Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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obeticholic acid, 5mg and 10mg film-coated tablets (Ocaliva®)

SMC No (1232/17)

Intercept Pharma UK & Ireland

05 May 2017

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 Scotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan medicine process

obeticholic acid (Ocaliva®) is accepted for use within NHS Scotland.

Indication under review: primary biliary cholangitis (also known as primary biliary cirrhosis) in combination with ursodeoxycholic acid in adults with an inadequate response to ursodeoxycholic acid or as monotherapy in adults unable to tolerate ursodeoxycholic acid.

In a randomised, double-blind, phase III study of patients with early stage primary biliary cholangitis and poor response or intolerance to ursodeoxycholic acid, treatment with obeticholic acid (+/- concomitant ursodeoxycholic acid) was associated with a greater biochemical response rate at 12 months when compared with placebo.

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

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

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

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Indication

For the treatment of primary biliary cholangitis (also known as primary biliary cirrhosis) in combination with ursodeoxycholic acid in adults with an inadequate response to ursodeoxycholic acid or as monotherapy in adults unable to tolerate ursodeoxycholic acid.[1]

Dosing Information

The starting dose is 5mg once daily. Based on the assessment of tolerability after six months, the dose should be increased to 10mg once daily to achieve optimal response. No dose adjustment of concomitant ursodeoxycholic acid is required in patients receiving obeticholic acid.

Obeticholic acid should be taken orally, with or without food.

Refer to the summary of product characteristics for dosage advice in relation to managing pruritus, drug interactions and in patients with moderate or severe liver disease.[1]

Product availability date

January 2017.
Obeticholic acid meets SMC orphan criteria
Obeticholic acid has conditional marketing authorisation from the European Medicines Agency.

Summary of evidence on comparative efficacy

Primary biliary cholangitis (PBC) is a rare, serious, life-threatening liver disease characterised by cholestasis with progressive impairment of bile flow in the liver that results in increased hepatocellular bile acid concentrations which are toxic.[2] Obeticholic acid is a selective and potent agonist for the nuclear farnesoid X receptor (FXR), a key regulator of bile acid inflammatory, fibrotic, and metabolic pathways, which is expressed at high levels in the liver and intestine. Activation of FXR limits the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.[1, 2]

The key evidence for obeticholic acid in the management of PBC is the POISE study. This randomised, double-blind, multi-centre, phase III study recruited adults with a definite or probable diagnosis of PBC (as per American and European liver disease guidelines) and with biochemical derangement (alkaline phosphatase [ALP] ≥1.67 times the upper limit of normal [ULN], and/or total bilirubin between one and two times the ULN). Patients were required to have taken ursodeoxycholic acid for at least 12 months at a stable dose for at least three months, or they were intolerant to ursodeoxycholic acid. Patients with clinical complications of PBC or significant hepatic decompensation, including history of liver transplantation were excluded.[3]

Patients taking ursodeoxycholic acid at baseline, continued at their stable dose of 13 to 15mg/kg/day. Patients were randomised in 1:1:1 ratio to once-daily obeticholic acid 10mg (n=73), obeticholic acid titration (n=71), or placebo (n=73) for 12 months. The titration group commenced on obeticholic acid 5mg for six months; patients who did not meet the biochemical response

(composite primary outcome) and were tolerating treatment were eligible to be titrated to 10mg daily for the next six months of the study. The titration group represents the licensed dosing for obeticholic acid. Randomisation was stratified for intolerance to ursodeoxycholic acid (yes or no), and according to Paris I risk criteria (ALP >3xULN, and/or aspartate aminotransferase level >2xULN, and/or a total bilirubin >ULN).[3]

The primary outcome was the biochemical composite end point of ALP<1.67xULN with a concomitant reduction of at least 15% from baseline, and total bilirubin ≤ULN at 12 months, and this was assessed in the intention-to-treat population (all randomised patients who had received at least one dose of treatment). The primary analysis was the comparison of obeticholic acid 10mg (fixed-dose) versus placebo. Both obeticholic acid dosage schedules were associated with significantly greater proportions of patients meeting the primary endpoint when compared with placebo (p<0.001 for both comparisons); 46%, 47% and 10% in the obeticholic acid titration group (licensed dose), fixed-dose group and placebo groups, respectively.[2, 3]

A number of secondary outcomes planned within the study investigated either biochemical markers for liver disease/inflammation, or non-invasive tests for liver fibrosis. Compared with placebo, obeticholic acid (titration group) was associated with statistically significant reductions from baseline in ALP, gamma-glutamyl transferase, transaminases (AST and ALT), and bilirubin levels at six and twelve months. No statistically significant differences between treatment groups were observed for changes from baseline in albumin, international normalised ratio or in prothrombin time although these markers for liver synthesis were not deranged at baseline. There was no significant difference between obeticholic acid (titration group) and placebo for the liver fibrosis outcomes (transient elastography measured by Fibroscan device, and enhanced liver fibrosis score).[3] Biochemical response criteria have been developed to support the prediction of long-term clinical outcomes and disease prognosis; response rates for obeticholic acid (titration group) and placebo are presented in Table 1. Within the economic case presented to SMC, low-risk of disease progression was attributed to meeting the Mayo II criteria.

