

abemaciclib 50mg, 100mg and 150mg tablets (Verzenios®)

Eli Lilly and Company

5 April 2019

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 full submission assessed under the end of life process

abemaciclib (Verzenios®) is accepted for restricted use within NHSScotland.

Indication under review: For the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with fulvestrant* as initial endocrine-based therapy or in women who have received prior endocrine therapy.

SMC restriction: for use in women who have progressed on or after (neo) adjuvant endocrine therapy, or progressed during first-line endocrine-based therapy for advanced breast cancer

In a phase III randomised study in women with HR-positive, HER2-negative advanced breast cancer who had received prior endocrine therapy, abemaciclib in combination with fulvestrant significantly increased progression-free survival compared with endocrine monotherapy.

This SMC advice takes account of the benefit of Patient Access Schemes (PAS) that improve the cost effectiveness of abemaciclib and fulvestrant. 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.

* For SMC advice relating to the use of abemaciclib in combination with an aromatase inhibitor in this setting, please refer to SMC2135.

Indication

For the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with fulvestrant as initial endocrine-based therapy or in women who have received prior endocrine therapy.

Dosing Information

The recommended dose of abemaciclib is 150mg twice daily when used in combination with endocrine therapy. Please refer to the Summary of Product Characteristics of the endocrine therapy combination partner for the recommended posology.

In pre- or peri-menopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Abemaciclib is given orally at approximately the same times each day as a tablet to be swallowed whole with or without food. It should not be taken with grapefruit or grapefruit juice.

Abemaciclib should be taken continuously as long as the patient is deriving clinical benefit from therapy or until unacceptable toxicity occurs.

Abemaciclib should only be initiated and supervised by physicians experienced in the use of anti-cancer therapies. Please refer to the summary of product characteristics for further information.¹

Product availability date

October 2018

Abemaciclib meets SMC end of life criteria for this indication.

Summary of evidence on comparative efficacy

Abemaciclib is a cyclin-dependent kinase (CDK) 4 and 6 inhibitor. Oestrogen receptor induced proliferation requires cyclin D and increases with CDK 4 and 6 activity, which may promote cell cycle progression. Inhibition of CDK 4 and 6 disrupts this pathway and diminishes breast cancer cell growth. Continuous inhibition is associated with sustained growth arrest or apoptosis.²

The licensed indication for abemaciclib includes two distinct populations for use; 'in combination with an aromatase inhibitor as initial endocrine-based therapy or in women who have received prior endocrine therapy' and 'in combination with fulvestrant as initial endocrine-based therapy or in women who have received prior endocrine therapy'. This detailed advice document (DAD)

refers to the second of these populations. The first population (abemaciclib in combination with an NSAI) is covered in a separate DAD (SMC2135).

For this indication the submitting company has requested that SMC considers abemaciclib when positioned for use in combination with fulvestrant for women who have progressed on or after (neo) adjuvant endocrine therapy, or progressed during first-line endocrine-based therapy for advanced breast cancer.

Key evidence for this indication is from MONARCH 2, a double-blind, randomised, controlled, phase III study investigating the efficacy and safety of abemaciclib in combination with fulvestrant in women with HR-positive, HER2-negative advanced breast cancer. The study was conducted in women with post-menopausal status, including pre- and peri-menopausal women with ovarian function suppression, with confirmed HR-positive, HER2-negative locoregional or metastatic breast cancer not suitable for surgical resection. Patients had measurable disease or non-measurable bone-only disease as per Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1, adequate organ function and an Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 1 . Patients were required to have disease progression while receiving neoadjuvant or adjuvant endocrine therapy, ≤ 12 months after the end of adjuvant endocrine therapy, or while receiving endocrine therapy for advanced breast cancer.^{2,3}

