

# Regorafenib for previously treated advanced hepatocellular carcinoma

Technology appraisal guidance

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[www.nice.org.uk/guidance/ta555](https://www.nice.org.uk/guidance/ta555)

## Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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This guidance replaces TA514.

# 1 Recommendations

- 1.1 Regorafenib is recommended as an option for treating advanced unresectable hepatocellular carcinoma in adults who have had sorafenib, only if:
- they have Child–Pugh grade A liver impairment and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and
  - the company provides it according to the [commercial arrangement](#).
- 1.2 This recommendation is not intended to affect treatment with regorafenib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

## Why the committee made these recommendations

Advanced unresectable hepatocellular carcinoma is mostly treated with sorafenib in the NHS. For people who cannot tolerate sorafenib, or whose disease progresses on sorafenib, the only current option is best supportive care. Regorafenib is a possible treatment option after sorafenib instead of best supportive care.

Clinical trial evidence comes from people who have advanced hepatocellular carcinoma that has been treated with sorafenib, and who have an ECOG performance status of 0 or 1 and Child–Pugh grade A liver impairment. This shows that people having regorafenib live longer than people having best supportive care. However, the trial does not include people who cannot tolerate sorafenib, or who have more severe liver disease or a poorer performance status. So it can't be assumed that these people would get the same benefits from regorafenib as the people in the trial.

Regorafenib meets NICE's criteria to be considered a life-extending treatment at the end of life. The most plausible cost-effectiveness estimates are within the range that NICE

normally considers an acceptable use of NHS resources for end-of-life treatments. Therefore it is recommended for people with hepatocellular carcinoma who have had sorafenib, and have an ECOG performance status of 0 or 1 and Child–Pugh grade A liver impairment.

## 2 Information about regorafenib

### Marketing authorisation indication

- 2.1 Regorafenib (Stivarga, Bayer) is indicated as 'monotherapy for the treatment of adult patients with hepatocellular carcinoma who have been previously treated with sorafenib'.

### Dosage in the marketing authorisation

- 2.2 160 mg (4×40 mg tablets) orally once daily for 3 weeks followed by 1 week off therapy. A 4-week period is considered a treatment cycle.

### Price

- 2.3 The list price per treatment cycle for 160 mg of regorafenib is £3,744.00 (excluding VAT; British national formulary online [accessed October 2018]). The company has a [commercial arrangement](#). This makes regorafenib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

## 3 Committee discussion

The appraisal committee ([section 5](#)) considered evidence submitted by Bayer and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

### Unmet need

#### People with advanced hepatocellular carcinoma would welcome a new treatment option

- 3.1 Advanced unresectable hepatocellular carcinoma is often diagnosed late in life and has a poor survival prognosis. It is a debilitating condition with many distressing symptoms. The clinical and patient experts noted that people with advanced unresectable hepatocellular carcinoma have limited treatment options and will have been through many unsuccessful treatments in a long treatment pathway. They noted that improving quality of life and even small extensions to length of life are of considerable importance to this patient group. The committee agreed that people with advanced unresectable hepatocellular carcinoma who have already had sorafenib have an unmet clinical need, and would welcome other treatment options.

### Treatment pathway

#### Regorafenib is a potential option for advanced unresectable hepatocellular carcinoma after sorafenib

- 3.2 If surgical or locoregional treatments fail or are unsuitable, systemic therapy with sorafenib is the most often used treatment option for people with hepatocellular carcinoma. [NICE's technology appraisal guidance on sorafenib](#) recommends it as an option for treating advanced hepatocellular carcinoma only for people with Child–Pugh grade A liver impairment. During the appraisal of sorafenib, the committee noted that

current clinical experience suggests that people need both adequate liver function and performance status to have sorafenib in clinical practice in England, and concluded that treatment should be restricted to people with Child–Pugh grade A liver function and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2. The clinical expert explained that best supportive care or clinical trials are the only options for people whose disease progresses despite taking sorafenib, or who cannot tolerate it. There are no second-line therapies available and a palliative care approach is taken for these patients. The committee noted that regorafenib offered a potential second-line treatment option for people who cannot tolerate, or whose disease progresses on, sorafenib.

