Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2399

# pemigatinib 4.5mg, 9mg, and 13.5mg tablets (Pemazyre®)

Incyte Biosciences UK Ltd

14 January 2022

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 process

**pemigatinib (Pemazyre®)** is accepted for use within NHSScotland.

**Indication under review:** for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.

In a phase II, single-arm study, pemigatinib demonstrated anti-tumour activity in patients with advanced/metastatic or surgically unresectable cholangiocarcinoma with a FGFR2 fusion or rearrangement who have progressed on at least one line of prior systemic therapy.

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

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

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

## Indication

For the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or rearrangement that have progressed after at least one prior line of systemic therapy.[1]

## Dosing Information

The recommended dose of pemigatinib is 13.5mg orally once daily for 14 days followed by 7 days off therapy. Treatment should be continued as long as the patient does not show evidence of disease progression or unacceptable toxicity.

FGFR2 fusion positivity status must be known prior to initiation of pemigatinib.

Therapy should be initiated by a physician experienced in the diagnosis and treatment of patients with biliary tract cancer. Dose modifications or interruption of dosing should be considered for the management of toxicities. See Summary of product characteristics (SPC) for more details.[1]

## Product availability date

25 August 2021

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

In January 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) published a positive Early Access to Medicines Scheme (EAMS) scientific opinion for pemigatinib monotherapy for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or rearrangement that is relapsed or refractory after at least one line of systemic therapy. This EAMS scientific opinion was withdrawn in April 2021 when marketing authorisation was granted.

Pemigatinib has conditional marketing authorisation from the MHRA.

## Summary of evidence on comparative efficacy

Cholangiocarcinoma is a rare malignant growth that originates in the epithelial lining of the biliary tree. FGFR2 fusions/rearrangements are strong oncogenic drivers and are commonly found in patients with cholangiocarcinoma.[2] Pemigatinib is an inhibitor of FGFR1, 2 and 3 which inhibits FGFR phosphorylation and signalling and decreases cell viability in cells expressing FGFR genetic alterations.

FIGHT-202 is a multicentre, open-label, single-arm, phase II study which evaluated the efficacy and safety of pemigatinib in patients with advanced/metastatic or surgically unresectable cholangiocarcinoma who have progressed on at least one line of prior systemic therapy. Patients

had histologically or cytologically confirmed disease, radiographically measurable disease, and an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2. Patients were assigned to cohorts based on tumour FGF/FGFR status; cohort A (n=107) includes participants with FGFR2 rearrangement or fusions and will be the only cohort discussed in this document.[3]

Patients received pemigatinib orally at a starting dose of 13.5mg once daily (21-day cycle; 14 days on, 7 days off). Treatment was to continue until radiological disease progression, unacceptable toxicity, withdrawal of consent, or physician choice. Dose interruptions up to 14 days and dose modifications were permitted to manage adverse events.[3]

The primary outcome was the proportion of patients with FGFR2 fusions or rearrangements who achieved an objective response (best overall response of confirmed complete response or confirmed partial response as per Response Evaluation Criteria in Solid Tumours version [RECIST] 1.1 criteria), assessed by independent central review. Efficacy was assessed in all patients with centrally confirmed FGF/FGFR status who received at least one dose of pemigatinib.[3]

After a median follow-up of 15.4 months (data cut-off 22 March 2019), 36% of patients treated with pemigatinib achieved a centrally confirmed objective response; 2.8% achieved complete response and 33% achieved partial response. Results from a later data-cut off (07 April 2020) were broadly consistent. See Table 1 for more details.[3, 4]