Patients were randomised 2:1 to treatment with abemaciclib 150mg oral twice daily (n=446) or matching placebo (n=223) and were stratified by metastatic site (visceral, bone only, or other) and sensitivity to endocrine therapy (primary resistance or secondary resistance). Primary resistance required disease relapse while receiving the first 2 years of (neo) adjuvant endocrine therapy or experienced progression while receiving the first 6 months of endocrine therapy for advanced breast cancer. Patients out with the primary resistance criteria were considered as having secondary resistance.^{2,3} Patients in both groups received fulvestrant 500mg intramuscularly on days 1 and 15 of cycle 1 and on day 1 only of subsequent cycles. Assigned medicines were taken in continuous 28-day cycles and treatment was to continue until disease progression, patient withdrawal or death. Dose interruptions and reductions were permitted in accordance with the study protocol.^{2,3} The study initially randomised patients to abemaciclib 200mg twice daily, however the protocol was changed to a dose of 150mg twice daily following a review of safety data and dose reduction rates. All patients already receiving the 200mg dose had it reduced to 150mg. Patients were allowed to discontinue abemaciclib/placebo or fulvestrant and continue the other medicine.²

The primary outcome was investigator-assessed progression-free survival, defined as the time from randomisation until objective disease progression, according to RECIST version 1.1, or death in the intention-to-treat population which included all randomised patients.^{2,3} Patients were censored at the time of their last tumour assessment or the time of randomisation if baseline or post baseline assessments were missing.³ The results of the final progression-free survival analysis are presented in Table 1. PFS was significantly longer in the abemaciclib plus fulvestrant group compared with the placebo plus fulvestrant group.^{2,3}

Table 1. Final analysis of progression-free survival, the primary outcome of MONARCH 2.^{2, 3}

		abemaciclib plus fulvestrant (n=446)	placebo plus fulvestrant (n=223)
Final PFS analysis, data cut-off 14 February 2017, median follow-up 19.5 months			
PFS assessed by investigator	PFS events, n (%)	222 (50%)	157 (70%)
	Median PFS, months (95% CI)	16.4 (14.4 to 19.3)	9.3 (7.4 to 11.4)
	HR 0.55 (0.45 to 0.68), p<0.001		

PFS=progression-free survival, CI=confidence interval, HR=hazard ratio

Analyses of PFS across pre-specified subgroups were consistent with the results of the final analysis of PFS.^{2, 3} A sensitivity analysis which excluded patients who received 200mg twice daily as their starting dose of abemaciclib was consistent with the analysis in the ITT population.² Important secondary outcomes are presented in Table 2.

Table 2. Results of key secondary outcomes of MONARCH 2.^{2, 3}

		abemaciclib plus fulvestrant (n=446)	placebo plus fulvestrant (n=223)
Overall survival (OS), data cut-off 14 February 2017	OS Events, n (%)	85 (19%)	48 (22%)
	Median OS, months (95% CI)	NR	NR
	HR 0.85 (0.60 to 1.22), p=0.39		
Objective response rate, % (95% CI)		35% (31 to 40)	16% (11 to 21)
	OR 2.8, p<0.001		
Median duration of response, months (95% CI)		NR (18.05 to NR)	25.6 (11.9 to 25.6)
Clinical benefit rate, % (95% CI)		72% (68 to 76)	56% (50 to 63)
	OR 2.0, p<0.001		

OS=overall survival, NR=not reached, CI=confidence interval, HR=hazard ratio, OR=Odds ratio. Clinical benefit definition includes patients with complete response, partial response, or stable disease for 6 months or more.