## Clinical evidence

### **Regorafenib is more clinically effective than best supportive care in the clinical trial population**

- 3.3 The company's clinical evidence came from 1 trial. RESORCE (n=573) was an international, phase III, multicentre, randomised, double-blind, placebo-controlled trial comparing regorafenib (plus best supportive care) with placebo (plus best supportive care). The trial included people whose disease had progressed on sorafenib, who had either 160 mg regorafenib orally once daily for weeks 1 to 3 of each 4-week treatment cycle, or best supportive care. Up to 2 regorafenib dose reductions because of toxicity were allowed (from 160 mg to 120 mg to 80 mg). The primary outcome was overall survival, with secondary outcomes including progression-free survival. The committee noted that the results showed a small and statistically significant median overall survival gain of 2.8 months for regorafenib (10.6 months; 95% confidence interval [CI] 9.1 to 12.1) compared with best supportive care (7.8 months; 95% CI 6.3 to 8.8). The committee noted that the hazard ratio for overall survival for regorafenib compared with best supportive care was 0.63 (95% CI 0.50 to 0.79) and that regorafenib offered an important survival benefit for people with advanced hepatocellular carcinoma. Median progression-free survival was statistically significantly better for regorafenib (3.1 months, 95% CI 2.8 to 4.2) than for best supportive care (1.5 months,



95% CI 1.4 to 1.6). The committee noted that the hazard ratio for progression-free survival for regorafenib compared with best supportive care was 0.46 (95% CI 0.37 to 0.56), which represented a clinically relevant reduced risk of progression for the regorafenib group. It also heard that quality-of-life scores were generally similar across treatment arms with different measures, including EQ-5D. Scores were slightly worse for regorafenib than for best supportive care but these differences did not pass the 'minimally important difference' threshold established in the literature. The committee noted that there were 5 clinical trial centres in the UK, with 20 patients randomised to treatment in 4 of the centres. The ERG noted that RESORCE was a high-quality randomised controlled trial, with a low risk of selection, performance, attrition and reporting bias. Therefore, the committee concluded that regorafenib offered an important gain in progression-free and overall survival compared with best supportive care.

## **The benefits of regorafenib cannot be generalised outside the trial population**

3.4 RESORCE included people with advanced unresectable hepatocellular carcinoma who:

- previously tolerated treatment with sorafenib
- mostly had Child–Pugh grade A liver impairment
- had an ECOG performance status of either 0 or 1.

The committee noted that regorafenib's marketing authorisation is broader than the trial population, because the trial did not include people who:

- had Child–Pugh grade B liver impairment
- had an ECOG performance status of 2 or more

- could not tolerate sorafenib.

In RESORCE, tolerating sorafenib was defined as having had at least 400 mg a day for 20 days or more, in the 28 days before stopping treatment with sorafenib. The clinical expert noted that RESORCE included a highly selected population who could tolerate sorafenib well. They also highlighted that post-trial studies investigating survival outcomes for sorafenib, which included patients outside of the strict trial criteria, showed lower survival than predicted in the main sorafenib trial. The clinical expert stated that the toxicity and efficacy of regorafenib in people who could not tolerate sorafenib, with Child–Pugh grade B liver impairment and with an ECOG performance status of 2 or more, was unknown. The committee therefore concluded that benefits could not be extrapolated outside the trial population because of the uncertainty in survival benefit for people excluded from RESORCE but covered by the marketing authorisation for regorafenib.

