

## encorafenib 50mg and 75mg hard capsules (Braftovi®)

Pierre Fabre Ltd

10 January 2020

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 resubmission assessed under the end of life and orphan medicine process

**encorafenib (Braftovi®)** is accepted for use within NHSScotland

**Indication under review:** In combination with binimetinib for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Progression-free survival was significantly longer in the encorafenib plus binimetinib group compared with BRAF inhibitor monotherapy in a phase III study of patients with unresectable or metastatic BRAF V600 melanoma.

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

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

**Chairman**  
**Scottish Medicines Consortium**

## Indication

In combination with binimetinib for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.<sup>1-3</sup>

## Dosing Information

The recommended dose for commencing on encorafenib is 450mg orally once daily when used in conjunction with binimetinib.<sup>1, 2</sup>

The recommended dose of binimetinib is 45mg orally twice daily, approximately 12 hours apart. A missed dose should be omitted if the next scheduled dose is due within six hours. Capsules should be swallowed whole with water. Binimetinib can be taken with or without food.<sup>3</sup>

Due to adverse effects, treatment with encorafenib and binimetinib may require dose reduction, temporary discontinuation or permanent discontinuation. See summary of product characteristics (SPC) for information on dose modifications for adverse events.<sup>1-3</sup>

It is recommended that patients continue treatment with encorafenib and binimetinib until patients no longer derive benefit or the development of unacceptable toxicity.

Before taking encorafenib and binimetinib, patients must have confirmation of BRAF V600 mutation using a validated test. The efficacy and safety of encorafenib in conjunction with binimetinib has not been established in patients with wild-type BRAF melanoma therefore encorafenib and binimetinib should not be used in patients with BRAF wild-type melanoma.<sup>1-3</sup>

Encorafenib treatment in combination with binimetinib should be initiated and supervised under the responsibility of a physician experienced in the use of anticancer medicinal products.<sup>1-3</sup>

## Product availability date

3 October 2018

Encorafenib in combination with binimetinib meets SMC end of life and orphan equivalent criteria.

## Summary of evidence on comparative efficacy

Encorafenib is a serine/threonine-protein kinase inhibitor, suppressing serine/threonine-protein kinase (RAF)/ mitogen-activated extracellular signal-regulated kinase (MEK)/ extracellular signal-regulated kinase (ERK) pathways in tumour cells that express BRAF V600 E, D and K mutations. Binimetinib has reversible inhibitory activity on MEK1 and MEK2, which act as upstream regulators of the ERK pathway. BRAF mutations are known to activate the proliferative ERK pathway, both in melanoma and other forms of cancer. The combination of encorafenib with binimetinib (a BRAF/MEK inhibitor) inhibits these pathways, producing higher levels of anti-tumour activity.<sup>1-3</sup> This resubmission is for encorafenib in combination with binimetinib, for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation, which was previously not recommended by SMC in July 2019 (SMC2145).

The evidence supporting the efficacy and safety of encorafenib plus binimetinib comes from COLUMBUS, a multicentre, randomised, open-label, active-controlled phase III study. The study had two parts: part 1 compared encorafenib plus binimetinib with encorafenib monotherapy and vemurafenib monotherapy whilst part 2 evaluated the contribution of binimetinib to combination therapy and is not relevant to the current submission. COLUMBUS recruited adult patients with histologically confirmed locally advanced, unresectable, metastatic cutaneous melanoma, or unknown primary melanoma. Patients were required to have BRAF V600E and/or V600K mutation confirmed by central laboratory and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Both treatment naïve patients and patients who had progressed on or after first-line immunotherapy were included in the study.<sup>4,5</sup>

Patients were randomised equally to receive encorafenib 450mg orally once daily plus binimetinib 45mg orally twice daily (n=192), encorafenib 300mg orally once daily (n=194), or vemurafenib 960mg orally twice daily (n=191), and were stratified according to disease stage (American Joint Committee on Cancer [AJCC] stage IIIB, IIIC, IVM1a, IVM1b or IVM1c), performance status (ECOG score 0 or 1) and prior first-line immunotherapy use (yes or no). Encorafenib 300mg monotherapy is not a licensed treatment and will not be discussed further.<sup>4,5</sup>

