-dependent cell-mediated cytotoxicity. In pre-clinical studies, it has shown a synergistic effect with trastuzumab, an anti-HER2 monoclonal antibody, which binds to the HER2 receptor at subdomain IV.[1-4]

A double-blind phase III study (CLEOPATRA) recruited 808 patients with HER2-positive, unresectable locally recurrent or metastatic breast cancer who had not received chemotherapy or biologic therapy for metastatic disease. They were randomised in a 1:1 ratio to placebo or pertuzumab 840mg intravenous (IV) infusion, then 420mg IV infusion every three weeks until disease progression or unmanageable toxicity. These were administered in combination with IV infusions of trastuzumab 8mg/kg then 6mg/kg every three weeks and docetaxel 75mg/m^2 every three weeks. The docetaxel dose was increased to 100mg/m^2 if the initial dose was well tolerated.

The primary endpoint, progression-free survival (PFS), was defined as the time from randomisation to first documented radiographic evidence of progressive disease assessed by an independent review facility using Response Evaluation Criteria in Solid Tumours (RECIST), or death from any cause within 18 weeks of the last independent assessment of tumours. PFS was analysed via a log-rank test in the intention-to-treat (ITT) population, which comprised all randomised patients. Tumour assessments were conducted every 9 weeks.[2-4]

After a median follow-up of 19.3 months, data cut-off in May 2011, the primary analysis indicated that independently-assessed PFS was significantly improved with pertuzumab compared with placebo, with median PFS of 18.5 and 12.4 months in the respective groups and a hazard ratio (HR) for progression or death of 0.62 (95% confidence interval [CI]: 0.51 to 0.75).

At the May 2011 data cut-off, there had been 165 deaths (43% of the pre-specified number for the final analysis of overall survival). There were fewer deaths in the pertuzumab group compared with the placebo group: 69 (17%) versus 96 (24%), with a HR of 0.64 (95% CI: 0.47 to 0.88, p=0.005). This did not meet the stopping boundary. At the final analysis of overall survival, data cut-off in February 2014, after a median follow-up of 49.5 and 50.6 months, 168 (42%) and 221 (54%) patients in the pertuzumab and placebo groups, respectively, had died. Overall survival was significantly increased in the pertuzumab group compared with placebo, with a HR 0.68 (95% CI: 0.56 to 0.84, p<0.001). Kaplan-Meier estimated median survival with pertuzumab was 56.5 months and was 40.8 months in the placebo group. This analysis did not adjust for treatment switching; 48 patients from the placebo group crossed-over to the pertuzumab group. When data from these patients were censored at crossover, the HR was 0.63 (95% CI: 0.52 to 0.78) and median overall survival was 56.5 and 39.6 months in the respective groups.[2-5]

Objective response rate, defined as an independently-assessed complete or partial response as per RECIST on two consecutive occasions at least four weeks apart, was analysed in patients who had measurable disease at baseline. At the cut-off for the primary PFS analysis in May 2011, the objective response rate was significantly greater with pertuzumab compared with placebo, 80% versus 69%, with a treatment difference of 11% (95% CI: 4.2% to 18%).[2-4] Pre-specified analyses of the Functional Assessment of Cancer Therapy-for Breast Cancer (FACT-B) questionnaire did not indicate a difference between treatment arms in quality of life.[3]

Summary of evidence on comparative safety

Almost all patients in both groups of the pivotal study experienced at least one adverse event and the majority were treatment-related. Adverse events that occurred with a higher incidence (at least 5%) in the pertuzumab group compared with the placebo groups were diarrhoea (67% versus 46%), rash (34% versus 24%), mucosal inflammation (28% versus 20%), febrile neutropenia (14% versus 7.6%) and dry skin (11% versus 4.3%). These were mainly mild to moderate in severity and occurred less frequently after discontinuation of docetaxel. Serious adverse events were reported by 34% and 26% of patients in the pertuzumab and placebo groups, respectively. The most common were febrile neutropenia (11% and 5%) and infections (11% and 7.3%).[2-4]

