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ribociclib 200mg film-coated tablets (Kisqali®)  

Novartis Pharmaceuticals UK Ltd

9 February 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 NHS Scotland. The advice is summarised as follows:

**ADVICE**: following a full submission assessed under the end of life and orphan medicine process

ribociclib (Kisqali®) is accepted for use within NHS Scotland.

**Indication under review**: In combination with an aromatase inhibitor, for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer as initial endocrine-based therapy.

A phase III double-blind, randomised controlled study demonstrated that ribociclib plus an aromatase inhibitor significantly improved progression-free survival compared with aromatase inhibitor monotherapy in postmenopausal women with HR-positive, HER2-negative locally advanced or metastatic breast cancer who had not previously received systemic therapy for advanced disease.

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

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

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium
**Indication**
In combination with an aromatase inhibitor, for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer as initial endocrine-based therapy.¹

**Dosing Information**
Ribociclib 600mg orally once daily for 21 consecutive days followed by seven days off treatment, resulting in a complete cycle of 28 days. The treatment should be continued as long as the patient is deriving clinical benefit from therapy or until unacceptable toxicity occurs. The tablets should be swallowed whole (not chewed, crushed or split) and can be taken with or without food. Ribociclib should be taken with an aromatase inhibitor which is taken orally once daily continuously throughout the 28-day cycle.¹

Ribociclib should be taken with 2.5mg letrozole or another aromatase inhibitor (AI). The AI should be taken continuously.

Dose modification of ribociclib is recommended based on individual safety and tolerability. Management of some adverse events may require temporary dose interruptions, reduction or discontinuation as per dose reduction guidelines.

Complete blood counts should be performed prior to initiating treatment, every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, then as clinically indicated.

Treatment with ribociclib should be initiated by a physician experienced in the use of anticancer therapies.

See summary of product characteristics (SPC) for further details.

**Product availability date**
November 2017

Ribociclib meets SMC end of life criteria and orphan equivalent criteria for this indication.

**Summary of evidence on comparative efficacy**
Ribociclib is an oral, selective, small-molecule inhibitor of cyclin-dependent kinases (CDK) 4 and 6 that are essential to signalling pathways leading to cell cycle progression and cellular proliferation.² CDK4/6 inhibitors were developed to reduce resistance to aromatase inhibitors.¹ Most post-menopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer receive first line treatment with an aromatase inhibitor; letrozole, anastrozole or exemestane,³ but resistance develops in a large proportion of patients, reducing the effectiveness of treatment.⁴

The evidence supporting the marketing authorisation is from an ongoing phase III, double-blind, randomised, placebo-controlled study, MONALEESA-2 that recruited postmenopausal women with locally confirmed, HR-positive, HER2-negative recurrent or metastatic breast cancer who had not received prior systemic therapy for advanced disease.⁴ Disease was measurable according to
Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 or there was ≥1 predominantly lytic bone lesion. Patients had good Eastern Cooperative Oncology Group (ECOG) performance status (0 or 1) and adequate bone marrow and organ function. Patients were randomised equally, stratified according to the presence or absence of liver or lung metastases, to receive ribociclib 600mg or placebo once daily on days 1 to 21 of a 28 day cycle. All patients also received continuous treatment with letrozole 2.5mg daily. Treatment was continued until disease progression or unacceptable toxicity. The ribociclib daily dose could be reduced to 400mg or to 200mg to manage treatment-related adverse events.\textsuperscript{4}

The primary outcome was progression-free survival (PFS), assessed by the local investigator according to RECIST version 1.1 and analysed in the intention to treat population, comprising all randomised patients.\textsuperscript{4} At the initial data cut-off, after a median follow-up of 15.3 months, 36\% (243/668) of all patients had (investigator assessed) disease progression or had died; 28\% (93/334) in the ribociclib group and 45\% (150/334) in the placebo group.\textsuperscript{2, 4} The primary outcome was achieved: median PFS (Kaplan-Meier method) was not reached in the ribociclib group (95\% confidence interval [CI]: 19.3 to not estimable) versus 14.7 months (95\% CI: 13.0 to 16.5) in the placebo group; HR 0.56; (95\% CI: 0.43 to 0.72; p<0.001).\textsuperscript{4} A blinded, independent central review identified substantially fewer disease progression events than the investigators. In about 60\% of cases, progressive disease diagnosed by the investigator was not confirmed in the central review. This discrepancy was balanced between treatment arms (60\% ribociclib group and 61\% placebo group) and did not affect the HR: 0.59 (95\% CI: 0.41 to 0.85; p=0.002), which was similar to the primary analysis.\textsuperscript{2, 4}

Two updated PFS analyses have been performed; the first at a median follow-up of 20.1 months, after 297 (investigator assessed) PFS events and the second at a median follow-up of 26.4 months, after 345 (investigator assessed) PFS events.\textsuperscript{2, 5} See Table 1 below.