The primary outcome was progression free survival (PFS), defined as the time from randomisation to the date of the first documented disease progression or death from any cause, whichever occurred first. PFS was assessed in the intention-to-treat population (ITT) which included all randomised patients, with data censored most commonly for patients who were alive without evidence of disease progression, and for patients who commenced a new antineoplastic medicine.<sup>4,6</sup>

Encorafenib plus binimetinib was associated with a significant improvement in PFS compared with vemurafenib in the ITT population. Results from the latest data cut-off (November 2018) for PFS were consistent with previously reported figures.<sup>7</sup> Table 1 presents the primary outcome results of COLUMBUS.

**Table 1. Primary outcome results of COLUMBUS in the ITT population.<sup>4, 7</sup>**

	<b>Encorafenib plus binimetinib (n=192)</b>	<b>Vemurafenib (n=191)</b>
<b>Progression-free survival (data cut-off May 2016)</b>		
Median follow-up (months)	16.7 months	14.4 months
Events (n)	98	106
Median PFS	14.9 months	7.3 months
KM estimate of PFS at 2 years	32%	24%
Hazard ratio (95% CI)	0.54 (95% CI: 0.41 to 0.71) <sup>A</sup>	
<b>Progression-free survival (data cut-off November 2018)</b>		
Median follow-up (months)	NR	NR
Events (n)	NR	NR
Median PFS	14.9 months	7.3 months
KM estimate of PFS at 2 years	37%	20%
Hazard ratio (95% CI)	0.51 (95% CI: 0.39 to 0.67) <sup>B</sup>	

<sup>A</sup> = p<0.001; <sup>B</sup> = p-value not reported; CI = confidence interval; KM = Kaplan-Meier; NR = not reported; PFS = progression-free survival

A hierarchical statistical testing strategy was applied for the key secondary outcomes of this study. When assessed by independent review, median PFS for encorafenib plus binimetinib was numerically greater compared with encorafenib 300mg monotherapy but failed to achieve statistical significance (14.9 months versus 9.6 months; HR 0.75 95% CI: 0.56 to 1.00; two-sided p=0.051).<sup>5</sup> As this analysis did not achieve statistical significance, subsequent secondary analyses in the hierarchy (Part 2 PFS analysis, interim overall survival analysis and final overall survival analysis) could not be formally tested for significant differences and are therefore presented for descriptive purposes only. Important secondary outcomes are described in Table 2. Median overall survival for encorafenib plus binimetinib and for vemurafenib was unchanged at the latest data cut-off (November 2018), resulting in an unchanged HR. Other secondary results were broadly consistent with previously reported findings (see Table 3 for secondary outcomes results from data cut-off November 2018).<sup>7</sup>

**Table 2. Descriptive analyses of secondary outcomes of COLUMBUS in the ITT population (Data cut-off May 2016).<sup>4</sup>**

	<b>Encorafenib plus binimetinib (n=192)</b>	<b>Vemurafenib (n=191)</b>
<b>Median overall survival</b>	33.6 months	16.9 months
<b>Confirmed overall response rate<sup>A</sup></b>	63%	40%
<b>Confirmed best overall response</b>		
Complete response	8%	6%
Partial Response	55%	35%
<b>Disease control rate<sup>B</sup></b>	92%	82%
<b>Median time to response</b>	1.9 months	2.1 months
<b>Duration of response</b>	16.6 months	12.3 months

A: Overall response rate includes complete response and partial response.