Particular attention was given to potential cardiac adverse events by the study investigators. In the pertuzumab group compared with placebo, there was a lower incidence of left ventricular systolic dysfunction of any grade (4.4% versus 8.3%) and of grade 3 or above (1.2% versus 2.8%). Among patients who had left ventricular ejection fraction (LVEF) assessed post-baseline, significant decline, defined as a reduction of at least 10% to an LVEF less than 50%, was reported by 3.8% and 6.6% in the pertuzumab and placebo groups, respectively.[2-4]

Summary of clinical effectiveness issues

HER2-positive metastatic breast cancer is an aggressive subtype of breast cancer despite the introduction of trastuzumab. It often affects younger women and clinical experts consulted by SMC considered that pertuzumab fills an unmet need in this therapeutic area due to the associated survival benefit. Pertuzumab meets SMC orphan-equivalent criteria.

Pertuzumab is a first-in-class medicine that produces improvements of 6 months in median PFS and 16 months in overall survival, compared with current first-line treatment of HER2-positive metastatic breast cancer. An increase in overall survival of this magnitude has acknowledged clinical relevance. The data supporting these benefits derive from a well-designed and conducted double-blind, randomised controlled study, with an independently-assessed primary outcome.[2-5]

In the CLEOPATRA study, the proportion of patients who had received prior (neo-) adjuvant therapy with trastuzumab was lower than expected in clinical practice: 12% (n=47) in the pertuzumab group and 10% (n=41) in the placebo group. Current adjuvant treatment of women with HER2-positive, node-positive breast cancer or women with HER2-positive node-negative tumours >1cm in size would include trastuzumab. The patients in the study who had received (neo-) adjuvant trastuzumab were mainly from North America and the EU and had demography similar to entire European and ITT study populations. Exploratory post-hoc analysis in this subgroup indicated that the treatment effects on independently-assessed PFS, HR 0.62 (95% CI: 0.35 to 1.07) and overall survival, HR 0.68 (95% CI: 0.30 to 1.55) were similar to those in the total study population. At the time of the final analysis the HR for overall survival within the 88 women

previously treated with trastuzumab in the (neo-) adjuvant setting was 0.80 (95% CI: 0.44 to 1.47), the interaction p-value was not reported for this subgroup analysis.[5]

Similarly, only 14% (109/808) of patients had their docetaxel dose up-titrated to 100mg/m^2. However, treatment effect for PFS in the subgroup who did not have dose escalation, HR 0.62 (95% CI: 0.50 to 0.76), was similar to that in the subgroup who did, HR 0.65 (95% CI: 0.37 to 1.13).[3]

Subgroup analyses suggested lower efficacy in patients with non-visceral disease compared with visceral disease. There was large variability in the estimate and the sample size was small therefore the indication was not restricted to exclude these patients.[5]

At the primary analysis the proportions of patients receiving subsequent treatment for breast cancer after discontinuing the study regimen were 76% (225/298) in the pertuzumab group and 77% (260/338) in the placebo group. Patients and investigators remained unaware of treatment allocation and pertuzumab was not allowed as a subsequent breast cancer treatment. After a subsequent interim analysis of overall survival at cut-off May 2012, patients in the placebo group without disease progression could cross over to receive pertuzumab and 48 patients crossed over. At the final analysis for overall survival, 77% (258/335) and 79% (291/369) of patients initially assigned to the pertuzumab and placebo groups had received treatment after discontinuing study treatment, with 73% (188/335) and 72% (208/369), respectively, having anti-HER2 therapy. The treatments received and the pattern of use of cytotoxic agents were generally balanced between the groups.[5]

The study population contained only 19 patients with locally recurrent disease and 19 patients aged 75 years or more. Therefore, there are limited data in these groups.[3]

The addition of pertuzumab to trastuzumab and docetaxel did not appear to increase cardiac toxicity. However, it should be noted that median LVEF was 65%, and only 7.8% of the study population had LVEF of 50% to 55%. Also, only a minority of patients had been exposed to anthracyclines in the adjuvant setting.[3]