The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30: diarrhoea, appetite loss, and nausea and vomiting subscales indicated patients in the abemaciclib group reported greater impact on quality of life than patients in the control group.³ The systemic therapy side effect item of EORTC QLQ-BR23 indicated that more patients treated with abemaciclib experienced adverse effects than those treated with placebo.³ For the index value and visual

analogue scale items of the EQ-5D-5L tool there was no evidence of difference between the abemaciclib and control groups in change from baseline.³

Summary of evidence on comparative safety

The median duration of exposure in the abemaciclib plus fulvestrant and fulvestrant groups were recorded as 13 and 9 months respectively. In the safety population the following were reported for patients randomised to abemaciclib plus fulvestrant (n=441) and fulvestrant (n=223) respectively: adverse events (AEs) related to study treatment 95% versus 60%, serious AEs related to study treatment 8.8% versus 1.3%, discontinued treatment due to a study treatment related AE 6.8% versus 1.8%,³ dose reductions due to AEs 43% versus 1.3% and dose interruptions due to AEs 52% versus 12%.² The most common AEs in the same groups respectively were; diarrhoea (86% and 25%), neutropenia (46% and 4%), nausea (45% and 23%), fatigue (40% and 27%), abdominal pain (35% and 16%), anaemia (29% and 3.6%), leukopenia (28% and 1.8%), and vomiting (26% and 10%).²

Antidiarrhoeals were required for the majority of patients treated with abemaciclib.⁴

Summary of clinical effectiveness issues

Breast cancer is the most common cancer in women. The expression of certain receptors, such as HR and HER-2, by breast cancer cells plays an important role in determining the therapeutic efficacy of treatments.³ Most women with HR-positive, HER2-negative advanced breast cancer receive first line treatment with endocrine therapy, with or without a CDK 4/6 inhibitor, unless the disease is considered to be imminently life-threatening or requires early relief of symptoms due to significant visceral organ involvement, in which case chemotherapy may be used. Endocrine therapy options include anastrozole, letrozole, exemestane, fulvestrant and tamoxifen.^{5, 6} The choice of first-line endocrine therapy for advanced breast cancer depends on which treatment was used in the (neo) adjuvant setting, the duration of that treatment as well as the time elapsed from the end of the (neo) adjuvant treatment. The CDK inhibitors, palbociclib and ribociclib, and everolimus are licensed for use as add-on therapies to endocrine therapies. In most patients progressive disease ultimately develops, either as early failure to respond to endocrine therapy (primary or de novo resistance) or as relapse/progression following an initial response (acquired resistance).^{3, 5} The median overall survival for advanced breast cancer is approximately 3 years,⁵ and abemaciclib meets SMC end of life criteria.

For this indication the submitting company has requested that SMC considers abemaciclib when positioned for use in combination with fulvestrant for women who have progressed on or after (neo) adjuvant endocrine therapy, or progressed during first-line endocrine-based therapy for advanced breast cancer.

In MONARCH 2 median progression-free survival was 7.1 months longer in patients treated with abemaciclib plus fulvestrant compared with fulvestrant monotherapy. The difference between treatments was statistically significant and clinically meaningful. Overall survival data are immature with an event rate of approximately 20% reported at the data cut-off for the final analysis of PFS.^{2,3}

Favourable effects on survival are the most persuasive outcome of a clinical study for an anti-cancer medicine, however prolonged progression-free survival is considered to be of benefit to the patient.⁷ In the context of advanced breast cancer, the possible benefits of improvements in progression-free survival include; a delay in the worsening of disease symptoms and a delay in the time to treatment with poorly tolerated chemotherapy.³ Diarrhoea had a meaningful adverse impact of quality of life outcomes for patients treated with abemaciclib compared with the control group in MONARCH 2.³

Over 50% of patients in MONARCH 2 were white/Caucasian and approximately 30% were Asian which is not representative of the overall Scottish population. Subgroup analyses reported similar improvements in PFS in Asian and white/Caucasian patients.^{2,3}

Many patients with advanced breast cancer receive CDK 4/6 inhibitors in combination with endocrine therapy as first line treatment. It is unlikely that patients treated with a CDK 4/6 inhibitor as first line treatment would be considered for a CDK 4/6 inhibitor as second line treatment following disease progression. The MONARCH 2 population reflects this through the exclusion of patients who had prior treatment with a CDK 4/6 inhibitor. As the proportion of patients receiving a CDK 4/6 inhibitor as first line treatment increases, it is likely the proportion of patients eligible to receive abemaciclib plus fulvestrant as a second line treatment following disease progression will decrease.