**Table 1. Efficacy results of FIGHT-202 (Efficacy evaluable population) (Independent central review as per RECIST 1.1).[3, 4, 7]**

| | **Cohort A: FGFR2 fusion or rearrangement** | |
|---|---|---|
| **Data cut-off** | **22 March 2019** | **07 April 2020** |
| Median follow-up | 15.4 months | 27.9 months |
| N | 107 | 108 |
| Overall response rate | 36% | 37% |
| **Best overall response** | | |
| Complete response | 2.8% | 3.7% |
| Partial response | 33% | 33% |
| Stable disease | 47% | 45% |
| Progressive disease | 15% | 15% |
| **Progression-free survival** | | |
| Events (n) | 71 | * |
| Median PFS | 6.9 months | 7.0 months |
| KM estimate of PFS at 12 months | 29% | * |
| **Overall survival** | | |
| Events (n) | 40 | * |
| Median overall survival | 21.1 months | 17.5 months |
| KM estimate of overall survival at 12 months | 68% | * |
| **Duration of response** | | |
| Median DOR | 7.5 months | 8.1 months |

DOR = duration of response; FGFR2 = fibroblast growth factor receptor 2; KM = Kaplan Meier; PFS = progression-free survival; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours version 1.1 *SMC is unable to present these results

Quality of life was assessed using EORTC QLQ-C30 and QLQ-BIL21. Mean and median changes from baseline in EORTC QLQ-C30 and QLQ-BIL21 scores varied, and no consistent trends were found.[2]

The submitting company conducted an unanchored matching-adjusted indirect comparison (MAIC) to compare pemigatinib with chemotherapy regimen mFOLFOX (a modified regimen of oxaliplatin, L-folinic acid, and fluorouracil) with or without active symptom control [ASC], and ASC alone. Individual patient data from FIGHT-202[3] were matched to aggregate data from ABC-06[6], a phase III, open-label, randomised study that recruited patients with locally advanced or metastatic biliary tract cancer (FGFR2 status unknown) with disease progression following first-line treatment. The outcomes assessed were PFS and overall survival. Results favoured pemigatinib; overall survival weighted hazard ratio (HR) versus mFOLFOX plus ASC = 0.2 (95% confidence interval [CI]: 0.2 to 0.3); PFS weighted HR versus mFOLFOX plus ASC = 0.4 (95% CI: 0.3 to 0.6).

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

## Summary of evidence on comparative safety

No comparative safety data are available. Refer to the summary of product characteristics for details.[1]

In the FIGHT-202 study at data cut-off 22 March 2019, the median duration of treatment was 15.4 months in the cohort of patients with FGFR2 fusion or rearrangement (n=107). Any treatment-emergent adverse event (TEAE) was reported by 100% of patients and these were considered treatment-related in 94%; patients reporting a grade 3 or higher TEAE were 60%; patients with a reported serious TEAE were 40%; patients with a dose reduction due to TEAEs were 16%; the proportion of TEAEs that led to dose interruptions were 44%; and patients discontinuing therapy due to a TEAE were 4.7%.[2]

The most frequently reported TEAEs (>20%) in patients from cohort A were alopecia (59%), hyperphosphataemia (55%), diarrhoea (52%), dysgeusia (48%) and fatigue (45%), nausea (40%), constipation (40%), stomatitis (38%), dry mouth (38%), dry eye (32%), vomiting (31%), decreased appetite (30%), arthralgia (29%), dry skin (25%), hypophosphataemia (24%), pain in extremity (23%), back pain (22%) and abdominal pain (22%).[2]

Hyperphosphataemia is a pharmacodynamic effect expected with pemigatinib administration, which when prolonged can cause hypocalcaemia, soft tissue mineralisation, anaemia, secondary hyperparathyroidism, muscle cramps, seizure activity, QT interval prolongation, and arrhythmias.

