Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2362

nivolumab 10mg/mL concentrate for solution for infusion (Opdivo®)

Bristol-Myers Squibb Pharmaceuticals Ltd

09 July 2021

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 and orphan equivalent medicine process

nivolumab (Opdivo®) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based combination chemotherapy.

In a phase III study, treatment with nivolumab significantly improved overall survival compared with taxane chemotherapy in patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma.

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

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

Chairman
Scottish Medicines Consortium

Indication

As monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based combination chemotherapy.[1]

Dosing Information

The recommended dose is 240mg every 2 weeks administered as an intravenous infusion over 30 minutes. Treatment should be continued as long as clinical benefit is observed or until treatment is no longer tolerated by the patient.

Dose adjustment is not recommended. Adverse effects should be managed though dosing delay or discontinuation. Please see Summary of product characteristics (SPC) for further information.

Treatment must be initiated and supervised by physicians experienced in the treatment of cancer.[1]

Product availability date

20 November 2020
Nivolumab meets SMC end of life and orphan equivalent criteria for this indication.

Summary of evidence on comparative efficacy

Nivolumab is a human monoclonal antibody that potentiates T-cell responses, including anti-tumour responses, through blockage of the programmed death-1 (PD-1) receptor binding to PD-L1 and PD-L2 ligands. PD-L1 and PD-L2 are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, engagement with PD-1 results in inhibition of T-cell proliferation and cytokine secretion. PD-L1 expression is enriched in oesophageal squamous cell carcinoma.[2, 3]

Evidence to support the efficacy and safety of nivolumab for this indication comes from ATTRACTION-3, a multicentre, randomised, open-label, phase III study. The study recruited patients aged ≥20 years with unresectable oesophageal cancer, whose major current or previously resected lesion was in the cervical or thoracic oesophagus (including the oesophagogastric junction) and was pathologically confirmed as squamous or adenosquamous cell carcinoma. Eligible patients were refractory or intolerant to fluoropyrimidine and platinum based chemotherapy, had previously received one treatment regimen and were not indicated for a radical resection. Additionally, patients had at least one measurable or non-measurable lesion per Response Evaluation Criteria in Solid Tumours (RECIST), version 1.1, had a life expectancy of at least three months and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.[2, 3]

Patients were randomised equally to receive intravenous nivolumab 240mg every two weeks (n=210) or investigators' choice of chemotherapy of either intravenous docetaxel 75mg/m^2 every three weeks or intravenous paclitaxel 100mg/m^2 once weekly for six weeks (followed by one week off). Pre-specified dose reductions were permitted for paclitaxel and docetaxel for toxicities but not for nivolumab. Treatment was to continue until disease progression as assessed by the investigator per RECIST 1.1, or unacceptable toxicity. Treatment beyond initial disease progression was permitted in both treatment groups based on the investigator's judgement. Randomisation was stratified according to location (Japan versus the rest of the world), number of organs with metastases (≤1 versus ≥2) and expression of PD-L1 (<1% versus ≥1%).[2, 3]

The primary outcome was overall survival, defined as the time from randomisation until death from any cause. A hierarchical statistical testing strategy was applied to two key secondary outcomes: investigator-assessed objective response rate (ORR) and progression-free survival (PFS), with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Efficacy analyses for overall survival and progression-free survival (PFS) were performed in the intention-to-treat (ITT) population, which included all patients who underwent randomisation. Selected secondary outcomes including ORR were assessed in the response evaluable set (RES) population which consisted of all randomly assigned patients from the ITT who are not Good Clinical Practice (GCP) non-compliant and had target lesion measurements at baseline.[3]

The primary analysis (data cut-off: November 2018) was conducted after a median follow-up of 10.5 months for the nivolumab group and 8.0 months for the control group. Nivolumab demonstrated a significant benefit in overall survival compared with taxane chemotherapy (docetaxel or paclitaxel). Key secondary outcomes were not supportive and these favoured the taxane chemotherapy group.[2, 3] Results for the primary and selected secondary outcomes are presented in Table 1.