## **An audit of sorafenib use shows differences between the RESORCE trial population and the population in clinical practice in England**

- 3.5 A 2017 audit of sorafenib use in the UK by King et al. found that sorafenib is used in patients who have an ECOG performance status of 2 or more and Child–Pugh grade B liver impairment (21 and 16% of the audit population respectively). The committee noted that sorafenib is recommended as an option for treating advanced hepatocellular carcinoma only for people with Child–Pugh grade A liver impairment, but that people progressing on sorafenib are likely to have further deterioration in liver impairment (Child–Pugh status) and ECOG performance status. The clinical expert explained that because sorafenib and regorafenib are both tyrosine kinase inhibitors with similar mechanisms of action, people who cannot tolerate sorafenib may also be unable to tolerate regorafenib (although there are no data to support this). Therefore, an estimated 30 to 50% of the population whose disease progressed on sorafenib would be eligible for regorafenib. The committee also noted that all patients had a treatment-related adverse event, and that quality of life was only maintained rather than improved with regorafenib treatment. The committee acknowledged comments received during consultation that use of regorafenib should be restricted

based on the eligibility criteria in the RESORCE trial. It concluded that given the lack of evidence in people with an ECOG performance status of 2 or more, or with Child–Pugh B liver impairment or who cannot tolerate sorafenib, there was considerable uncertainty in the efficacy of regorafenib in populations not included in RESORCE but covered by its marketing authorisation.

## **The company's economic model**

### **The model structure is appropriate for decision making**

- 3.6 The company used a partitioned survival model with 3 health states (progression free, progressed disease and death). The committee noted the uncertainty in the model about people covered by the marketing authorisation for regorafenib who were excluded from RESORCE. The committee understood that all efficacy and clinical parameters in the model were derived using patient-level data from RESORCE. The committee noted that data for progression-free survival from RESORCE represented a full pattern of progression, so no extrapolation was needed and the progression-free survival curve was taken directly from the observed trial's Kaplan–Meier data. The committee accepted that standard parametric curve fitting was done using patient-level data from RESORCE for overall survival.

## **Overall survival extrapolation in the economic model**

### **The Weibull distribution is preferred but is associated with uncertainty**

- 3.7 In the company's original base case, a dependent log-normal curve was used to model overall survival. The ERG disagreed with this choice of curve and the fitting of dependent models because the log-normal function is an accelerated failure time model. The ERG also considered the choice of the log-normal curve to be inappropriate, based on its clinical expert's advice that the model-predicted sustained difference in

overall survival between the regorafenib and best supportive care curves beyond 35 cycles was unrealistic in a population with progressed hepatocellular carcinoma. At the appraisal committee meeting, the clinical expert explained that the 5-year survival suggested by the log-normal curve was implausible because the modelled population was elderly, with advanced disease refractory to most previous treatments. [NICE's reference case](#) places most significance on clinical plausibility and so the ERG preferred the Weibull curve based on clinical opinion and goodness-of-fit to observed data. The Cancer Drugs Fund clinical lead highlighted a recent study reporting mature follow-up data for people having sorafenib (plus other treatments) in specialist centres. This showed relatively high 5-year survival rates of 5 to 8%, suggesting that some people may have indolent disease. The committee noted that this study included people having sorafenib and that the population having regorafenib are likely to have lower 5-year survival rates because they are further along the treatment pathway. The committee concluded that the company's preferred dependent log-normal curves were technically incorrect and overly optimistic. It preferred the use of independent Weibull curves, but recognised that these were associated with uncertainty.

## **The Weibull distribution is the most appropriate for extrapolating overall survival**

- 3.8 The committee considered that the Weibull distribution remained the most appropriate choice for extrapolating overall survival because no new evidence was provided during consultation. However, in its updated analyses, the company extrapolated overall survival with independently fitted Gompertz and exponential distributions, as well as the Weibull distribution. The company noted that the ERG's clinical expert also considered the Gompertz and exponential extrapolations to be clinically plausible, so it provided cost-effectiveness results for these 3 distributions individually combined with its updated assumptions. The ERG explained that its preference for the Weibull distribution was not based only on clinical opinion of its plausibility, but also on goodness-of-fit to the observed data and the empirical hazards. The committee noted that based on the empirical hazards (particularly in the best supportive care arm), an exponential curve was not appropriate and that the Akaike

information criterion/Bayesian information criterion for Weibull fitted better than Gompertz by more than 5 points. The committee noted that no further information was provided by the company to support the use of an exponential or Gompertz curve. The committee reiterated that the Weibull was the most appropriate distribution for extrapolating overall survival, in preference to the Gompertz and exponential curves.