### Table 1: PFS results from MONALEESA-2\textsuperscript{2, 4, 5}

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ribociclib plus letrozole N=334</th>
<th>Placebo plus letrozole N=334</th>
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<tbody>
<tr>
<td>Investigator assessed PFS; median follow-up 15.3 months*</td>
<td>NE (95% CI: 19.3 to NE)</td>
<td>14.7 months (95% CI: 13.0 to 16.5)</td>
</tr>
<tr>
<td></td>
<td>HR 0.56; (95% CI: 0.43 to 0.72); p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>BIRC assessed PFS; median follow-up 15.3 months</td>
<td>22.9 months (95% CI: NE to NE)</td>
<td>NE (95% CI: NE to NE)</td>
</tr>
<tr>
<td></td>
<td>HR: 0.59 (95% CI: 0.41 to 0.85; p=0.002)</td>
<td></td>
</tr>
<tr>
<td>Investigator assessed PFS; median follow-up 20.1 months</td>
<td>22.4 months (95% CI: 20.8 to NE)</td>
<td>15.3 months (95% CI: 13.4 to 16.7)</td>
</tr>
<tr>
<td></td>
<td>HR 0.56; (95% CI: 0.44 to 0.71; p&lt;0.001)</td>
<td></td>
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<tr>
<td>Investigator assessed PFS; median follow-up 26.4 months</td>
<td>25.3 months (95% CI: 23.0 to 30.3)</td>
<td>16.0 months (95% CI: 13.4 to 18.2)</td>
</tr>
<tr>
<td></td>
<td>HR 0.57 (95% CI: 0.46 to 0.70; p&lt;0.001)</td>
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\*primary analysis; PFS=progression-free survival; CI=confidence interval; N=number; NE=not estimable; HR=hazard ratio; BIRC=blinded, independent review committee
Investigator assessed PFS benefit was observed across all predefined subgroups. These included age (<65 or ≥65 years); race (Asian or non-Asian); ECOG performance status (0 or 1); presence or absence of liver or lung metastases; bone only disease or not; newly diagnosed disease or not; previous endocrine therapy or not; previous (neo)adjuvant chemotherapy or not.\textsuperscript{4}

Results for the key secondary outcome of overall survival (OS) are not yet mature. At a median follow-up of 15.3 months (primary PFS analysis), 6.9% (23/334) of patients in the ribociclib group and 6.0% (20/334) of patients in the placebo group had died.\textsuperscript{4} Updated results at a median follow-up of 26.4 months found that 15% (50/334) of patients in the ribociclib group and 20% (66/334) of patients in the placebo group had died.\textsuperscript{5} Median OS (Kaplan-Meier estimate) was not reached (95% CI: not reached to not reached) in the ribociclib group versus 33.0 months (95% CI: 33.0 to not reached) in the placebo group; HR 0.75 (95% CI: 0.52 to 1.08; p=0.059).\textsuperscript{2}

Overall (either complete or partial) response in the ribociclib group was significantly (p<0.001) higher than in the placebo group, see table 2.\textsuperscript{4}

Table 2: Response outcomes from MONALEESA-2 \textsuperscript{4}

<table>
<thead>
<tr>
<th></th>
<th>Ribociclib + Letrozole</th>
<th>Placebo + Letrozole</th>
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<tbody>
<tr>
<td>Complete response</td>
<td>2.7% (9/334)</td>
<td>2.1% (7/334)</td>
</tr>
<tr>
<td>Partial response</td>
<td>38% (127/334)</td>
<td>25% (85/334)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>28% (95/334)</td>
<td>33% (111/334)</td>
</tr>
</tbody>
</table>