Table 1: Primary and selected secondary outcomes from ATTRACTION-3 in the ITT and RES population at November 2018 data cut-off.[2, 3]

ITT population	**Nivolumab (n=210)**	**Docetaxel or Paclitaxel (n=209)[A]**
Median overall survival, (95% CI)	10.9 months	8.4 months
Deaths, n	160	173
Hazard ratio (95% CI)	0.77 (0.62 to 0.96), p=0.019	
KM estimated overall survival at 12 months	47%	34%
KM estimated overall survival at 18 months	31%	21%
Median PFS (investigator-assessed as per RECIST 1.1)	1.7 months	3.4 months
Number of events	187	176
Hazard ratio (95% CI)	1.08 (0.87 to 1.34)	
KM estimated PFS at 12 months, (%)	12%	7.2%
KM estimated PFS at 18 months, (%)	9.0%	4.0%
Response evaluable set population[B]	**Nivolumab (n=171)**	**Docetaxel or Paclitaxel (n=158)**

Objective response rate (investigator-assessed as per RECIST 1.1), n(%)	19%	22%
Odds ratio, (95% CI)	0.88 (0.51 to 1.50), p=0.632	
Confirmed best overall response		
Complete response (%)	0.6%	1.3%
Partial response (%)	19%	20%
Stable disease (%)	18%	41%
Progressive disease (%)	55%	32%
Not evaluable	7.6%	5.1%

ITT=intention to treat, HR=hazard ratio, CI=confidence interval, KM=Kaplan-Meier, PFS=progression free survival, RECIST= Response Evaluation Criteria in Solid Tumours. [A] Investigator's choice of docetaxel or paclitaxel[B] Response evaluable set population consisted of the ITT patients with target lesion measurements at baseline. All responses were investigator-assessed.

The lines on the Kaplan-Meier curve for overall survival cross at approximately five months and after this favour nivolumab.[3] At the latest data cut-off (May 2020) median overall survival was 10.9 months in the nivolumab group compared with 8.5 months in the control group (HR 0.79, [95% CI: 0.64 to 0.97]).[4]

Health Related Quality of Life (HRQoL) was assessed using the EuroQol 5-dimension 3-level (EQ-5D-3L) questionnaire comprising a visual analogue scale (VAS) and descriptive system, which is used to generate the utility index. The mean difference between treatment groups for the utility index and VAS, numerically favoured nivolumab at all treatment points and exceeded clinically meaningful thresholds at weeks 24, 30, 36 and 42 for the utility index and at weeks 18, 24 and 30 for VAS.[2, 3]

The submitting company presented a Bayesian network meta-analysis (NMA) to compare the efficacy of docetaxel, paclitaxel and best supportive care (BSC) in adult patients with unresectable, advanced oesophageal cancer where standard chemotherapy has failed. The NMA included four studies and compared overall survival between treatments. The results of the NMA indicated that BSC is estimated to be less efficacious than docetaxel, and paclitaxel is estimated to be more efficacious than docetaxel. The results of the NMA were used in the economic case to inform a scenario analysis comparing nivolumab with BSC.

Summary of evidence on comparative safety

Overall, the EMA noted that adverse events (AEs) reported in ATTRACTION-3 were consistent with the known safety profile of nivolumab and that the incidence of AEs and serious AEs compares favourably with chemotherapy. It was also indicated that selected AEs observed with nivolumab are often of low grade and generally manageable with immune-modulating therapy. There were two patient deaths in ATTRACTION-3 attributable to drug-related pneumonitis.[2]

In ATTRACTION-3, the median duration of treatment in the nivolumab and control group was 2.6 months. Any treatment-emergent AEs was reported by 90% (189/209) of patients in the nivolumab group and 99% (205/208) in the control group (docetaxel or paclitaxel) and these were

considered treatment-related in 66% and 95% respectively. In the nivolumab and control groups respectively, treatment-related AEs that were grade 3 or higher were 18% versus 64%, and considered serious in 16% versus 23%. The proportion of treatment-related AEs that led to dose interruptions were 16% versus 50% and treatment discontinuations were 9% in both groups.[2, 3]

The most frequently reported treatment-related AEs of any grade with an incidence >10% in the nivolumab group versus the control group were: rash (11% versus 15%), diarrhoea (11% versus 10%), decreased appetite (7.7% versus 27%), fatigue (7.2% versus 21%), malaise (4.3% versus 22%), stomatitis (2.4% versus 12%), nausea (1.9% versus 16%), alopecia (1.4% versus 47%), arthralgia (1.4% versus 10%), decreased neutrophil count (1.4% versus 36%), anaemia (2.4% versus 24%), decreased white blood cell count (1.0% versus 35%), neutropenia (0.5% versus 19%), peripheral sensory neuropathy (0.5% versus 23%), febrile neutropenia (0.0% versus 11%), peripheral neuropathy (0% versus 11%).[2, 3]