Recommendations for management of hyperphosphataemia include dietary phosphate restriction, administration of phosphate-lowering therapy, and dose modification when required. Severe hypophosphataemia has also been reported. An additional AE of special interest is serous retinal detachment reactions, which may present with symptoms such as blurred vision, visual floaters, or photopsia. Regular ophthalmological examinations are recommended.[1]

## Summary of clinical effectiveness issues

Cholangiocarcinoma originates in the epithelial lining of the biliary tree and it is classified as intrahepatic or extrahepatic based on the location of the primary tumour; intrahepatic is the most common location. Prognosis is generally poor with a median survival of around 6 months in patients who have progressed after first-line therapy. There are no established treatment options for patients with cholangiocarcinoma who have progressed after first-line therapy; patients in Scotland may receive CAPOX (capecitabine and oxaliplatin) or FOLFOX chemotherapy regimens in this setting however there is limited evidence to support their use. Pemigatinib meets SMC end of life and orphan criteria for this indication.[2]

The key strengths and uncertainties of the clinical evidence are summarised below:

*Key strengths*

- ORR of 37% at latest data cut-off. ORR is an appropriate outcome for a phase II study and is an adequate marker of anti-tumour activity.
- Potential for bias was mitigated by use of independent central review and RECIST 1.1 criteria for efficacy outcomes ORR and PFS.
- FIGHT-202 recruited a relatively large number of patients considering the rarity of the disease.
- When indirectly compared with mFOLFOX plus ASC, pemigatinib appeared to be associated with benefits in both PFS and overall survival.

*Key uncertainties*

- FIGHT-202 was a single-arm study which is a major limitation of the submission. Although anti-tumour activity seems probable, it is very difficult to assess the magnitude of any benefit associated with pemigatinib compared with other treatment options. mFOLFOX can be considered a relevant comparator; however, patients in Scotland may receive other less frequently used chemotherapy regimens such as CAPOX, which have not been indirectly compared with pemigatinib.[2]
- There are limitations to the MAIC presented. Firstly the study populations from FIGHT-202 and ABC-06 differed; FIGHT-202 recruited patients with FGFR2 fusions or rearrangements only (Cohort A) whereas ABC-06 did not test for FGFR2 status. There is some evidence to suggest that patients with FGFR2 genetic alterations may have better prognosis [2], therefore creating uncertainty in the results of the MAIC. Secondly, the effective sample size following matching was small (n=54). Furthermore, only four variables were matched which weakens the analysis; important factors such as FGFR2 status, subtype of cancer, stage, and prior therapies were not matched. Confidence intervals were tight, suggesting that uncertainty has not been fully accounted for in the analysis. Lastly, the MAIC did not examine safety or quality of life outcomes thus making a risk-benefit evaluation of the two treatments uncertain. Although there are limitations and uncertainties to the MAIC, it is acknowledged that there is a paucity of robust evidence available for this rare condition.

- The primary outcome of FIGHT-202, ORR, is a surrogate outcome and is not a direct measure of patient benefit. HRQoL data were inconclusive due to the open-label, uncontrolled study design.[2, 4]
- 40% of patients in the FIGHT-202 study reported a serious TEAE. The main safety concerns are related to the lack of characterisation of important identified risks such as serous retinal detachments and hyperphosphatemia. Despite these uncertainties, the safety profile was deemed acceptable by regulatory authorities and risk minimisation measures have been implemented. Further data are required as part of the specific obligations for conditional marketing authorisation.[2]
- Only one patient in cohort A had extrahepatic cholangiocarcinoma. It is acknowledged that extrahepatic cholangiocarcinoma is rare in patients with FGFR2 rearrangements or fusions. Efficacy in this subpopulation is therefore uncertain; more data are required.[2]

Clinical experts consulted by SMC considered that pemigatinib fills an unmet need, and is a therapeutic advancement for patients with locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or rearrangement.

Companion diagnostic required: contact local laboratory for information.