B: Disease control rate includes complete response, partial response, stable disease, non-progressive disease and non-complete response

**Table 3. Descriptive analyses of secondary outcomes of COLUMBUS in the ITT population (Data cut-off November 2018).<sup>7</sup>**

	<b>Encorafenib plus binimetinib (n=192)</b>	<b>Vemurafenib (n=191)</b>
<b>Median overall survival</b>	33.6 months	16.9 months
<b>Confirmed overall response rate<sup>A</sup></b>	64%	41%
<b>Confirmed best overall response</b>		
Complete response	13%	8%
Partial Response	51%	32%
<b>Disease control rate<sup>B</sup></b>	92%	81%

A: Overall response rate includes complete response and partial response.

B: Disease control rate includes complete response, partial response, stable disease, non-progressive disease and non-complete response

Various sensitivity analyses were conducted to support the primary analysis including investigator assessment, per-protocol set analysis, unstratified log-rank and Cox regression tests and “actual event analysis”. The results of these analyses were in line with the primary analysis. The results were also consistent across reasonably sized subgroups.<sup>4, 8</sup>

Health Related Quality of Life (HRQoL) was assessed using three questionnaires: Functional Assessment of Cancer Therapy-Melanoma (FACT-M), European Organisation for Research and Treatment of Cancer (EORTC) quality of life 30 item questionnaire (QLQ-C30), and the 5-level European Quality of Life 5 Dimensions questionnaire (EQ-5D-5L). At baseline, scores between treatment groups were similar for all three questionnaires. In two of the three questionnaires (FACT-M and EORTC QLQ-C30), patients’ health status scores deteriorated sooner than in the vemurafenib group compared with the encorafenib plus binimetinib group. Both treatment groups had similar results over time with the EQ-5D-5L questionnaire.<sup>4, 9</sup>

The submitting company presented Bayesian network meta-analyses (NMA) to compare encorafenib plus binimetinib with dabrafenib plus trametinib in patients with unresectable or metastatic BRAF V600 mutation-positive melanoma (seven studies in the base case network). The network also included other BRAF inhibitors (vemurafenib monotherapy, dabrafenib monotherapy, and vemurafenib plus cobimetinib) and dacarbazine. Additionally, a simple Bucher indirect comparison (ITC) was conducted comparing encorafenib plus binimetinib with dabrafenib plus trametinib via vemurafenib monotherapy. Outcomes that were assessed in the NMA included investigator assessed progression free survival, overall survival, EQ-5D change from baseline, discontinuation due to adverse events, serious adverse events, and any adverse event grade  $\geq 3$ . Results from the NMA were similar for both treatments for all assessed efficacy outcomes and safety outcomes, suggesting that encorafenib plus binimetinib is likely to be similar to dabrafenib plus trametinib.

### Summary of evidence on comparative safety

Overall the safety profile of encorafenib plus binimetinib was consistent with known safety profiles of other BRAF/MEK inhibitors and most of the reported adverse events were considered manageable.<sup>4</sup>

The safety analysis set included all randomised patients who had received at least one dose of study medication and had at least one post-baseline assessment (n=570). Overall, 98% of patients in the encorafenib plus binimetinib group reported at least one adverse event (AE) of any grade compared with 100% in the vemurafenib group. In both groups, 58% and 63% of AEs were grade 3 or 4 in severity respectively, and 34% and 37% were classed as serious AEs. Adverse events that led to treatment dose adjustment were reported in 53% of the encorafenib plus binimetinib group and 62% of the vemurafenib group. Similar numbers of study drug discontinuations related to AEs were observed in each group (15% versus 17% respectively). The safety data reported in the COLUMBUS study were comparable despite notable differences in median duration of exposure to study treatment, which was 51.2 weeks in the encorafenib plus binimetinib group compared with 26.3 weeks in the vemurafenib group. At November 2018 data cut-off, a higher number of grade 3 or 4 AEs were reported compared to previous data cut-offs; 68% in the encorafenib plus binimetinib group and 66% of the vemurafenib group experienced a grade 3 or 4 AE. Other safety outcomes were broadly consistent with previously reported results.<sup>4, 7, 8, 10</sup>