Summary of clinical effectiveness issues

Patients with unresectable advanced or metastatic oesophageal squamous cell carcinoma are considered for palliative treatment with radiotherapy (e.g. brachytherapy) or endoscopic therapies (e.g. stents) for the symptomatic relief of obstruction and dysphagia. Chemotherapy can be given to prolong survival in selected patients with good performance status. The value of palliative chemotherapy in this patient population is not well established and, therefore, best supportive care may also be considered, especially for less fit patients. A fluoropyrimidine and platinum-based chemotherapy regimen is considered an acceptable first-line option. There is no standard second-line treatment for patients that progress beyond first line and are suitable for further treatment.[2, 3, 5] Clinical experts consulted by SMC advised that taxane monotherapy, possibly further treatment with fluoropyrimidine/platinum chemotherapy or best supportive care are the treatment options most commonly used in this setting. They considered that nivolumab fills an unmet need in this therapeutic area following prior fluoropyrimidine- and platinum-based combination chemotherapy due to limited treatment options. Nivolumab meets SMC orphan equivalent and end of life criteria for this indication.

In ATTRACTION-3, nivolumab demonstrated superiority over taxane chemotherapy (docetaxel or paclitaxel) for overall survival in patients with unresectable advanced or recurrent oesophageal squamous cell carcinoma. The median overall survival gain was small at 2.5 months but was considered clinically relevant by the EMA given the poor prognosis of patients with advanced disease. Overall survival data were sufficiently mature. Kaplan-Meier overall survival curves crossed after five months, only afterwards favouring nivolumab. In general, secondary outcomes did not support the primary outcome, only duration of response numerically favoured nivolumab compared with taxane chemotherapy.[1-3]

The study population of ATTRACTION-3 was predominantly Asian (96%) which could affect generalisability of study results. Overall, the EMA concluded that Western patients with

oesophageal squamous cell carcinoma are likely to benefit from second-line nivolumab but the precise magnitude of benefit to patients has not been established.[2]

A further limitation of the generalisability of the ATTRACTION-3 study was the inclusion criteria specified that patients should have an ECOG performance status of 0 or 1. Thirty-four percent of the study population had received at least two prior systemic anti-cancer therapy regimens and approximately half received subsequent anti-cancer treatment. This may indicate that the study population is likely to be fitter than many patients seen in clinical practice.[2]

ATTRACTION-3 had an open label study design, which may have biased assessment and reporting of safety and patient reported outcomes. There were also limitations with HRQoL outcomes including lack of specificity of the EQ-5D-3L tool and thresholds to detect clinically meaningful change not pre-defined in the statistical analysis plan which may affect the validity of results.[2]

ATTRACTION-3 compared nivolumab with paclitaxel and docetaxel which are the most relevant comparators in Scottish practice. However, best supportive care (BSC) may also be a relevant option, especially for patients with poorer performance status. The NMA was associated with a number of limitations. There was no indirect comparison between nivolumab and BSC and only one outcome was included. There was considerable methodological and clinical heterogeneity that could not be adjusted for. The NMA did not represent a patient population that may be considered for nivolumab but were not fit enough for taxanes. Due to these limitations the company's conclusions are uncertain.

Clinical experts consulted by SMC considered that nivolumab is a therapeutic advancement because of the survival benefit compared with taxane chemotherapy. They indicated it would be used as a second-line treatment in patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma. The introduction of nivolumab would require patients and carers to attend hospital every two weeks for intravenous administration. Nivolumab may have additional resource implications due to frequency of administration compared with taxane chemotherapy. A more favourable toxicity profile compared with taxanes may mean fewer admissions to manage serious AEs. The number of eligible patients for this treatment will 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 **nivolumab**, 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 advanced, recurrent or metastatic oesophageal squamous cell carcinoma that has progressed after prior chemotherapy has an extremely poor prognosis. Symptoms are commonly severe and include difficulty swallowing, weight loss, vomiting, pain and

general deterioration in health, which often progresses very rapidly after diagnosis. This condition has a severely negative impact on quality of life and may cause frustration, anger, depression and social withdrawal. Patients often require intensive input from health services and support from family and carers.

- There is a significant unmet need in this patient group as treatment options are limited. Patients who are fit enough are offered further chemotherapy, likely with taxane monotherapy, however the benefit is limited and treatment is associated with debilitating side effects. Hospital admissions are required in the majority of patients to manage toxicity, which has a negative impact on quality of life, and is especially relevant in this patient population with short life expectancy.
- Nivolumab is the first immunotherapy treatment for these patients. Patients who respond are expected to have improved disease control, live longer and have improved quality of life. This would provide additional time for patients to spend with their family. PACE clinicians noted that some patients have sustained durable type responses which are entirely unprecedented in this disease and transformative to patients and their families when they occur.
- Nivolumab is well tolerated and associated with a better safety profile compared with taxane monotherapy. This will reduce treatment discontinuations and hospital admissions to manage severe toxicities, enabling patients to live and function more independently and reduce the burden of care for their families. The introduction of nivolumab is not expected to have significant service implications.