In the absence of direct evidence comparing abemaciclib with relevant comparators the submitting company presented Bayesian network meta-analyses (NMAs) for the intended population. Data from 19 studies were used to inform the networks for the following outcomes; progression-free survival, overall survival, objective response rate and clinical benefit rate. The comparators of interest were exemestane plus everolimus, fulvestrant 500mg and exemestane. The networks also included nine other treatments which are not considered to be relevant comparators for Scottish practice. The results of the NMAs were presented for each treatment relative to fulvestrant 500mg and only abemaciclib plus fulvestrant was statistically likely (had credible intervals did not include 1.0) to have an advantage over fulvestrant for progression-free survival and clinical benefit rate. Abemaciclib plus fulvestrant and exemestane plus everolimus had a statistically likely advantage over fulvestrant for objective response rate and there were likely no differences between the comparator treatments and fulvestrant for overall survival. SUCRA scores or rank probabilities were not provided. A sensitivity analysis of PFS was conducted using data for abemaciclib plus fulvestrant, exemestane plus everolimus, exemestane alone and fulvestrant alone with the results presented using abemaciclib plus fulvestrant as the reference treatment. Abemaciclib plus fulvestrant was likely to have similar efficacy to exemestane plus everolimus, and

was likely to be more effective than exemestane monotherapy and fulvestrant monotherapy. An adjusted indirect comparison was conducted to generate a relative treatment effect for tamoxifen versus fulvestrant 500mg; there was no significant difference in treatment effect for either progression-free survival/time to progression or overall survival.

Points to consider when interpreting the NMA results include; the networks included studies of treatments not considered to be relevant Scottish comparators, the impact of adding these studies to the networks is uncertain; heterogeneity between studies in terms of populations, disease characteristics, year of reporting and tumour assessments; the proportional hazards assumption did not hold for all studies included; and overall survival data from some of the studies were immature meaning firm conclusions cannot be drawn. The indirect comparison did not compare safety and health-related quality of life; this may be clinically relevant when considering the risk/benefit of the treatments.

Abemaciclib would provide clinicians and patients with an additional treatment option. It requires continuous twice daily administration, while both everolimus and exemestane require continuous once daily oral administration.

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 abemaciclib, as an end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Metastatic breast cancer is an incurable and life-limiting condition. Disease progression can cause a significant symptom burden, both physical (such as pain and fatigue) and psychological (such as anxiety and distress), which impacts on the quality of life of the patient, their carers and their family
- Abemaciclib would be the first cyclin-dependent kinase (CDK) 4/6 inhibitor routinely available in this setting. Compared with a relevant comparator it is associated with a delay in disease progression and may postpone the need for toxic chemotherapy, helping to maintain normal functioning for longer.
- Supporting patients to live independently, and contribute to social and financial aspects of family life for longer, would be greatly beneficial to the patients, carers and family.
- The adverse event profile of abemaciclib may be favourable compared to some alternative treatment options. Diarrhoea is common with abemaciclib but clinicians are familiar with managing this and other the adverse effects which are associated with CDK 4/6 inhibitors.
- Abemaciclib is an oral treatment which may support the development of new models of care delivery associated with more efficient resource use.

Additional Patient and Carer Involvement

We received a joint patient group submission from Breast Cancer Now and Breast Cancer Care Scotland, which are both registered charities. Breast Cancer Care Scotland has received 0.69% pharmaceutical company funding in the past two years, with none from the submitting company. Breast Cancer Now has received 10% pharmaceutical company funding in the past two years with none from the submitting company. A representative from Breast Cancer Now participated in the PACE meeting. The key points of the joint submission from Breast Cancer Now and Breast Cancer Care Scotland 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 abemaciclib in combination with fulvestrant with fulvestrant alone, exemestane plus everolimus, tamoxifen and exemestane alone. The company requested SMC consider abemaciclib in combination with fulvestrant when positioned for use in woman who have progressed on or after (neo) adjuvant endocrine therapy, or progressed during first-line endocrine-based therapy for advanced breast cancer. SMC clinical expert responses suggest fulvestrant and exemestane plus everolimus are the predominant treatments for these patients.