Table 1: Alternative biochemical response criteria response rates.[2]

Response criteria	**Response rates at month 12, %**		**odds ratio (CI)**
	obeticholic acid (titration group)	**placebo**	
Paris I ALP≤3xULN AST≤2xULN Total bilirubin ≤ULN	64%	18%	9.4 (2.8 to 31.0)
Paris II ALP≤1.5xULN AST≤1.5xULN Total bilirubin ≤ULN	27%	4.1%	9.1 (2.5 to 32.6)
Mayo II ALP≤1.67xULN Total bilirubin ≤ULN	46%	15%	5.7 (2.5 to 13.1)
Toronto II ALP≤1.76xULN	51%	16%	7.2 (3.0 to 17.2)

Rotterdam Total bilirubin ≤ULN Albumin ≥ lower limit of normal.	17%	5.9%	4.3 (0.3 to 58.8)

ALP = alkaline phosphatase, AST = aspartate aminotransferase, ULN = upper limit of normal, CI = confidence interval.

Patient reported outcomes investigated pruritus via a visual analogue scale and with a validated questionnaire (5-D) that evaluated five specific dimensions of pruritus (degree, duration, disability, distribution and direction). At month 12 there was no difference between the groups for the pruritus visual analogue scale and the 5D questionnaire, although overall a greater proportion of patients in the obeticholic acid group reported pruritus when compared with placebo (56% [39/70] versus 38% [28/73], respectively).[3]

Patients also completed the PBC-40, a validated 40-item questionnaire covering six domains: fatigue, itch, general symptoms, emotional, social, and cognitive function. There was no significant difference between the treatment groups for any of the six PBC-40 domains.[3]

A long-term, open-label, follow-up phase (up to five years) was offered to all eligible patients who completed the 12-month double-blind phase of the study. All patients continuing on the long-term safety extension (LTSE) study were given obeticholic acid 5mg daily with titration at three-monthly intervals of 5mg/day according to tolerability and response, to a maximum of 25mg per day (unlicensed dose titration schedule). Of the 198 patients who completed the double-blind phase, 97% (193/198) entered the open-label extension. A durable response (in terms of sustained reductions in ALP and total bilirubin) through two years of treatment was observed in patients originally randomised to obeticholic acid. In the patient group originally assigned to placebo reductions in ALP and total bilirubin were observed upon initiation and titration of obeticholic acid.[3]

Summary of evidence on comparative safety

During the double-blind phase of the POISE study, the proportion of patients experiencing an adverse event that was considered to be possibly, probably or definitely related to treatment was higher in the obeticholic acid titration group than in the placebo group (60% [42/70] and 52% [38/73] respectively). Discontinuation from the study due to an adverse event was infrequent, and occurred in 7.1% (5/70) of obeticholic acid titration group patients and in 2.7% (2/73) of placebo patients.[2]

The majority of treatment-emergent adverse events across treatment groups were mild or moderate in severity, however a higher proportion of patients randomised to the obeticholic acid titration group experienced severe adverse events compared with patients randomised to placebo (31% and 12%, respectively), a difference largely attributable to pruritus. Treatment-related pruritus was recorded for 50% (35/70) of patients in the obeticholic acid titration group compared with 37% (27/73) of patients in the placebo group. Discontinuation due to pruritus was reported in one patient in the licensed obeticholic acid group.[2]

Serious adverse events occurred in a greater proportion of patients randomised to the obeticholic acid titration group compared with the placebo group (16% and 4.1%, respectively); these were mainly associated with disease and none were considered related to obeticholic acid treatment.[2, 3]

The safety profile that was observed with obeticholic acid during the open-label extension was similar to that in the double-blind phase.[3]

Summary of clinical effectiveness issues

PBC is a rare disease which progresses slowly, complications of which include hepatic fibrosis, cirrhosis, decompensation and eventually death. Advanced PBC is a common indication for liver transplantation. Symptoms of PBC include pruritus and fatigue. Biochemical disturbance is seen with elevated ALP in early disease, with raised bilirubin and transaminases as hepatocellular damage increases..[2, 4] Obeticholic acid is a designated EMA orphan medicine so meets SMC orphan criteria.