Quality of life was assessed using the standardised international instruments: European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaire core 30 (QLQ-C30), EORTC breast cancer specific quality of life questionnaire (QLQ-BR23), the five-level version of the EuroQol five-dimensional score (EQ-5D-5L) and time to deterioration of ECOG performance status.\textsuperscript{4} HRQoL (global health status/QoL score) was maintained and similar in both treatment arms. Time to definitive 10% deterioration of HRQoL was similar between treatment groups, slightly favouring the ribociclib arm, with an HR of 0.890 (95% CI: 0.67 to 1.182). No statistically or clinically relevant differences were observed for key symptoms using EORTC QLQ-C30 including fatigue, nausea and vomiting.\textsuperscript{11}

Summary of evidence on comparative safety

The rate of adverse events was similar in both treatment groups: 98% (329/334) of ribociclib patients versus 97% (320/330) of placebo patients and these were grade 3 in 66% versus 32% and grade 4 in 15% versus 0.9% of the respective groups. Adverse events considered to be treatment related occurred in 96% (319/334) of ribociclib patients versus 75% (249/330) of placebo patients. Serious adverse events were reported in 21% (71/334) of ribociclib patients versus 12% (39/330) of placebo patients; with 7.5% (25/334) versus 1.5% (5/330), respectively, considered to be treatment related.\textsuperscript{2, 4}

In the ribociclib group, 77% (257/334) of patients had an interruption of ribociclib treatment and 40% (132/334) of patients had an interruption of letrozole treatment. In the placebo group 41% (134/330) of patients had an interruption of placebo treatment and 32% (107/330) had an interruption of letrozole treatment. The dose of ribociclib was reduced in 54% (180/334) of patients and the dose of placebo was reduced in 7.0% (23/330) of patients; and this was due to adverse events in 51% (169/334) and 4.2% (14/330) of patients, respectively. Treatment was discontinued in 42% (139/334) of patients in the ribociclib group and in 54% (176/330) of patients in the placebo group; and this was due to progressive disease in 26% (87/334) and 44% (146/330) and to adverse events in 7.5% (25/334) and 2.1% (7/330) of patients in the respective groups.\textsuperscript{4}
Treatment related adverse events (incidence ≥20%), and/or (grade 3/4 treatment related adverse events [incidence ≥2%]) which were more common in the ribociclib than placebo group were: neutropenia (74% versus 5.2%, [59% versus 0.9%]); nausea (52% versus 28%, [2.4% versus 0.6%]); fatigue (36% versus 30%, [2.4% versus 0.9%]); diarrhoea (35% versus 22%, [1.2% versus 0.9%]); leucopenia (33% versus 3.9%, [21% versus 0.6%]); alopecia (33% versus 16%, [0 versus 0%]); vomiting (29% versus 16%, [3.6% versus 0.9%]); constipation (25% versus 19%, [1.2% versus 0%]); headache (22% versus 19%, [0.3% versus 0.3%]); back pain (20% versus 18%, [2.1% versus 0.3%]); rash (20% versus 8.2%, [0.9% versus 0%]); abnormal liver function test (18% versus 5.5%, [9.6% versus 2.4%]); lymphopenia (10.5% versus 2.1%, [6.9% versus 0.9%]) hypophosphataemia (4.2% versus 0.9%, [3.6% versus 0.6%]).

The European Medicines Agency identified the following as the main adverse events of special interest for ribociclib: neutropenia, anaemia, leucopenia, thrombocytopenia, nausea, vomiting, infections, diarrhoea, hepatobiliary toxicity, renal toxicity, QT corrected (QTc) interval prolongation, pulmonary embolism, reproductive toxicity.

Ribociclib tablets contain soya lecithin and should be avoided in patients allergic to peanuts or soya.

### Summary of clinical effectiveness issues

Breast cancer is the most common cancer in women. Most post-menopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer receive first line treatment with endocrine therapy, initially aromatase inhibitor monotherapy, unless the disease is imminently life-threatening or requires early relief of symptoms due to significant visceral organ involvement, in which case chemotherapy may be used. Progressive disease ultimately develops in all patients, either as early failure to respond to endocrine therapy (primary or de novo resistance) or as relapse/progression following an initial response (acquired resistance). Ribociclib is the second selective CDK inhibitor to be licensed in the UK. Palbociclib was licensed for the indication under review in 2016 and was accepted for use by SMC in 2017. Ribociclib meets SMC end of life and orphan equivalent criteria for this indication.