A partitioned survival model was conducted over a 25-year time horizon which included three health states: PFS, post-progression survival, and death. The model used weekly cycles and a half-cycle correction.

For the comparison with fulvestrant, clinical data were taken from the MONARCH 2 study which compared abemaciclib plus fulvestrant with fulvestrant alone. The primary outcome was investigator-assessed PFS and the results showed a significant increase in PFS with abemaciclib plus fulvestrant. Overall survival was included as a secondary endpoint but the data are immature and median survival had not yet been reached.^{2,3} For the comparisons with exemestane, exemestane plus everolimus and tamoxifen, the relative treatment effects from the NMA or adjusted indirect comparison were applied to the fulvestrant curve to provide the clinical data for these comparisons. The results of the NMAs were presented for each treatment relative to fulvestrant and only abemaciclib plus fulvestrant was statistically likely to have an advantage over fulvestrant for PFS and clinical benefit rate. Abemaciclib plus fulvestrant was likely to have similar efficacy to exemestane plus everolimus but note that the numerical differences between these treatments were included in the economic model.

The clinical data were extrapolated using parametric models fitted to the PFS and overall survival data. Goodness of fit statistics were used to assess the fit of the curves to the study data along with visual inspection and comparison of extrapolated estimates with published studies. The Weibull model was selected in the base case for PFS, overall survival and time on treatment. For overall survival, the company noted that using the Weibull distribution for the duration of the model may not be appropriate due to uncertainties regarding the long-term extrapolation of

fulvestrant and the long-term treatment effect. Therefore, in the base case analysis the Weibull distribution was used for the initial extrapolation phase, then long-term external data from the CONFIRM study were used to inform the extrapolation phase of the model beyond the maximum follow up of the MONARCH 2 study.⁸ In addition, the treatment effect of abemaciclib plus fulvestrant versus fulvestrant was assumed to taper whereby the hazard ratio gradually increased to one. Alternative extrapolation approaches and time points for tapering the treatment effect were explored in the sensitivity analysis. For the other comparisons, overall survival estimates were obtained by applying the relative treatment effects from the NMA to the fulvestrant overall survival curve.

EQ-5D-5L data were collected in the MONARCH 2 study and used in the model to estimate utility values. These data were 'cross-walked' to the EQ-5D-3L scale using a published method and then valued using the standard UK value set. However, only the pre-progression utility value was used in the model. The company argued that the post-progression utility data were not appropriate to use in the model due to the immaturity of the data and therefore the post-progression utility value was taken from a published study.⁹ The value used in the base case was 0.505, which the company noted was similar to that used in other relevant SMC and NICE appraisals.

The analysis included medicine acquisition and administration costs, best supportive care costs, follow-up care, hospitalisations, post-progression therapy, terminal care, and adverse event management costs. Medicine costs were estimated by combining the dosing regimens, relative dose intensities (RDI) and mean body surface area data. A number of post-progression treatments were included as a weighted average cost based on the proportion of patients receiving each treatment in the MONARCH 2 study, the key studies in the NMA and clinical opinion.

A patient access scheme (PAS) was proposed by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. PASs are also in place for fulvestrant and everolimus and these were included in the results used for decision-making by using an estimate of the relevant PAS prices.

SMC is unable to present the results provided by the company which used an estimate of the PAS price for fulvestrant and everolimus, or the results using the list prices of the medicines due to commercial confidentiality and competition law issues.