Commonly reported AEs Grade 1 and 2 reported most frequently ( $\geq 20\%$  of patients) in the encorafenib plus binimetinib group (n=192) were nausea (40%), diarrhoea (34%), vomiting (28%), fatigue (27%), arthralgia (25%), constipation (22%) and headache (20%).<sup>5</sup> The most common Grade 3 and 4 AEs (reported in  $\geq 2\%$  of patients) were increased gamma glutamyltransferase (9%), increased blood creatinine phosphokinase (7%), hypertension (6%), increased alanine aminotransferase (5%), and pyrexia (4%).<sup>5</sup>

## Summary of clinical effectiveness issues

Cutaneous melanoma is the fifth and sixth most common type of cancer in females and males respectively in Scotland, and the incidence is rising.<sup>11</sup> Ultra violet (UV) light exposure (both natural and artificial sunlight) is considered to be the main risk factor for cutaneous melanoma. It has a relatively young age distribution and often affects people of working age. About 90% of melanoma cases are diagnosed as primary tumours, with no evidence of metastasis.<sup>12</sup> These cases can be cured if recognised and treated with surgery at an early stage. However, for patients with advanced melanoma, prognosis is poor, with 5-year survival rates ranging between 40% and 80%.<sup>11, 13</sup> Recurrence rates remain high for patients with local or distant metastasis, despite surgical intervention. Approximately 45% of patients with cutaneous melanoma express a BRAF V600 mutation, and median overall survival for advanced BRAF V600 melanoma patients on current treatments (dabrafenib plus trametinib) is estimated at 26.1 months.<sup>14</sup> Current treatment options include targeted treatment in the form of BRAF and MEK inhibitors and immunotherapies. For patients in whom BRAF/MEK inhibitor is indicated, the combination of dabrafenib and trametinib is recommended.<sup>11</sup> Dabrafenib in combination with trametinib is restricted to first line use (SMC 1161/16). Comments from clinical experts consulted by SMC highlight the absence of an SMC accepted second-line targeted treatment that can be used following immunotherapy. Encorafenib in combination with binimetinib meets SMC orphan equivalent and end of life criteria.

In the COLUMBUS study, in adult patients with advanced BRAF V600 melanoma, blinded independent review committee assessment of PFS was significantly longer in the encorafenib plus binimetinib group than the vemurafenib group (median PFS 14.9 months versus 7.3 months). The European Medicines Agency (EMA) accepts PFS as a primary outcome in cancer studies provided that overall survival is also investigated as a secondary outcome.<sup>15</sup> Median overall survival data numerically favoured encorafenib plus binimetinib compared with vemurafenib (33.6 months versus 16.9 months), but could not be tested inferentially due to a failed hierarchical testing strategy. Overall survival data from COLUMBUS may have been confounded by subsequent treatments, which were received by 34% in the encorafenib plus binimetinib group and 40% of the vemurafenib group. The PFS and overall survival improvements seen in the encorafenib plus binimetinib group compared with vemurafenib were described as statistically significant and clinically meaningful by the EMA.<sup>4</sup>

COLUMBUS was an open-label study, which may have biased efficacy, safety, and patient reported outcomes. The risk of assessment bias was mitigated by the use of blinded, independent review for key primary and secondary outcomes. Sensitivity analyses were also conducted to provide further reassurance. However, the open-label design may have contributed to the higher rates of drop-out observed in the vemurafenib group. Throughout the treatment period, 15% (28/191) of the vemurafenib group dropped out of the study by physician or patient/guardian decision, compared with 8% (15/192) of the encorafenib plus binimetinib group.<sup>5</sup> The EMA felt that higher drop-out rates from the single agent treatment groups were inevitable given that current best

practice for these patients is the combination of both a BRAF and MEK inhibitor. However, the EMA accepted that at the time of study design this was not standard of care.<sup>4,5</sup>