## **Time-to-treatment discontinuation in the economic model**

### **Treatment discontinuation in RESORCE may not represent NHS clinical practice**

- 3.9 The committee noted that the number of people continuing treatment with regorafenib despite disease progression was high in RESORCE and that time-to-treatment discontinuation did not equate to time to progression. The clinical expert explained that this did not represent clinical practice in England because 80% of patients would stop treatment on progression. They highlighted that the number of people continuing treatment despite disease progression and the efficacy of treatment in these patients was uncertain. The committee concluded that the rate of treatment discontinuation in RESORCE was unlikely to represent NHS clinical practice.

### **Including the survival benefits but excluding the costs of post-progression treatment is not appropriate**

- 3.10 The company agreed that most people would stop treatment if their disease progressed, and accepted that people would have less treatment in practice than in RESORCE. The company did a new survey, which investigated post-progression treatment, and found that 8 of the 9 respondents would stop treatment at progression. In response to consultation, the company presented a scenario whereby an area under the log-logistic, time-to-treatment discontinuation curve was applied. This was adjusted for 80% of patients stopping treatment at or before progression and 20% having treatment post-progression. This resulted in

people having an average of approximately 1 cycle of post-progression treatment. The ERG explained that although current practice in England may differ from that in RESORCE, the survival estimates observed in RESORCE may have been influenced by the post-progression treatment. Therefore it was inappropriate to include health benefits associated with post-progression treatment, but to exclude a proportion of the costs associated with generating those health gains. The committee concluded that adjusting for cost alone for 20% of people having treatment post-progression was not appropriate.

## Costs in the economic model

### Assuming additional days of drug wastage to model drug cost is arbitrary and associated with uncertainty

- 3.11 The company's original base case included cost savings from dose reductions and treatment interruptions for regorafenib. The ERG's clinical advisers noted that NHS prescribing practices do not account for reduced frequency of individual prescriptions for patients with leftover tablets. Cost reductions included in the company's model would therefore probably not be fully realised in clinical practice. The clinical expert explained that despite efficiency measures in the NHS, it would be reasonable to assume some drug wastage in clinical practice even if the patient's dose were reduced. This was also supported by the Cancer Drugs Fund clinical lead who stated that people are normally given a month's supply of a drug, and any leftover tablets cannot be used for other patients. Therefore, a month's supply should be modelled to take wastage into account. The company provided evidence from pharmacists from 2 of the largest tertiary centres in the UK supporting pack splitting to minimise wastage of sorafenib and other oral tyrosine kinase inhibitors. Healthcare at Home, which distributes sorafenib in England, also provided a supportive statement after consultation. The committee acknowledged that although wastage could be minimised, the pharmacists' evidence provided by the company suggested that it could not be eliminated entirely. In response to consultation, the company presented a scenario whereby costs for the actual treatment taken (as average doses in RESORCE) were modelled but with an assumption that

every patient wastes additional days of medicine at the maximum daily dose over the course of their treatment. This wastage was applied as a one-off cost to every patient and reflected an assumption in between the original company base case and committee-preferred analysis. The committee considered the assumption of drug wastage to be arbitrary and therefore associated with significant uncertainty. The ERG did 2 exploratory analyses: a pessimistic scenario in which drug costs were assumed to be 160 mg per day (full pack dose), and an optimistic scenario in which drug costs were assumed to be 160 mg multiplied by relative dose intensity to account for this uncertainty (see [section 3.15](#)). The ERG also highlighted 2 further concerns with the company's modelling of drug costs. It noted that the projected log-logistic, time-to-treatment discontinuation curve and the Weibull overall survival curves crossed at around 4 years. This is not logical because it indicates that patients are still incurring drug costs after they have died. In addition, the modelled relative dose intensity followed an unusual pattern for which no rationale was provided. The committee concluded that the company's approach to modelling drug wastage was associated with uncertainty.