There are limited treatment options for patients with PBC; currently ursodeoxycholic acid is the only medicine licensed for this rare disease. Ursodeoxycholic acid is the standard first-line treatment for PBC. Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area, namely a lack of treatment options when ursodeoxycholic acid is either not tolerated or sufficiently effective.

The POISE study provided comparative data against placebo for 12 months of treatment. Obeticholic acid was associated with a greater biochemical response rate compared with placebo. The primary outcome was a surrogate marker for disease severity and prognosis. Data of ursodeoxycholic acid use in PBC suggests that ALP and total bilirubin are associated with disease progression and lower levels of these markers are associated with liver-transplant-free survival. The levels for response used in the composite outcome were extrapolated from two PBC cohorts. The outcome measures were considered acceptable by the European Medicines Agency (EMA). Obeticholic acid, compared with placebo, was not associated with any symptomatic benefit as measured by the disease-specific PBC-40 questionnaire.[2, 3]

The POISE study was not designed to measure relevant direct health outcomes such as liver transplant, decompensation or death; sufficient events for a meaningful comparison were unlikely within the 12-month timeframe of the study given the rate of disease progression associated with PBC. The EMA has asked for this limitation in the evidence base to be addressed through a phase III study investigating clinical outcomes (expected to be completed in 2023) as part of the conditional marketing authorisation for obeticholic acid.[2] Meta-analysis of long-term cohort studies of patients with PBC suggests that ALP and bilirubin levels are predictive of transplant-free and overall survival with ALP<2x ULN and Bilirubin ≤1x ULN associated with better patient outcomes. This was observed in patients whether they were treated with ursodeoxycholic acid or not.[5]

POISE recruited patients with relatively early-stage disease; those with clinical complications of PBC or significant hepatic decompensation were excluded from the study. Effectiveness of the medicine in patients with more advanced disease is uncertain. A phase IV study of patients with moderate or severe hepatic impairment is a requirement of the EMA's conditional marketing authorisation.[2]

The majority of patients recruited to POISE took study treatment (obeticholic acid or placebo) in combination with ursodeoxycholic acid (93%); evidence for obeticholic acid monotherapy (ie in ursodeoxycholic acid intolerant patients) is limited.[3]

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 obeticholic acid as an orphan medicine, in the context of treatments currently available in NHS Scotland

The key points expressed by the group were:

- PBC is an incurable autoimmune condition primarily affecting the liver. Symptoms include chronic fatigue, pruritus, joint and bone pain. Both physical symptoms and the psychological aspect of living with the disease can adversely affect quality of life, impact being greater in patients in whom ursodeoxycholic acid is ineffective. Life expectancy for patients with untreated PBC is approximately ten years.

- As PBC progresses to end-stage liver disease, patients experience a range of serious complications and a proportion of patients require a liver transplant with associated high patient and carer burden.

- Obeticholic acid addresses an unmet need for patients in whom there are no other treatment options. PACE participants highlighted high correlation between surrogate biochemical markers and long-term clinical outcomes; obeticholic acid is therefore expected to delay disease progression, delay / avoid the requirement for liver transplantation, and improve life expectancy.

- Slowing the progression of PBC has a positive impact on patient quality of life with respect to engagement with work, family, friends, and wider society. In addition, patients are less dependent on their family and carers.

- Anecdotal evidence from patients indicates that pruritus associated with obeticholic acid has minimal impact and normalises over time.

- PACE participants also noted that minimising liver transplantation from PBC would result in more donor livers being available for transplantation in patients with other conditions.

Additional Patient and Carer Involvement
We received a patient group submission from the PBC Foundation, which is a registered charity. The PBC Foundation has received 8% pharmaceutical company funding in past two years, including from the submitting company. A representative from the PBC Foundation participated in the PACE meeting. The key points of the submission have been included in the full PACE statement.

Summary of comparative health economic evidence

The submitting company provided a cost-utility analysis using a Markov state-transition model structure comparing obeticholic acid tablets titrated from 5mg to 10mg, given daily, in two subsets of patients with primary biliary cholangitis (PBC) who have failed to show adequate control with ursodeoxycholic acid: patients with inadequate response to ursodeoxycholic acid, and ursodeoxycholic acid intolerant patients. For patients with inadequate response to ursodeoxycholic acid, the analysis consisted of a comparison of obeticholic acid + ursodeoxycholic acid vs. ursodeoxycholic acid alone and for patients intolerant to ursodeoxycholic acid the analysis consisted of a comparison of obeticholic acid vs. no treatment (placebo). A lifetime horizon was adopted with a mean starting age in the model cohort of 56 years, based on the POISE study.