Patients were required to have an ECOG performance status of 0 or 1 therefore it is unclear whether the results would apply to patients with a poorer performance status ( $\geq 2$ ). Additionally, the study had low numbers of patients who had previously been treated with immunotherapies. Subsequent subgroup analysis favoured encorafenib plus binimetinib in patients previously treated with immunotherapy, however confidence intervals were wide (HR 0.4 95% CI: 0.10 to 1.64) and subgroup size small (n=15). Less than 1% of the study population (3/577) had been previously treated with anti-programmed cell death protein 1 (PD1)/programmed cell death ligand 1 (PDL1) immunotherapies, and 3.3% (19/577) had previously received ipilimumab for metastatic disease. Similarly, COLUMBUS had low numbers of patients with baseline brain metastases (3.5%), potentially differing from what would be seen in Scottish practice.<sup>4,5</sup> Vemurafenib monotherapy was the key comparator in COLUMBUS part 1, however the relevant comparator in Scottish practice is considered to be dabrafenib in combination with trametinib.<sup>11</sup>

There were some relevant limitations to the NMA. The open-label design of five out of the seven studies may have been susceptible to bias, particularly in subjective outcomes such as investigator-assessed PFS, patient reported outcomes (including health-related quality of life), and adverse effects. Furthermore, differences in median length of follow up between studies may add uncertainty. Wide credible intervals may also suggest uncertainty in the results. However, on balance it would appear that the results of the NMA, and the supportive Bucher ITC, suggest that encorafenib plus binimetinib is likely to be similar to dabrafenib plus trametinib.

Clinical experts consulted by SMC considered that encorafenib plus binimetinib is an alternative option to existing BRAF/MEK inhibitor treatment. Potential to use a BRAF/MEK inhibitor after immunotherapy, as per the licensed indication, was noted. As both combinations are oral therapies, clinical experts believe that implications for the service would be low.

### 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 encorafenib plus binimetinib, as an orphan-equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Unresectable/metastatic melanoma is a severe, aggressive form of cancer that is associated with a very poor prognosis. It often leads to complex and severe symptoms as secondary tumours can spread to the brain, lung, and bones. It can also have a psychological toll, causing stress, anxiety and depression. Advanced melanoma affects a disproportionate number of

younger patients, who may be parents and/or providing care for older members of their family. The diagnosis can therefore have a considerable emotional, psychological, and financial impact on the family.

- Treatment options are limited in advanced melanoma. Encorafenib plus binimetinib would offer patients with BRAF V600 mutation another effective treatment option, and if approved for the full licensed indication would allow clinicians the flexibility to prescribe treatments according to individual clinical circumstances i.e. first-line or second-line after immunotherapy.
- Unlike some current treatments, encorafenib plus binimetinib can be taken with or without food, and does not require fasting. Fasting can be particularly challenging for some patients as they may be taking concomitant steroids which require a full stomach before ingestion. Additionally, encorafenib plus binimetinib does not require to be stored in a refrigerator, increasing convenience for patients, especially when travelling, working or spending extended periods of time away from home.
- Encorafenib plus binimetinib may offer a more favourable side effect profile than other BRAF/MEK inhibitors with respect to some side effects such as pyrexia, which has been reported less frequently with encorafenib plus binimetinib. Pyrexia can be difficult to manage and has been known to cause hospitalisations.

#### **Additional Patient and Carer Involvement**

We received patient group submissions from Melanoma UK and Melanoma Action and Support Scotland (MASScot). Melanoma UK is a registered charity and MASScot is a Scottish Charitable Incorporated Organisation (SCIO). Melanoma UK has received 8.3% pharmaceutical company funding in the past two years, with none from the submitting company. MASScot has received 2.3% pharmaceutical company funding in the past two years, with none from the submitting company. Representatives from both organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

### **Summary of comparative health economic evidence**

The submitting company presented a cost-minimisation analysis (CMA) comparing encorafenib plus binimetinib to dabrafenib plus trametinib in the licensed population. SMC clinical experts have indicated this was an appropriate comparator treatment.