Clinical experts consulted by SMC considered that there is unmet need in this area as patients inevitably progress on initial endocrine therapy.

The MONALEESA-2 study demonstrated that the addition of ribociclib to letrozole produced a significant increase in PFS compared with letrozole monotherapy. The latest results (investigator assessed PFS) at median follow-up 26.4 months showed an increase of 9.3 months. In about 60% of cases, progressive disease identified by the investigator was not confirmed in central review, although this was balanced between treatment groups and did not affect the HR. OS data are still immature. Patient reported quality of life was a secondary end point; no statistically or clinically relevant differences between treatment groups were observed for key symptoms.

Clinical experts consulted by SMC considered that adding ribociclib to aromatase inhibitor treatment is a therapeutic advancement due to prolongation of PFS which would have the advantage of delaying chemotherapy and its associated toxicity.

The addition of ribociclib to aromatase inhibitors would provide an additional treatment option for patients with advanced breast cancer. The introduction of CDK inhibitors has service implications as treatment should be initiated and supervised by a physician experienced in the use of anticancer medicinal products (i.e. secondary care) unlike hormone therapy which can be managed in primary care.

The Summary of Product Characteristics provides recommendations on monitoring including complete blood counts, liver function tests, ECG (QTc interval prolongation), serum electrolytes and drug interactions e.g. with strong CYP3A4 inhibitors.
Unlike palbociclib, ribociclib is not licenced for use in pre- or peri-menopausal women or in combination with fulvestrant in women who have received prior endocrine therapy.

**Summary of 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 ribociclib, as an orphan-equivalent and end of life medicine, in the context of treatments currently available in NHS Scotland.

The key points expressed by the group were:

- Metastatic breast cancer is a chronic and progressive life-limiting disease with a median survival of less than three years and it has a very significant physical and psychological negative impact on the lives of patients and their families.
- First-line therapy is usually with aromatase inhibitor monotherapy. Subsequent endocrine treatments may be tried after failure of initial treatment, however all patients will eventually progress and will only have the option of traditional chemotherapies which have substantial adverse effects such as hair loss, vomiting and cognitive impairment.
- The combination of ribociclib plus an aromatase inhibitor, compared with aromatase inhibitor monotherapy, significantly prolongs median progression free survival by over nine months. This delay in disease progression, and therefore delay in the need for toxic chemotherapy, translates to highly valued additional quality time for patients and their families.
- Ribociclib has a manageable adverse effect profile, allowing patients to maintain a reasonable quality of life, both physically and psychologically.
- Ribociclib has the convenience of being an oral medication which can be taken at home, therefore disruption to normal life is minimised for the patient and family.
- Visits to hospital clinics are required for monitoring, so there would be some impact on the outpatient service compared with endocrine monotherapy.

**Additional Patient and Carer Involvement**

We received a joint patient group submission from Breast Cancer Now and Breast Cancer Care, both are registered charities. Breast Cancer Care has received 1.94% pharmaceutical company funding in the past two years, including from the submitting company. Breast Cancer Now has received 9.5% pharmaceutical company funding in the past two years, including from the submitting company. Representatives from both charities 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 submitting company presented a cost-utility analysis comparing ribociclib in combination with letrozole to letrozole monotherapy for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy (i.e. first-line treatment).
A state-transition approach model was used, comprising four health states. Patients entered the model in the first line progression-free survival (PFS1) health state and on progression, moved to the second line progression-free survival (PFS2) health state. From PFS2, patients moved to progressed disease. Patients could die at any time. A lifetime time horizon (40 years) was adopted. The model structure assumed any incremental gain in PFS resulted in an identical gain in OS.

Parametric distribution curves were fitted to model PFS and time to discontinuation (TTD) in the PFS1 health state. Patient-level data from the pivotal study informed the curve selections but were not modelled directly.

Second-line treatment varied between arms, with initial treatment, being a mix of:

- Everolimus plus exemestane
- Exemestane monotherapy
- Chemotherapy (capecitabine)

Usage was advised by clinical experts. Scenario analyses used the same treatment in each arm.

Patient-level data from a head-to-head study of everolimus in combination with exemestane, compared with exemestane were used to model TTD, assumed to be a proxy for PFS, and OS for these treatments. A Weibull distribution was fitted to the combination arm and a hazard ratio applied to obtain the TTD exemestane curve. Post-discontinuation survival data from TTD to death were pooled for both arms of the everolimus combination study. A Weibull distribution was fitted to the patient data.