Additional Patient and Carer Involvement

We received patient group submissions from Guts UK Charity and OCHRE, which are both registered charities. Guts UK Charity has received 1.8% pharmaceutical company funding in the past two years, with none from the submitting company. OCHRE has not received any pharmaceutical company funding in the past two years. 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 company submitted a cost-utility analysis of nivolumab against taxane monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine and platinum-based combination chemotherapy. The base case analysis covered the entire disease population with no further sub-group analysis.

A partitioned survival cohort simulation model was used. The model consisted of three mutually exclusive health states; pre-progression, progressed disease (PD) and death. The cycle length was one week with patients either remaining in state, or transitioning to PD or death at the end of

each cycle. The model projected two primary outcomes –overall survival and PFS. An NHS perspective and a 40-year lifetime horizon were selected in the base case of the economic model.

The clinical effectiveness parameters for nivolumab were estimated from the most recent data-cut of the ATTRACTION-3 study[3]. This included parameters for overall survival, PFS, incidence of adverse events, treatment discontinuation, subsequent therapies and patient utilities. Outcomes data were limited to the duration of the study and as such extrapolation of overall survival and PFS was required. The hazard profile showed two distinct sections and therefore a semi-parametric approach was preferred as it allowed the most stable portion of the observed data to inform the parametric component and extrapolated portion. Switching to parametric extrapolation from 25 weeks onwards used the maximum number of events to inform long-term extrapolation and describe the lower long-term hazard.

The log-normal distribution was selected to model PFS in the nivolumab arm. This approach predicted a median PFS of 7.3 weeks and a mean PFS of 44 weeks. In order to model PFS in the taxane arm, extrapolation using the Weibull distribution provided an appropriate fit. This approach predicted a median PFS of 14.6 weeks and a mean PFS of 22.9 weeks.

For modelling overall survival on nivolumab, the log-logistic distribution was deemed appropriate as it provided an adequate fit to the data, providing a median overall survival of 47 weeks and a mean overall survival of 170.4 weeks. In order to model overall survival in the taxanes arm, the Weibull distribution was deemed appropriate as it provided an adequate fit to the data, providing a median overall survival of 35.8 weeks and a mean overall survival of 59 weeks.

Utility values were based on EQ-5D-3L data from the ATTRACTION-3 study. State specific utilities were derived but were also contingent on treatment arm. The company defended the decision to apply treatment-specific utility based on the novel mechanism of action of nivolumab. Patient-assessed quality of life data were collected with varying frequency through the study, dependent upon treatment status, which was closely associated with progression status. Imputation was required to account for missing information.

Acquisition costs for nivolumab and taxanes were included in the analysis, as were the costs associated with any subsequent treatments (i.e. BSC). Unit costs for disease management, managing adverse events, end of life care were also accounted for. Clinicians were surveyed to provide estimates of resource use associated with disease management.

A Patient Access Scheme (PAS) was submitted by the company and was assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount was offered on the list price for nivolumab.

The base case analysis (with PAS) presented by the submitting company produced an incremental cost-effectiveness ratio (ICER) of £41,201 per quality-adjusted life-year (QALY) against taxanes.

The company provided probabilistic sensitivity analysis, deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, a range of parameters were tested included time horizon, discounting rate, baseline characteristics, health state costs, BSC costs, utility values and adverse event probabilities.

The company also conducted scenario analyses to test the impact of alternate survival extrapolations, stopping rules and using BSC as a comparator. Table 2 below contains some of the results from scenario analyses.

Table 2: Selected scenario analysis for the ITT and market authorisation populations

	Scenario	**ICER**
	Base case	£41,201
1	PFS nivolumab – Weibull extrapolation	£42,025
2	OS nivolumab – Generalised Gamma extrapolation	£48,681
3	OS taxanes – Log logistic extrapolation	£49,262
4	Time on treatment nivolumab - Log logistic extrapolation	£47,628
5	2 year stopping rule - nivolumab	£36,601
6	Nivolumab cessation at progression	£17,069
7	BSC comparator	£38,427
8	Alternate utility values – MCAR	£42,099
9	Alternate utility values – equal post-progression utility	£49,725
10	Hospitalisation costs based on full length of stay	£56,097