The CLEOPATRA study demonstrated benefits relative to trastuzumab plus docetaxel. There are no direct comparative data with the other standard first-line treatment of HER2-positive metastatic breast cancer, trastuzumab plus paclitaxel. Therefore, a naïve indirect comparison of docetaxel and paclitaxel in this setting was performed using data from the pivotal studies that supported the licensed indications for trastuzumab in combination with paclitaxel (H0648g) and docetaxel (M77001) in HER2-positive metastatic breast cancer.[6, 7] This was supported by data from a direct comparison of the taxanes in the adjuvant setting.[8] The assumption of similar clinical effectiveness for these treatment regimens derived from this is based on judgement, rather than analyses. Scottish clinical experts have advised that they tend to use 3-weekly docetaxel in patients with good performance status and weekly paclitaxel in patients who are less able to tolerate docetaxel, as the paclitaxel regimen appears to be associated with less severe adverse effects. The clinical

experts' responses did not indicate any perceived differences in efficacy. However, their treatment strategy appears to indicate that they prefer docetaxel where possible.

Clinical experts consulted by SMC considered that addition of pertuzumab to trastuzumab plus docetaxel represents a therapeutic advancement for patients with metastatic HER2-positive breast cancer given the size of the overall survival benefit observed in the CLEOPATRA study.

Trastuzumab can be given using an IV or a subcutaneous formulation with the subcutaneous formulation currently used routinely in clinical practice in Scotland. The summary of product characteristics for pertuzumab notes that it can be given in combination with IV or SC trastuzumab and IV docetaxel Experts noted that relative use of i-v and s-c trastuzumab might change in the future due to lower costs associated with biosimilar availability but service considerations associated with longer duration of administration for the i-v preparation would remain relevant.

Patient and clinician engagement (PACE)

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

The key points expressed by the group were:

- Secondary breast cancer is a severe and life-limiting condition. This HER2 positive subtype is aggressive with a poor prognosis. It commonly it affects women at a younger age. Disease progression results in increasingly difficult and debilitating symptoms which can have a significant effect on everyday activities, relationships and has a profound psychological impact.
- Pertuzumab significantly improves overall survival and the time gained is also of high quality. This longer response at first line delays the time to further chemotherapy which is highly valued as there would be fewer hospital visits and less reliance on carers and healthcare professionals as a result.
- Adverse effects of pertuzumab were reported as having little impact on patients' day to day lives.
- Patient groups advised that carers and families reported benefits of enabling the patient to enjoy a prolonged period of normality, where they are essentially well and can pursue a full life; returning to work, caring for families, resuming interests and social life, such family holidays and remaining fit and well for longer, contributing to society and the economy.
- The PACE group expressed very strong support for pertuzumab, describing it as a major advance. The normality of life observed in patients treated with this medicine has a wide ranging positive impact.
- The PACE group noted that there was an unmet need to maintain equity of care with other similar countries where pertuzumab is now part of standard treatment. It was highlighted that this presents a risk to the eligibility of Scottish oncology centres to participate in future

clinical studies of other new medicines, which could potentially increase inequity of care and reduce survival for Scottish patients compared with patients in other countries.

Additional Patient and Carer Involvement

We received a joint submission from Breast Cancer Care Scotland and Breast Cancer Now, which are both registered charities. Breast Cancer Care has received 0.69% pharmaceutical company funding in the past two years, including from the submitting company. Breast Cancer Now has received 10% pharmaceutical company funding in the past two years, with none from the submitting company. Representatives from Breast Cancer Care and Breast Cancer Now participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

Summary of comparative health economic evidence

The company submitted a cost-utility analysis comparing pertuzumab in combination with trastuzumab and docetaxel to trastuzumab plus docetaxel or trastuzumab plus paclitaxel, for the treatment of adult patients with HER2 positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy. SMC clinical experts confirmed the comparators were appropriate.

A partitioned survival model was used over a 25-year time horizon which included three health states: progression-free, progressed disease and death. The model used estimated parametric survival functions for both overall survival and PFS. The source of the clinical data was the CLEOPATRA study and the data from the final analysis were used in the model. [2-5] For the comparison with paclitaxel, the company assumed the results of the trastuzumab plus docetaxel arm would generalise to patients treated with paclitaxel. In order to extrapolate the clinical effects over time, the company used the log-logistic function to estimate PFS and the gamma function to estimate overall survival. The selection of these parametric functions was based on goodness of fit statistics and visual inspection of the curves.