The following limitations were noted:

- For the comparison with fulvestrant, although direct study data show abemaciclib is superior to fulvestrant in terms of PFS, overall survival data are immature and median survival has not yet been reached. There is a trend to increased survival but there is a lack of robust evidence to support the life-year gain for abemaciclib predicted by the economic model. The company provided some sensitivity analysis to test the overall survival gain but this had little impact on the results even when survival was reduced by 50%. The company explained that this unusual result was due to the approach taken in the sensitivity analysis where only the time in the post-progression health state was reduced as the PFS data were more mature and therefore

- considered less uncertain. As this health state is associated with higher costs and lower quality of life, reducing time in this health state did not have a large negative impact on the results.
- For the comparison with exemestane plus everolimus, the clinical data are based on a NMA which had some limitations and therefore the results of this comparison are more uncertain. In addition, the NMA showed there are no statistically significant differences between abemaciclib and exemestane plus everolimus but the numerical differences were included in the model resulting in a life-year gain with abemaciclib. As noted above, additional sensitivity analysis was provided to test the overall survival gain predicted by the model.
 - Sensitivity analysis was provided where the post-progression utility value was increased from 0.505 to 0.6 and this showed the results were relatively sensitive to changes in this parameter. The utility values used in the base case are comparable to those used in previous SMC submissions in this indication, but it was also noted that the post-progression utility value based on quality of life data from the MONARCH 2 study was not used in the model.
 - The CONFIRM study was used to extrapolate survival data over the longer term as this provided long-term data on patients treated with fulvestrant. However, the patients in this study were more heavily pre-treated than those in the MONARCH 2 study. Sensitivity analysis was provided using the Weibull distribution for the duration of the model time horizon and this showed some sensitivity to using an alternative extrapolation approach.

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

*Other data were also assessed but remain 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 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.⁶ The guideline predates the availability of abemaciclib.

In 2018 the European School of Oncology (ESO) and the European Society for Medical Oncology (ESMO) produced the 4th ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer. The guideline advises that for ER-positive advanced breast cancer pre-menopausal women should have adequate ovarian function suppression or ovarian function ablation and should then be treated in line with post-menopausal women. For patients with ER-positive/HER2-negative advanced breast cancer the preferred first line treatment in the majority of case is endocrine therapy; for patients with visceral crisis of endocrine resistance other treatments are likely to be preferred. Previous therapies and response to these therapies will guide the choice of endocrine therapy, monotherapy options include; aromatase inhibitors (exemestane, letrozole, anastrozole),

tamoxifen, or fulvestrant. The guideline suggests that there is some uncertainty around the optimal role of the CDK inhibitors - palbociclib, ribociclib and abemaciclib, in clinical practice.⁵

Additional information: comparators

Fulvestrant and everolimus plus exemestane are considered the predominant comparators but exemestane and tamoxifen may also be considered as lesser comparators in this setting

Cost of relevant comparators

Medicine	Dose Regimen	Cost per year (£)
abemaciclib plus fulvestrant	abemaciclib 150mg oral twice daily plus fulvestrant 500mg intramuscular every 2 weeks for the first 3 doses, then 500mg every month	45,664
fulvestrant	500mg intramuscular every 2 weeks for the first 3 doses, then 500mg every month	7,314
everolimus plus exemestane	everolimus 10mg oral once daily plus exemestane 25mg oral once daily	34,855
exemestane	25mg oral once daily.	106
tamoxifen	20mg oral once daily	34

Doses are for general comparison and do not imply therapeutic equivalence. Costs from BNF online (abemaciclib cost from MIMs online) on 14 January 2019. Costs do not take any patient access schemes into consideration. Regimens assume maximum licensed dose for the indication is tolerated.

Additional information: budget impact

The company estimated there would be 492 patients eligible for treatment each year 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.

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

References

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This assessment is based on data submitted by the applicant company up to and including 15 February 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*

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.