## 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 pemigatinib, as an orphan and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Advanced or metastatic cholangiocarcinoma patients who have progressed after first line chemotherapy have a very poor prognosis and median overall survival is 6 months. As symptoms may be vague, it is frequently diagnosed late and many patients find the terminal diagnosis very difficult to process. For family members/carers, understanding the diagnosis and its implications can be equally difficult for them.
- There are limited treatment options and traditional chemotherapy is only offered to patients who are fit enough. This provides limited benefit at the expense of significant toxicities. There is a large unmet need in this setting for effective treatments.
- Pemigatinib would be expected to improve quality of life by: improving symptom control (which may see some return to work); delaying tumour progression; having a more favourable safety profile compared with chemotherapy, and potentially improving overall survival.
- Local experience of using pemigatinib in this setting via early access arrangements support the clinical trial data that suggests rapid reduction in symptoms in some patients.

- Importantly, pemigatinib is an oral therapy that can be taken at home, which allows patients to spend more time at home with loved ones instead of in hospital receiving chemotherapy treatment.
- Patients and their carers think that for those with an FGFR2 fusion, pemigatinib offers a more personalised treatment, bringing with it the hope of extended survival over the more standard chemotherapies and/or best supportive care.
- At present patients are not tested for FGFR2 fusions or rearrangements. The introduction of FGFR2 testing may have service implications.

**Additional Patient and Carer Involvement**

We received a patient group submission from AMMF - The Cholangiocarcinoma Charity, which is a registered charity. AMMF has received 1.02% pharmaceutical company funding in the past two years, including from the submitting company. A representative from AMMF participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

## Summary of comparative health economic evidence

A cost-utility analysis was presented evaluating pemigatinib within its full licensed indication. Comparisons were made against mFOLFOX plus active symptom control, and active symptom control alone. Responses from clinical experts consulted by SMC suggested that these comparators were appropriate.

In the base case, a four-state partitioned survival model was used, comprising progression free (PF) on treatment, PF off treatment, progressed disease (PD) off treatment and death. A lifetime horizon was used and a one-week cycle length applied.

Clinical data for pemigatinib were derived from cohort A of the FIGHT-202 study, with extrapolation for the survival outcomes due to the immaturity of the data.[4] To select the base case survival functions, a range of standard parametric functions were considered in terms of statistical goodness-of-fit, evaluation of the hazard profiles versus the observed data, and clinical expert input received by the company. This led to the extrapolation of overall survival using log-logistic, progression-free survival using log-normal and time on treatment using Weibull. To derive survival estimates for the comparators, the company adjusted the survival functions using hazard ratios from the MAIC (described in the summary of comparative efficacy section) after deeming the proportional hazards assumption to hold based on inspection of log-cumulative hazard plots. No adjustment was made regarding the potential prognostic influence of FGFR2 fusion status.

Utility data were derived using EORTC QLQ-C30 data collected within the FIGHT-202 study, mapped to EQ-5D and valued according to the UK tariff.[3, 8] A number of linear mixed effects models were then fitted to the observed data, with the chosen model providing treatment-independent health state utility values. An administration disutility was applied for patients receiving mFOLFOX treatment due to the intravenous administration, and a number of adverse event disutilities applied.

Costs of medicines acquisition and administration (for mFOLFOX) were included with dosing applied according to respective Summary of Product Characteristics. Treatment duration for pemigatinib was extrapolated using a Weibull function as mentioned above (capped to the equivalent duration of PFS), whilst in the absence of data treatment duration for the comparators was assumed equivalent to PFS. mFOLFOX treatment was also capped at a maximum of 12 treatment cycles (24 weeks). No subsequent treatment costs were applied. Costs of healthcare resources were based on ESMO guidelines for biliary cancer and included outpatient consultations, monitoring such as regular computed tomography (CT) scans, and the additional cost of pain management in the progressed disease state. [5] End of life costs were applied as a separate one-off cost.

A screening cost for the identification of eligible patients with FGFR2 rearrangements or fusions was included in the pemigatinib arm, based on a unit cost of £34 per test (on the assumption that FGFR2 testing will be added to existing sequencing panels) and a prevalence of FGFR2 fusions and recombinations of 8.6% (based on the patients screened for inclusion in FIGHT-202) resulting in a total testing cost per eligible patient of £395.