## **Pooling estimates from the 2007 and 2015 surveys is appropriate for health state resource use costs**

- 3.12 In its original base case, the company used clinician surveys to estimate resource use associated with sorafenib and best supportive care. It assumed that the sorafenib results would also apply to regorafenib. The committee noted that the company used a survey from 2015 with 3 clinical experts to inform resource use in its original base case. The ERG highlighted that the company did not reference an earlier survey done in 2007 using 4 UK clinicians. The company reiterated its preference for the 2015 survey because estimates from 2007 preceded the availability of sorafenib and were not based on clinical experience. The committee considered that the new survey might have produced better estimates for the sorafenib arm because it would take into account experience with sorafenib. But it noted that estimates for the best supportive care arm from the original survey should be equally valid when compared with those of the new survey. The committee was not convinced of the robustness of the surveys and noted the small number of clinicians involved and the variability in the clinicians' responses.



Without any better quality data, the committee concluded that it would be more appropriate to pool estimates from the 2007 and 2015 surveys for health state resource use costs.

## **The hospital admission rate derived from the new survey is appropriate**

- 3.13 In response to consultation, the company provided results from a new survey designed to better understand the rate of hospitalisations in the NHS, and to address the ERG's concerns with how questions in the original surveys may have been interpreted. The results supported the statement from the clinical expert in the appraisal consultation document that few people are admitted to hospital. These results related to hospitalisations were then incorporated in the company's updated model. The ERG noted that in the new survey, resources associated with patients who have post-progression treatment with regorafenib are unlikely to be generalisable to those associated with people who stop regorafenib after progression. Nevertheless, the committee concluded that the hospital admission rates derived from the new survey were the best available data to be used in its decision making.

## **Utility values in the economic model**

### **Utility values derived from RESORCE using EQ-5D data are too high for a population with progressed disease**

- 3.14 The Cancer Drugs Fund clinical lead noted that the utility values appear high for a population of patients who enter the model after progressing on sorafenib even if the patients have an ECOG performance status of 0 or 1 at entry. The clinical expert said that most patients tend to have side effects from treatment that have a serious impact on their quality of life, which did not appear to be reflected in the utility values. There were concerns about the face validity of the utility values collected in RESORCE using EQ-5D data because the utility decrement for progression (−0.048) appeared low for an advanced hepatocellular population with progressed disease. The company obtained EQ-5D data directly from the trial as recommended in NICE's methods guide.



However, the ERG explained that the EQ-5D questionnaire was completed on the first day of each treatment cycle, when a patient had not had treatment for a week. So any adverse effects of regorafenib treatment may not have been fully captured. The committee noted that reducing the health state utility values would increase the incremental cost-effectiveness ratio (ICER), although an exact figure was not provided. The committee concluded that the high utility values used in the model did not seem clinically plausible despite EQ-5D data from the trial being used. This was likely to have resulted in an underestimate of the ICER.

## Cost-effectiveness results

### The most plausible ICER is below £50,000 per QALY gained

3.15 After consultation, the company submitted a further model using the committee's preferred assumptions, specifically:

- extrapolating overall survival using a Weibull distribution (see [section 3.7](#))
- pooling resource use estimates from the 2015 and 2007 surveys (see [section 3.12](#)) and
- fully extrapolating time-to-treatment discontinuation (see [section 3.9](#)).

The company also:

- used a revised rate of hospitalisations based on the new survey (see [section 3.13](#))
- assumed that 80% of people stop treatment at or before progression, with only 20% having treatment post-progression (see [section 3.9](#)) and

- included a confidential commercial arrangement.

