Regorafenib for previously treated advanced hepatocellular carcinoma

Technology appraisal guidance
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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 are 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.

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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1 Recommendations

1.1 Regorafenib is not recommended for treating advanced unresectable hepatocellular carcinoma in adults who have had sorafenib.

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

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

Clinical trial evidence in people with advanced hepatocellular carcinoma who have already had sorafenib, have an Eastern Cooperative Oncology Group (ECOG) performance status score of either 0 or 1, and Child-Pugh grade A liver impairment shows that people having regorafenib live longer than people having best supportive care. However, the survival benefit with regorafenib is unclear in people who cannot tolerate sorafenib, have a poorer ECOG performance status or more severe liver disease. These people were not included in the trial so it is uncertain whether the results of the trial would translate into similar benefits in the NHS.

The company responded to the committee’s preferred assumptions after consultation and submitted a further model incorporating these assumptions for overall survival extrapolation, full dose and pooled resource use surveys.

Regorafenib meets NICE’s criteria to be considered a life-extending treatment at the end of life. The most plausible cost-effectiveness estimates are higher than those NICE normally considers an acceptable use of NHS resources for end-of-life treatments. Therefore regorafenib cannot be recommended for routine use in the NHS.

Regorafenib is not recommended through the Cancer Drugs Fund because the uncertainties in the clinical and cost effectiveness cannot be resolved by data collection in the Cancer Drugs Fund, and regorafenib does not have plausible potential to be cost effective.
### 2 Information about regorafenib

| Marketing authorisation | Regorafenib (Stivarga, Bayer) is indicated as 'monotherapy for the treatment of adult patients with hepatocellular carcinoma who have been previously treated with sorafenib'.  
| | 'Regorafenib is not recommended for patients with severe hepatic impairment (Child-Pugh grade C) because it has not been studied in this population'. |
| Dosage in the marketing authorisation | 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 | The list price per treatment cycle for 160 mg of regorafenib is £3,744.00 (excluding VAT; British national formulary online [accessed October 2017]).  
| | The company has agreed a patient access scheme with the Department of Health. If regorafenib had been recommended, this scheme would provide a simple discount to the list price of regorafenib with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS. |
3 Committee discussion

The appraisal committee (section 4) 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 only active treatment option available for people with hepatocellular carcinoma. NICE technology appraisal guidance on sorafenib recommends it as an option for treating advanced hepatocellular carcinoma only in people with Child-Pugh grade A liver impairment. During the appraisal of sorafenib, the committee noted that people need both adequate liver function and performance status to have sorafenib in clinical practice in England, and 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 offers 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 only 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 offers an important gain in progression-free and overall survival compared with best supportive care.

The generalisability of the population included in the RESORCE trial to clinical practice in England is uncertain

3.4 RESORCE included people with advanced unresectable hepatocellular carcinoma who:

- previously had sorafenib
- mostly had Child-Pugh grade A liver impairment
- had an ECOG performance status score 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
- cannot tolerate sorafenib.

The clinical expert noted that RESORCE included a highly selective population who could tolerate sorafenib well and 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 not included in RESORCE but covered by the broader 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 at this time). 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 values were 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, with Child-Pugh B liver impairment and who cannot tolerate sorafenib, there is 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, however, 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 Kaplan–Meier data. The committee accepted that standard parametric curve fitting was done using patient-level data from RESORCE for overall survival.
The company submitted a model suitable for decision-making

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

- extrapolating overall survival using a Weibull distribution
- using the full dose of 160 mg per cycle
- resource use estimates from pooled 2015 and 2007 surveys
- full extrapolation of time-to-treatment discontinuation.

This model originally contained errors, which resulted in the company submitting several iterations of the economic model and response to consultation. The committee noted this divergence from NICE processes but accepted the company's model as suitable for decision-making.

Overall survival extrapolation in the economic model

The Weibull distribution is most appropriate for extrapolating overall survival

3.8 In the company's original base case, a dependent lognormal curve was used to model overall survival. The ERG disagreed with this choice of curve and the fitting of dependent models because the lognormal function is an accelerated failure time model. The ERG also considered the choice of the lognormal 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. The committee heard from the clinical expert that the 5-year survival suggested by the lognormal curve was implausible because the modelled population was elderly, with advanced disease refractory to most previous treatments. The ERG noted that the NICE reference case places most significance on clinical plausibility and 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 on patients 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 a sorafenib population 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 lognormal curves were overly optimistic and technically incorrect. It preferred the use of independent Weibull curves, but recognised that these were associated with significant uncertainty.

3.9 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 fit better than Gompertz by more than 5 points. The company provided no further information 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

3.10 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 is unlikely to represent NHS clinical practice.

Including the survival benefits but excluding the costs of post-progression treatment is unreasonable

3.11 The company agreed that most people will discontinue treatment if their disease progresses, 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 adjusting 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 observed 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 unreasonable.