PFS, TTD and OS for second-line chemotherapy, were modelled by applying hazard ratios to the curves for everolimus + exemestane using data from a retrospective study of patients treated with everolimus-based therapy (n=234) and with chemotherapy (n=137).

Quality of life data, using the EQ-5D instrument, were collected in the pivotal study and used to estimate the utility value for the PFS1 health state; no treatment-related disutilities were included. The value for the second PFS health state was taken from the company’s submission to SMC for everolimus in combination with exemestane, while the value for the progressed disease health state (0.505) was taken from the literature. A disutility of 0.113 for chemotherapy was applied which was also taken from the literature. Resource and cost data were provided for medicines, on-going care for breast cancer and serious adverse events except neutropenia. Resource use was based on prescribing guidelines, submissions to the National Institute for Health and Care Excellence (NICE) on this indication and clinical guidelines. Unit costs came from national databases.

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 NHS Scotland.

SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results. In addition, the company requested that the without-PAS figures to be considered as commercial in confidence material and therefore no cost-effectiveness results can be presented.
Deterministic sensitivity analyses showed ICERs were more sensitive to discount rates than any other factor. These showed the results were sensitive to a 5 year time horizon but not to a 10 year or longer time horizons. Varying the choice of curve adopted for PFS in first health state also resulted in upward sensitivity in the cost-effectiveness estimates.

The following limitations were noted:

- The model assumed the gain in PFS1 health state translated to a gain in OS. However, OS data are still immature and thus any predicted OS gain in the model is associated with uncertainty. With the PAS, removing the OS gain reduced costs in the progressed disease state for the ribociclib plus letrozole arm such that total costs were lower than those in the letrozole monotherapy arm. The QALY gain reduced, resulting in ribociclib plus letrozole dominating letrozole monotherapy.
- The extrapolated mean value of PFS in the first health state is materially higher than the mean TTD. This could result in medicine costs for ribociclib being underestimated. Additional sensitivity analysis was providing where the TTD was assumed to equal the observed PFS and this had the impact of increasing the ICER.
- The model structure is such that patients cannot move directly from first-line therapy to progressed disease. Rather all alive patients enter a second progression-free state for patients who progress on the ribociclib combination first-line. However, the results showed limited sensitivity to changes to the analysis to allow for such movements within the model.

The Committee considered the benefits of ribociclib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as ribociclib 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 modifier, the Committee accepted ribociclib for use in NHS Scotland.

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

### Additional information: guidelines and protocols

In August 2017 the National Institute for Health and Care Excellence updated its clinical guideline (CG 81): Advanced breast cancer: diagnosis and treatment. It recommends that an aromatase inhibitor be offered as first line treatment to postmenopausal women with oestrogen receptor (ER)-positive advanced breast cancer, unless their disease is imminently life-threatening or needs early symptomatic relief due to significant visceral organ involvement, in which case they should be offered chemotherapy.\(^\text{10}\)

The guideline predates the licensing of ribociclib.

### Additional information: comparators

Ribociclib is licensed for use in combination with an aromatase inhibitor (letrozole, anastrozole or exemestane). The relevant comparator is aromatase inhibitor monotherapy.
Cost of relevant comparators

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose Regimen</th>
<th>Cost per 28-day cycle (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ribociclib plus Letrozole</td>
<td>600mg once daily for 21 days in 28-day cycle plus letrozole 2.5mg once daily</td>
<td>2,954</td>
</tr>
<tr>
<td>Palbociclib plus Letrozole</td>
<td>125mg once daily for 21 days in 28-day cycle plus letrozole 2.5mg once daily</td>
<td>2,954</td>
</tr>
<tr>
<td>Letrozole</td>
<td>2.5mg once daily</td>
<td>4</td>
</tr>
</tbody>
</table>

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis, except for ribociclib from MIMS online, on 01 November 2017. Costs do not take any patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 728 patients eligible for treatment with ribociclib in year 1 rising to 1,291 patients in year 5 and assumed 70 patients would be treated in year 1 rising to 268 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.

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

6. Commercial in Confidence*

This assessment is based on data submitted by the applicant company up to and including 14 December 2017.

*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

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 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.