Abbreviations: ICER, incremental cost-effectiveness ratio; PFS, progression free survival; OS, overall survival; MCAR, missing completely at random

There were some limitations with the analysis which include the following:

- The greatest source of uncertainty in the model concerns treatment discontinuation. The base case analysis assumed that patients would continue on nivolumab until the occurrence of adverse events. However, alternate stopping rules may be preferred in clinical practice. The company explored the impact of a two-year stopping rule, as well as discontinuing nivolumab upon progression. Both scenarios led to a reduction in ICERs compared to the base case due to lower expenditure on nivolumab. However these scenarios assume that earlier treatment discontinuation has no impact on treatment effect and this may not necessarily be the case. Hence, an accurate ICER estimate for nivolumab will be contingent on preferences or guidelines for treatment discontinuation in clinical practice, but it must also account for potentially lower treatment effect because of their application.
- There are concerns about the face validity of PFS gains predicted by model when compared to study results. Median PFS was lower for nivolumab (1.68 months compared with 3.35 months), as was the overall response rate (19.3% compared with 21.5%). However, the model predicts a much larger gain in mean PFS. It is not clear what is driving the PFS gains in the model. The company has since provided some reassurance that the PFS gains predicted by the model are consistent with observed results. Whilst median PFS for nivolumab was lower, PFS at 12, 24, and 36-month time points was superior to taxanes. The company also highlighted that immunotherapy agents, such as nivolumab, often show delayed clinical responses.

- There remains some residual uncertainty about the validity of survival extrapolations. The application of some alternative and plausible overall survival curves and time on treatment extrapolations had an upward impact on the ICER. However, the company has used the most recent data cut providing evidence up to 36 months and their rationale for employing a semi-parametric model was satisfactory.
- The company estimated treatment-specific utilities before and after progression using a statistical model fit to EQ-5D data from the clinical study. Missing values were imputed under the assumption that they were missing at random. Both pre-and post-progression utility on nivolumab was substantially higher than that of taxanes. Much of this difference, particularly in the PFS state, can be explained by the better tolerability and adverse event profile of nivolumab. However, one might expect the difference in utility values post-progression to be narrower. Following NDC, the company provided additional validation of the treatment-specific utility values observed in the study.
- The model potentially underestimates the cost of inpatient treatment, which would have a significant upward influence on the ICER. The company's estimate for the cost of each episode of hospitalisation was £534. However, this estimate reflects an adjustment to the cost of hospitalisation being based on one bed day rather than the entire length of stay. The cost of hospitalisation based on entire length of stay is £3,380, which increases the ICER substantially. Whilst the higher cost is likely an overestimate, it is worth acknowledging that variation in hospitalisation costs in practice will influence the cost-effectiveness of nivolumab.
- There is a lack of robust evidence comparing nivolumab with BSC. BSC might be a relevant comparator in some cases in clinical practice. Whilst the company has provided a scenario analysis that includes BSC, the relative efficacy is based on the results of a weak NMA, which does not provide reliable results.

The Committee considered the benefits of nivolumab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as nivolumab 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 nivolumab for use in NHSScotland.

Additional information: guidelines and protocols

National Institute for Health and Care Excellence (NICE) published guidelines titles 'Oesophago-gastric cancer: assessment and management in adults' in 2018. These guidelines recommend that second-line palliative chemotherapy or a clinical trial should be considered for patients with locally advanced or metastatic oesophago-gastric cancer. No specific chemotherapy regimens are recommended.[6]

The European Society of Medical Oncology (ESMO) published guidelines titled 'Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up' in 2016. This guideline states that for patients with advanced and/or metastatic disease, palliative treatment with chemotherapy is indicated in select patients, particularly for patients with adenocarcinoma who have a good performance status. Platinum and fluoropyrimidine combinations are recommended, taxanes are also recommended in first-line combinations or as monotherapy in second-line therapy. In squamous cell carcinoma, the value of palliative chemotherapy is less evidenced and the guidelines state that best supportive care or palliative monotherapy should also be considered.[5]

Additional information: comparators

Taxane chemotherapy (potentially docetaxel) or best supportive care.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost for 12 weeks
Nivolumab	240mg every 2 weeks	£15,798

Costs from BNF online on 31 March 2021. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The company estimated there would be 18 patients eligible for treatment with nivolumab in year 1 rising to 25 in year 5. The estimated uptake rate was 53% in year 1 and 73% in year 5. This resulted in 9 patients estimated to receive treatment in year 1 rising to 18 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.**

References

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

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

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

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a

patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.