The utility values used in the model were estimated using a statistical model from a published study. [9] This study reported the results of 100 members of the public asked to value various health states and side effects associated with metastatic breast cancer using standard gamble methodology. To estimate utility values for patients in the PFS health state, the model included a treatment-specific weighted average of the published values for stable disease and treatment response based on the response rates in the pivotal study. This resulted in PFS utility values of between 0.792 and 0.810 and a progressed disease utility value of 0.503. Disutilties due to adverse events were also included.

Medicine acquisition costs were included in the analysis along with administration and monitoring costs associated with each treatment. In terms of administration, the base case analysis assumed all patients would receive trastuzumab IV (Herceptin®) infusion in the intervention arm and the

majority (86%) would receive SC trastuzumab in the comparator arms. The company also noted that biosimilar trastuzumab IV is available and explored the impact of including this in the model in a scenario analysis. Post-progression treatments applied in the model were trastuzumab emtansine, vinorelbine and capecitabine. Health state costs for PFS and post-progression survival consisted of GP, clinical nurse specialist and community nurse contact costs. The economic model included the cost associated with grade 3 and 4 adverse events. Palliative care costs were also included.

A complex patient access scheme (PAS) was proposed by the company and assessed by PASAG as acceptable for implementation in NHSScotland. A PAS is in place for trastuzumab IV (Herceptin®) and this was included in the analysis. The base case results are presented in table 1 below.

Table 1: Base case results (with PAS)

Pertuzumab plus trastuzumab plus docetaxel vs	Incremental cost	Incremental QALYs	ICER (with PAS)
Trastuzumab plus docetaxel	£52,723	0.93	£56,521
Trastuzumab plus paclitaxel	£46,774	0.93	£50,126

PAS = patient access scheme, ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life year

The company provided both deterministic and probabilistic sensitivity analyses. The key results of the deterministic sensitivity analysis for the comparison with trastuzumab and docetaxel are presented in table 2 below.

Table 2: Key sensitivity analysis results versus trastuzumab plus docetaxel (with PAS)

Parameter	ICER (with PAS)
Duration of treatment (until progression)	£76,552
Overall survival (estimated using Gompertz)	£73,469
Time horizon (10 years)	£69,577
Utility value for PFS state reduced in both arms (0.64 for in both arms)	£68,300

PAS = patient access scheme, ICER = incremental cost-effectiveness ratio, PFS = progression-free survival

In this resubmission the company provided a scenario analysis which explored the impact of including biosimilar trastuzumab IV in the model. In this scenario analysis, the cost of trastuzumab IV (Herceptin®) was replaced with the cost of biosimilar trastuzumab IV. The analysis assumed biosimilar trastuzumab IV would be available in practice at a discounted price. In this analysis the ICER (vs trastuzumab IV plus docetaxel) was estimated to be £44,413 based on an incremental cost of £41,428 and a QALY gain of 0.93. This additional analysis is provided for information only as SMC process requires companies to use list prices or accepted PAS discount prices.

The following limitations were noted:

- It may not be appropriate to assume the administration of trastuzumab would differ in each arm of the model. The company has assumed that trastuzumab would be given as an IV infusion when used in combination with pertuzumab, whereas in the comparator arm

84% of patients are assumed to receive SC trastuzumab and 16% trastuzumab IV. As pertuzumab and trastuzumab would be administered sequentially, the argument for using trastuzumab IV seems to be largely based on the availability of biosimilar trastuzumab IV at a discounted price and the potential cost savings this may offer. However, any switch to biosimilar trastuzumab IV in practice is uncertain, likely to be associated with variation across Scotland, and would be independent of the availability of pertuzumab. SMC clinical expert responses to date have indicated that there may be variation in how trastuzumab would be administered. The company provided on request a sensitivity analysis which assumes the same mode of administration in both arms. This increased the ICERs to £60,371- £66,982 (with PAS) depending on the assumptions made regarding treatment administration costs.