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

The base case results are shown in Table 2 below. Pemigatinib was estimated to result in an increase in QALYs, with the majority of these achieved in the progressed disease health state. The acquisition cost of pemigatinib represented the biggest additional cost, however resource use represented the second biggest additional cost.

**Table 2: Base case results (with PAS)**

| Pemigatinib versus | **Incremental LYGs** | **Pairwise ICER (£/QALY)** |
|---|---|---|
| mFOLFOX + ASC | 1.78 | 37,645 |
| ASC | 1.84 | 45,033 |
| Abbreviations: ASC: active symptom control, LYG: life-year gain, ICER: incremental cost-effectiveness ratio. | | |

A selection of key scenario analyses are summarised below in Table 3.

**Table 3: Key scenarios provided by company**

| **Scenario** | | **ICER (£/QALY) of pemigatinib vs** | |
|---|---|---|---|
| | | **ASC** | **mFOLFOX + ASC** |
| | Base case | 45,033 | 37,645 |
| 1. | Assume FGFR2 status HR adjustment for comparators (all stages Cox model) | 49,863 | 42,367 |
| 2. | Pemigatinib OS – Weibull | 61,622 | 51,984 |

| | | | |
|---|---|---|---|
| 3. | FGFR2 test cost = 100 | 45,662 | 38,292 |
| 4. | FGFR2 test cost = 300 | 47,570 | 40,251 |
| 5. | Utility decrement upon progression = 0.05 | 45,802 | 38,275 |
| 6. | Utility decrement upon progression = 0.10 | 48,302 | 40,314 |
| 7. | Combined 'upper bounds' scenario requested by NDC:<br>- Scenarios 1, 2 and 6 *plus*<br>- FGFR2 test cost = 200 | 78,210 | 67,597 |
| 8. | Combined 'upper bounds' scenario proposed by company:<br>- Scenarios 1 and 5 *plus*<br>- FGFR2 test cost = 200 *plus*<br>- OS extrapolation using generalised gamma function | 62,990 | 54,216 |
| Abbreviations: ASC, active symptom control; QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio;TOT, time on treatment; OS, overall survival;FGFR2 fibroblast growth factor receptor2 | | | |

The submission was subject to a number of limitations:

- The approach to extrapolating survival makes use of the log-logistic function for pemigatinib, with the company citing goodness-of-fit, a non-monotonic hazard profile (increasing then decreasing) and expert opinion regarding expectations of five year survival. However, minimal differences exist in the statistical goodness-of-fit for each of the six parametric functions evaluated, and inspection of the observed-versus-predicted hazard profiles suggests that a model with increasing hazards may be more appropriate (e.g. Weibull or generalised gamma). Given these observations, and the fact that log-logistic results is the second most optimistic survival estimates, it would seem equally reasonable to consider one of the more conservative models when extrapolating survival (Table 3, Scenario 2).
- According to the clinical study report for FIGHT-202, EORTC QLQ data were only collected until the end of treatment, which suggests that any decline in quality of life observed subsequently in the 'progressed disease' health state may not be captured. This results in a relatively small difference in utility between PFS and PD health states, which was smaller than the decline observed in previous oncology submissions. A greater decline in utility upon progression would reduce the QALY gain for pemigatinib, as a significant proportion of the additional life years modelled for pemigatinib are derived from the 'progressed disease' state (Table 3, Scenarios 5 and 6).