Effectiveness data for obeticholic acid in the model, for the two patient populations who had failed on ursodeoxycholic acid or were intolerant to ursodeoxycholic acid, were taken from POISE a 12-month multi-centre, phase III, randomised, double-blind, placebo-controlled study. POISE long-term safety extension (LTSE) was also used as evidence to support long-term clinical effectiveness.

Patients entered the model in either a PBC moderate or high risk of liver disease health state defined by surrogate biochemistry markers of ALP and bilirubin, with the high risk state also covering compensated cirrhosis. Transition probabilities between these health states and a low risk state were calculated for each three-month cycle for the first year only. Obeticholic acid patients could move to a low risk state, but ursodeoxycholic acid or no treatment comparator patients could only move to a high risk health state on the grounds that these patients entered the study as being inadequately controlled on ursodeoxycholic acid so would not be expected to move to a better health state. Due to the low patient numbers who received obeticholic acid monotherapy, the same transition matrices were used for the ursodeoxycholic acid intolerant patient population as for the ursodeoxycholic acid inadequate responders. Obeticholic acid regimen transition probabilities were taken from individual patient data in the POISE study but transition probabilities for the ursodeoxycholic acid alone comparator or no treatment (placebo only) comparator were based on global and UK observational data on disease progression in PBC patients, and other studies identified in the literature.[6, 7] Patients in the PBC high risk state experienced a probability of liver disease related outcomes of decompensated cirrhosis (DCC), a pre-liver transplant state (with follow-on probabilities of being in liver transplant and post liver transplant states), hepatocellular carcinoma (HCC) and liver related mortality, and probabilities of transitioning from DCC to pre-liver transplant, DCC to HCC, and risk of PBC re-emergence post liver transplant. The extrapolation was performed over a 44-year lifetime horizon, with the transition probabilities based on the observational data and various published sources, including those relating to hepatitis C virus (HCV).

No utility estimates specific to PBC were available for each health state, hence values from a published study in cholestatic disease for low and moderate risk states,[8] and for other health states a previous National Institute for Health and Care Excellence Single Technology Appraisal in HCV were used,[9] with an additional decrement applied to some of the health states based on expert clinical opinion that PBC has a larger impact on health-related quality of life than HCV for the same health states. The decrement was applied to the following states: DCC, pre-liver transplant, post-transplant. No disutility was applied for adverse events.

Medicine acquisition costs for both obeticholic acid and ursodeoxycholic acid were incorporated into the analysis, with administration costs omitted due to both being administered orally. Treatment was assumed to be continuous unless patients discontinue due to adverse events or other reasons. Other resource use, included outpatient appointments and follow-ups, blood tests, and the cost of treating the adverse event pruritus have been included.

A patient access scheme was submitted by the company and 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 price of the medicine. The corresponding base case incremental cost per quality adjusted life year (QALY) gained with the PAS discount for obeticholic acid and ursodeoxycholic acid vs. ursodeoxycholic acid alone in inadequate responders to ursodeoxycholic acid were £28,821/QALY and for the comparison of obeticholic acid vs no treatment in ursodeoxycholic acid intolerant patients were £21,821/QALY respectively, with incremental costs of £158k and £143k respectively, and incremental QALYs of 5.50 and 6.59 respectively. The results associated with key scenario and sensitivity analyses presented in the company submission or provided in response to requests are presented in Table 2.

Table 2: Results with PAS for obeticholic acid

Analysis	**Obeticholic acid vs. ursodeoxycholic acid in ursodeoxycholic acid inadequate responders**	**Obeticholic acid vs. no treatment in ursodeoxycholic acid intolerant patients**
Base case ICER	£28,821	£21,695
Scenario analysis: allowing PBC progression after 12 months in patients receiving obeticholic acid (9% probability of transitioning to high risk PBC over 15 years)	£31,068	£23,042
Scenario analysis: Using POISE data for ursodeoxycholic acid transition probabilities	£33,598	N/A
Sensitivity analysis: Simultaneous ±20% for all transition probabilities for PBC low, moderate and high risk states	£26,279 - £32,490	£20,373 - £23,667
Sensitivity analysis: Simultaneous ±20% for all transition probabilities for liver transplant/disease outcomes	£28,635 - £28,993	£21,623 - £21,735
Scenario analysis: No PBC adjustment of liver disease related utilities	£29,581	£22,455

The model structure appears appropriate. However, there are a number of limitations and uncertainties in the economic analysis:

- The modeling requires extrapolation of a single year of trial data over a long time horizon of 44 years. As such there is a high degree of inherent uncertainty associated with long term extrapolation based on surrogate markers and the use of a variety of published studies for the liver disease related outcomes. The probabilities of liver disease clinical events and death are applied 3-monthly for the whole model duration with large numbers of avoided liver transplants, DCC, HCC and liver related deaths predicted for obeticholic acid over the lifetime due to a much higher proportion of patients remaining in the PBC low- to -moderate risk states, translating to large life years and QALY gains estimated. This shows the key driver in the model is the lower probability relative to the comparators of being in the high- risk of progression state for the obeticholic acid patients but the extrapolation to the large long run clinical benefits is highly uncertain based on short term surrogate marker data.
- There are limited data for the comparison of obeticholic acid monotherapy versus no treatment (only 16 patients in POISE), and therefore an assumption is made that the transition probabilities for ursodeoxycholic acid inadequate responders analysis from POISE for obeticholic acid + ursodeoxycholic acid applies to obeticholic acid monotherapy in ursodeoxycholic acid intolerant patients, which is uncertain. The transition probabilities for no treatment are from a published study in PBC patients but relates to fibrotic and non-fibrotic/cirrhosis states that had to be assumed to be generalisable to compensated cirrhosis (CC) and DCC states in the model.
- The assumption that no more obeticholic acid patients can progress to the high risk state and hence be at risk of liver disease and transplants after 1 year is based on long run safety data from POISE, but is uncertain. The company was unable to use the long term data for obeticholic acid directly in the model due to patient- level data being not available. The company did however explore a scenario in which the transition from low and moderate risk PBC states was amended from 0% after 12 months for obeticholic acid to a 9% probability of transitioning to high risk of liver disease over a 15 year timeframe based on evidence in ursodeoxycholic acid responders. This resulted in an estimated ICER with PAS of £31,068/QALY in ursodeoxycholic acid inadequate responders, and £23,042/QALY in patients intolerant to ursodeoxycholic acid (Table 2).
- The transition probabilities for the ursodeoxycholic acid alone comparator in ursodeoxycholic acid inadequate responders were based on a calibration process using up to 20-year retrospective observational data in approximately 5,000 PBC patients. The company was also asked to perform a scenario analysis in which POISE data was used directly to estimate transition probabilities for the ursodeoxycholic acid comparator. This resulted in an estimated ICER of £33,598/QALY with PAS (Table 2).
- There was no consideration of disutilities associated with adverse events. Pruritus was considered to be the main adverse event incurring a cost, but a disutility has not been applied for this. The company claimed the impact on quality of life would be negligible. The company also provided additional scenario analyses reducing utility whilst on the pre-transplant waiting list over time, but this had only a small impact on the ICERs.
- A range of further scenario analysis including shorter time horizons and varying transition probabilities simultaneously was requested from the company to more fully explore the impact on the ICERs of uncertainty in translating short term surrogate outcome data into long run liver disease related events avoided. Using a 30 year time horizon, the ICERs increased to £29,671 with PAS in inadequate responders and £21,920 in patients intolerant to ursodeoxycholic acid; no shorter time horizons were considered. The impact of varying transition probabilities simultaneously by ±20%, is shown in table 2.

The Committee also considered the benefits of obeticholic acid in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for the absence of other treatments of proven benefit was satisfied. In addition, as obeticholic acid is an orphan medicine, SMC can accept greater uncertainty in the economic case.

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

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

Additional information: guidelines and protocols

The European Association for the Study of the Liver (EASL) Clinical Practice Guidelines for Management of cholestatic liver diseases, published in 2009 recommends ursodeoxycholic acid at 13 to 15mg/kg/day as the first-line pharmaco-therapy in all patients with PBC. If tolerated treatment should be lifelong. The guideline notes that there is no consensus on how to treat patients with a suboptimal biochemical response to ursodeoxycholic acid.[10] Revised guidelines from EASL published in April 2017 suggests obeticholic acid may be considered for use in accordance with its conditional marketing authorisation.[11]

Additional information: comparators

None.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
obeticholic acid	**5mg or 10mg orally once daily**	**£29,006**

Cost from eMC dictionary of medicines and devices browser. Cost does not take any patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 339 patients eligible for treatment with obeticholic acid in all years. The estimated uptake rate was 9% in year 1 (22 patients) rising to 59% in year 5 (139 patients) with a discontinuation rate of 30% applied in each year.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

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

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This assessment is based on data submitted by the applicant company up to and including 27 April 2017.

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

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These

contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a drug and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG, established under the auspices of NHS National Services Scotland reviews and advises NHS Scotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

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

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