- There is some uncertainty surrounding the overall survival extrapolation approach used in the base case and the validity of the overall survival estimates. The sensitivity analysis using alternative parametric functions showed that the results were not overly sensitive to most curves except using the Gompertz curve which increased the with-PAS ICER to £73,469. However, a simple comparison of median survival in the study with median survival estimated using alternative survival curves provided some support for the base case analysis where the gamma curve was used.

The Committee also considered the benefits of pertuzumab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for a substantial improvement in life expectancy was satisfied. In addition, as pertuzumab is an orphan-equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence, the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee accepted pertuzumab for use in NHSScotland.

Additional information: guidelines and protocols

The National Institute for Health and Care Excellence provides guidance on managing advanced breast cancer.[10] First-line treatment options for patients with HER2-positive advanced breast cancer include:

- Pertuzumab plus trastuzumab plus docetaxel
- Trastuzumab plus paclitaxel
- Trastuzumab emtansine in patients who have progressed within 6 months of completing adjuvant therapy.

Guidelines from the European Society for Medical Oncology and European School of Oncology were updated in 2018.[11] Anti-HER2 therapy should be offered early (as first-line) to all patients with HER2- positive advanced breast cancer, except in the presence of contraindications to the use of such therapy. Patients who have received any type of (neo) adjuvant anti-HER2 therapy remain

candidates for anti-HER2 therapies. The standard first-line therapy for patients previously untreated with anti-HER2 therapy is the combination of chemotherapy plus trastuzumab and pertuzumab, because it has proven to be superior to chemotherapy plus trastuzumab in terms of OS in this population (CLEOPATRA study). When pertuzumab is not given, first-line regimens for HER2 advanced breast cancer can include trastuzumab combined with vinorelbine or a taxane. Differences in toxicity between these regimens should be considered and discussed with the patient in making a final decision. Other chemotherapy agents can be administered with trastuzumab but are not as well studied and are not preferred.

The Scottish Intercollegiate Guidelines Network published recommendations for primary breast cancer in 2013; management of metastatic disease was outside the remit of this guideline.[12]

Additional information: comparators

Trastuzumab in combination with a taxane (docetaxel or paclitaxel)

Cost of relevant comparators

Medicine	Dose Regimen	Cost per 3-week cycle (£)
pertuzumab* trastuzumab docetaxel	**840mg, then 420mg IV every three weeks 8mg/kg, then 6mg/kg IV every three weeks 75mg/m^2, then 100mg/m^2 IV every three weeks**	**Cycle 1 = 6,858 Subsequent cycles = 4,188**
pertuzumab* trastuzumab docetaxel	**840mg, then 420mg IV every three weeks 600mg SC every three weeks 75mg/m^2, then 100mg/m^2 IV every three weeks**	**Cycle 1 = 6,614 Subsequent cycles = 4,210**
trastuzumab paclitaxel	8mg/kg, then 6mg/kg IV every three weeks 80mg/m^2 IV every week	Cycle 1 = 2,368 Subsequent cycles = 2,002
trastuzumab docetaxel	8mg/kg, then 6mg/kg IV every three weeks 100mg/m^2 IV every three weeks	Cycle 1 = 2,160 Subsequent cycles = 1,793
trastuzumab paclitaxel	8mg/kg, then 6mg/kg IV every three weeks 175mg/m^2 IV every three weeks	Cycle 1 = 2,135 Subsequent cycles = 1,768

*Doses are for general comparison and do not imply therapeutic equivalence. Costs from BNF online on 02 October 2018. Costs calculated using the full cost of vials / ampoules assuming wastage and based on 70kg body weight and 1.8m^2 body surface area. Costs do not take any patient access schemes into consideration. *Trastuzumab can be given as SC or IV formulation*

Additional information: budget impact

The company estimated there would be 245 patients eligible for treatment with pertuzumab in year 1 rising to 519 patients in year 5 to which confidential uptake rates were applied.

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.

References

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This assessment is based on data submitted by the applicant company up to and including 16 November 2018.

**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.