- The comparator data supporting the MAIC-derived hazard ratios do not present the proportion of patients with FGFR2 rearrangements or fusions, which limited evidence suggests could potentially have prognostic implications (with more favourable outcomes). If this were the case, the hazard ratio applied to derive comparator survival estimates may overestimate the difference between the treatments. A scenario analysis was provided that explored the influence of an improved prognosis associated with FGFR2 rearrangements or fusions, which results in an increased ICER (Table 3, Scenario 1). However, feedback received from experts during the PACE process suggested that FGFR2 fusions may not have a prognostic effect at the advanced, pre-treated disease stage covered by this submission.
- The costs of screening attributed to the identification of an eligible patient represent a key limitation. The submitting company based the unit cost upon an estimate agreed during the NICE appraisal, which was deemed relevant to screening pathways in NHS England. However, screening pathways differ in NHS Scotland and the use of next generation sequencing panels does not appear to be established practice. The use of higher costs was explored in additional sensitivity analyses, highlighting upwards sensitivity of the ICER to this assumption (Table 3, Scenarios 3 and 4).
- A combined analysis was presented to test a plausible 'upper bounds' estimate (Table 3, Scenario 7), with an alternative approach proposed by the submitting company using a less conservative approach to survival extrapolation and lower utility decrement upon progression (Table 3, Scenario 8).

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

## Additional information: guidelines and protocols

The European Society for Medical Oncology (ESMO) published "Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up: clinical practice guidelines" in 2016.[5] The guidance highlights that there is currently no licensed treatment for the second line treatment of advanced metastatic or surgically unresectable FGFR2 positive cholangiocarcinoma and that current management often involves fluoropyrimidine-based therapy, either as a monotherapy or in combination with other cytotoxics.

## Additional information: comparators

No standard of care. Modified FOLFOX or CAPOX chemotherapy regimens are used in practice.

## Additional information: list price of medicine under review

| Medicine | Dose Regimen | Cost per cycle (£) |
|---|---|---|
| **pemigatinib** | **13.5mg orally once daily for first 14 days in 21-day cycle** | **£7,159** |

*Costs from BNF online on 20 October 2021. Based on 21 day cycle. Costs do not take patient access schemes into consideration.*

## Additional information: budget impact

The company estimated there would be 5 patients eligible for treatment with pemigatinib 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 confidential.**

**References**


1. Incyte Biosciences UK Ltd. Pemigatinib (Pemazyre) 4mg, 9mg, and 13.5mg tablets. Summary of product characteristics. Electronic Medicines Compendium. www.medicines.org.uk Last updated 05 May 2021.

2. European Medicines Agency (EMA). Assessment Report. Pemazyre (Pemigatinib). Treatment of biliary tract cancer. 25 February 2021. EMEA/H/C/005266/0000 www.ema.europa.eu

3. Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro G, Melisi D, Al-Rajabi R, Paulson AS, Borad MJ, Gallinson D, Murphy AG, Oh DY. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. The Lancet Oncology. 2020 May 1;21(5):671-84.

4. Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro GM, Melisi D, Al-Rajabi RM, Paulson AS, Borad MJ, Gallinson DH, Murphy AG, Oh DY. Pemigatinib for previously treated locally advanced/metastatic cholangiocarcinoma (CCA): Update of FIGHT-202. Clin Oncol 39, 2021 (suppl 15; abstr 4086). 2021.

5. Valle JW, Borbath I, Khan SA, Huguet F, Gruenberger T, Arnold D. Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2016 Sep 1;27:v28-37.

6. Lamarca A, Palmer DH, Wasan HS, Ross PJ, Ma YT, Arora A, Falk S, Gillmore R, Wadsley J, Patel K, Anthoney A. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. The Lancet Oncology. 2021 May 1;22(5):690-701.

7. Incyte Corporation. Clinical Study Report Addendum: A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Advanced/Metastatic or Surgically Unresectable Cholangiocarcinoma Including FGFR2 Translocations Who Failed Previous Therapy (FIGHT-202) (data cut-off: 7 April 2020). 2020.

8. Dolan P. Modeling valuations for EuroQol health states. Med Care. 1997 Nov;35(11):1095-108. doi: 10.1097/00005650-199711000-00002. PMID: 9366889


This assessment is based on data submitted by the applicant company up to and including 12 November 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.*