Costs in the economic model

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

3.12 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 pills. 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 pills 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) was 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 reflects an assumption between the company's base case and committee's preferred assumptions. It was unclear in this scenario whether the observed reduced dosage in RESORCE reflected patients randomly missing tablets, or whether there had been a planned reduction in dose (in which case the reduction in regorafenib costs would be appropriate) because the company had not submitted any data on individual patient dosages which could reduce this uncertainty. 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 (RDI) to account for this uncertainty (see section 3.18). 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 logically inconsistent because it indicates that patients are still incurring drug costs after they have died. In addition, the modelled RDI 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 significant uncertainty.

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

3.13 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 committee heard from the ERG that the company did not reference an earlier survey done in 2007 using 4 UK clinicians. It noted that 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 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

3.14 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 were then incorporated in the company’s updated model. The ERG was broadly satisfied with the new survey, but it noted that 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 is the best available data.

Utility values in the economic model

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

3.15 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. The ERG had 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 the NICE 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 ERG noted that reducing the health state utility values will 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 and that this was likely to have resulted in an underestimate of the ICER.

The company's updated economic analysis

The company's ICER for regorafenib compared with best supportive care ranges from £42,788 to £50,456 per QALY gained

3.16 The company's updated base-case deterministic ICER, provided in response to consultation, included both the committee's preferred assumptions from the appraisal consultation document and a number of company-preferred assumptions, specifically:

- using a revised rate of hospitalisations based on the new survey
- assuming that each patient wastes additional days of medicine at the maximum daily dose
- assuming that 80% of people stop treatment at or before progression, with only 20% having treatment post-progression.

3.17 The company considered that using these assumptions and extrapolating overall survival using Weibull, Gompertz and exponential distributions would produce plausible ICERs. The deterministic ICERs range from £42,788 to £50,456 per quality-adjusted life year (QALY) gained for regorafenib compared with best supportive care (probabilistic ICERs were not provided).
The ERG’s updated exploratory economic analyses

The ERG’s exploratory ICER for regorafenib compared with best supportive care ranges from £55,829 to £68,137 per QALY gained

3.18 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 included corrections of 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 cost of full pack (160 mg) dosing.
- Analysis 2: analysis 1, plus using company-modelled RDI 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 RDI extrapolation instead of modelling RDI for regorafenib in the unusual pattern (as in the company model).

When combining all 4 analyses, the deterministic ICER was £55,829 per QALY gained.

3.19 The ERG also presented the most optimistic (analysis 4) and pessimistic (analysis 1) scenarios in terms of drug wastage in exploratory analyses using Weibull, Gompertz and exponential distributions. The ICERs for regorafenib compared with best supportive care ranged from £55,829 to £68,137 per QALY gained for the Weibull distribution and £48,510 to £60,910 per QALY gained using the Gompertz and exponential distributions.

The updated most plausible ICER after consultation

The most plausible ICER is above the range normally considered a cost-effective use of NHS resources

3.20 The committee accepted the ERG’s corrections to the errors in the company’s model. It noted that the ERG's most optimistic and pessimistic scenarios (in
terms of drug wastage), using the committee-preferred Weibull distribution, produced ICERs for regorafenib compared with best supportive care of £55,829 to £68,137 per QALY gained. The committee concluded that the most plausible ICER, incorporating the confidential patient access scheme for regorafenib compared with best supportive care, was over £50,000 per QALY gained and substantially above the range normally considered a cost-effective use of NHS resources.

**End of life**

**Regorafenib meets NICE’s end-of-life criteria when used in adults who have already sorafenib**

3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE’s Cancer Drugs Fund technology appraisal process and methods.

- 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. It heard from the ERG 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.
Cancer Drugs Fund

Regorafenib does not meet the criteria to be included in the Cancer Drugs Fund

3.22 Having concluded that regorafenib could not be recommended for routine use, the committee then considered if it could be recommended for treating hepatocellular carcinoma within the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides. The committee understood that the company had not made a specific case for regorafenib to be considered for funding through the Cancer Drugs Fund. It also considered that the most plausible ICERs were substantially higher than the range normally considered to be a cost-effective use of NHS resources and that the data presented were mostly mature. The committee discussed whether a recommendation through the Cancer Drugs Fund could allow for data collection for the full population covered by the marketing authorisation, but agreed that the relevant data to inform a decision would not be collected within 2 years. The committee therefore concluded that regorafenib did not have plausible potential to satisfy the criteria for routine use, and that the clinical uncertainties could not be resolved through data collection within the Cancer Drugs Fund. Regorafenib did not meet the criteria to be included in the Cancer Drugs Fund.

Innovation

There is no evidence of any additional benefits of regorafenib

3.23 The patient and clinical experts explained that there is 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 is currently the only treatment option available for people whose disease progresses with sorafenib, or who cannot tolerate it, and that regorafenib offers 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 not recommended

3.24 The committee concluded that the most plausible ICER for regorafenib compared with best supportive care was over £50,000 per QALY gained, which is higher than the range usually considered a cost-effective use of NHS resources, even for end-of-life treatments. Regorafenib also did not meet the criteria to be recommended for use in the Cancer Drugs Fund. The committee concluded that it could not recommend regorafenib for treating advanced unresectable hepatocellular carcinoma in adults who have already had sorafenib.
4 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

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