The clinical evidence to support the use of a CMA was the NMA and ITC analyses described above. On the basis of the findings of these analyses, the company assumed that treatment outcomes and adverse effects would not differ between the two arms of the model and thus a CMA was appropriate. The company did provide a secondary analysis using a cost-utility analysis with quality adjusted life year (QALY) gains derived from the numerical differences estimated from the indirect comparison but the CMA was the focus of the submission and used for decision-making.

Costs in the CMA related to medicines acquisitions costs only. Treatment duration was assumed equivalent between treatments at 11.8 months based on the median duration of treatment

exposure in the COLUMBUS study and on the assumption that comparable efficacy would be achieved with an equivalent time on treatment for the comparator (which the submitting company noted was supported by clinical expert opinion). Dose intensity was assumed to be the same for each treatment (100%).

Patient access schemes (PAS) for encorafenib and binimetinib were proposed by the submitting company and accepted by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Patient access schemes are also in place for dabrafenib and trametinib.

At list prices for all medicines, the results showed no difference between the two treatment regimens (i.e. costs were identical at list price).

The results presented do not take account of the PAS for encorafenib plus binimetinib or the PAS for dabrafenib plus trametinib 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 prices for dabrafenib plus trametinib due to commercial confidentiality and competition law issues.

No sensitivity analysis was provided given the simplicity of the CMA based on medicines acquisition costs only.

There were a number of limitations noted with the analysis:

- There is no direct evidence against dabrafenib plus trametinib. Indirect comparison was necessary to support the use of the cost-minimisation analysis. As noted above, there were weaknesses and limitations with this indirect evidence but overall, it was considered a reasonable basis to conclude similar efficacy.
- The treatment duration was assumed to be the same between the arms of the model, as was the relative dose intensities of all medicines (100%). While reasonable in terms of the indirect evidence used to support the CMA, in practice there could be variations in these parameters.
- On the basis of the findings of the indirect comparison, the CMA assumed similarity of adverse events between the treatment regimens and thus no account was taken of any possible differences in the relative costs of treating adverse events in practice.

The Committee considered the benefits of encorafenib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as encorafenib is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted encorafenib for use in NHSScotland.

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

## Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published Cutaneous melanoma: A national clinical guideline (SIGN 146) in January 2017.<sup>11</sup> SIGN 146 recommends trametinib in combination with dabrafenib for patients with unresectable stage IIIC or stage IV melanoma with a BRAF V600 mutation, and recommends ipilimumab, pembrolizumab and nivolumab monotherapy or ipilimumab/nivolumab combination therapy for patients with unresectable stage IIIC and IV melanoma. SIGN 146 states that optimal choice, sequence, and combination of therapies is yet to be determined.

## Additional information: comparators

Dabrafenib in combination with trametinib is the main comparator. Immunotherapies e.g. nivolumab, ipilimumab or pembrolizumab (alone or in combination) are generally used in the second-line setting.

## Cost of relevant comparators

Medicine	Dose Regimen	Cost per 28 day cycle (£)
<b>Encorafenib and binimetinib</b>	<b>Encorafenib: 450mg once daily orally</b> <b>Binimetinib: 45mg twice daily orally</b>	<b>£10,080</b>
Dabrafenib and trametinib	Trametinib: 2mg once daily orally Dabrafenib: 150mg twice daily orally.	£10,080

*Doses are for general comparison and do not imply therapeutic equivalence. Costs from MIMS online/BNF online on 7 November 2019. Costs do not take any patient access schemes into consideration. Median duration of exposure in the encorafenib plus binimetinib group in COLUMBUS was 11.7 months.<sup>4</sup>*

## Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 89 patients in year 1 rising to 96 in year 5 and the treated patient population to be 9 patients in year 1 and 48 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 confidential.\**

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This assessment is based on data submitted by the applicant company up to and including 09 December 2019.

*\*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](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.*