The ERG did 4 exploratory analyses that investigated the effect of individual assumptions on the ICER for regorafenib compared with best supportive care. All 4 analyses extrapolated overall survival using a Weibull distribution and corrected errors in the company model (specifically when additional progression-free survival data points had erroneously been excluded from calculations, and when emergency department visits accrued no cost):

- Analysis 1: using costs of full pack (160 mg) dosing.
- Analysis 2: analysis 1, using costs based on patients having the mean dose in RESORCE instead of full pack dosing.
- Analysis 3: analysis 2, plus incorporating a logical consistency constraint to account for the projected log-logistic, time-to-treatment discontinuation curve and the Weibull overall survival curve crossing at around 4 years.
- Analysis 4: analysis 3, plus using last observation carried forward relative dose intensity extrapolation instead of modelling relative dose intensity for regorafenib as in the company's model.

The committee noted that the ERG's most optimistic (analysis 4) and pessimistic (analysis 1) scenarios (in terms of drug wastage), using the committee-preferred Weibull distribution, and with the commercial arrangement, produced ICERs for regorafenib compared with best supportive care of £44,296 and £51,868 per quality-adjusted life year (QALY) gained respectively. The committee agreed that analysis 1 was unlikely to reflect clinical practice, because the dose reductions in the trial were planned, so it was more likely that wastage would be minimised in clinical practice. It agreed that the most plausible ICER would be between the 2 figures and likely closer to £44,296 than to £51,868 per QALY gained. The committee concluded that the most plausible ICER, incorporating the confidential commercial arrangement for regorafenib compared with best supportive care, was below £50,000 per QALY gained.

## End of life

### Regorafenib for treating advanced unresectable hepatocellular carcinoma in adults who have had sorafenib meets both NICE's end-of-life criteria

- 3.16 The committee considered the advice about life-extending treatments for people with a short life expectancy in [NICE's guide to the methods of technology appraisal](#). The committee discussed whether life expectancy without regorafenib would be less than 24 months. It noted that median overall survival was 7.8 months for best supportive care in RESORCE and that the mean modelled overall survival from the company model was 10.8 months. The ERG explained that any changes relating to parametric overall survival functions would not change the conclusions for this end-of-life criterion. The committee concluded that the short life expectancy criterion was met. The committee discussed whether a survival benefit of over 3 months could be expected for regorafenib compared with best supportive care. It noted that the median survival in the regorafenib arm of RESORCE was extended by 2.8 months. It also recalled that the average number of months of life gained with regorafenib, as estimated by the company's economic model, was 6.24 months compared with best supportive care. On balance, the committee agreed that it was reasonable to assume that the survival benefit of regorafenib is likely to exceed 3 months and concluded that the extension-to-life criterion was met.

## Innovation

### There is no evidence of additional benefits of regorafenib

- 3.17 The patient and clinical experts explained that there was a significant unmet need for people with advanced unresectable hepatocellular carcinoma because of the limited treatment options available to them. The committee noted that best supportive care was currently the only treatment option available for people whose disease progresses with sorafenib, or who cannot tolerate it, and that regorafenib offered a

valuable second-line treatment option. It concluded that regorafenib would be beneficial for patients, but it had not been presented with evidence of any additional benefits that were not captured in the measurement of QALYs.

## Conclusion

### Regorafenib is recommended for routine NHS use

- 3.18 The committee concluded that, with the discount agreed in the commercial arrangement, the most plausible ICER was within the range that NICE normally considers an acceptable use of NHS resources for a life-extending treatment at the end of life. It therefore recommended regorafenib for use in the NHS, for the population in RESORCE. That is, for treating advanced unresectable hepatocellular carcinoma in adults who have had sorafenib, only if they have Child–Pugh grade A liver impairment and an ECOG performances status of 0 or 1 (see [section 3.4](#)).

## 4 Implementation

- 4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.
- 4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has advanced unresectable hepatocellular carcinoma with Child–Pugh grade A liver impairment and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and has had sorafenib, and the doctor responsible for their care thinks that regorafenib is the right treatment, it should be available for use, in line with NICE's recommendations.

## 5 Appraisal committee members and NICE project team

### Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The [minutes of each appraisal committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

### NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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## Accreditation

