NICE National Institute for Health and Care Excellence

Regorafenib for previously treated advanced hepatocellular carcinoma

Chair's presentation

TA514 - rapid review
Committee C
ERG: ScHARR, The University of Sheffield
NICE technical team: Kirsty Pitt, Alex Filby
Company: Bayer
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Regorafenib (Bayer)

Marketing authorisation	Indicated in adults with hepatocellular carcinoma previously treated with sorafenib
Administration & dose	Oral,160 mg once daily for 3 weeks followed by 1 week off therapy
Mechanism of action	Tyrosine kinase inhibitor (TKI) which inhibits multiple protein kinases involved in oncogenesis, tumour cell proliferation and tumour vasculature. Also inhibits angiogenic kinase receptors which play a central role in angiogenesis thereby preventing the proliferation of cancer cells
Price	List price per 4 week treatment cycle: £3,744 A simple discount PAS price has been agreed with NHS England

TA514 final guidance recommendation

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

Committee's key considerations in TA514

Issue	Committee's conclusion
Generalisability of trial	Benefits can't 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. Trial did not include patients who: • had Child-Pugh grade B • had ECOG of 2 or more • could not tolerate sorafenib
Most plausible ICER	£55,829 to £68,137 per QALY gained, depending on drug wastage assumptions used
End of life criteria	Both criteria met
Cancer Drugs Fund	Criteria not met because relevant data for the full population in the marketing authorisation would not be collected within 2 years

Drug wastage in the model

Upper bound ICER → Costs based on maximum daily dose being received (160mg). Patient receives full pack of regorafenib each month and all unused medication disposed at end of each cycle.

Lower bound ICER → Costs based on patients receiving mean dose in the RESORCE trial – accounts for dose reductions used in the trial in response to toxicity.

TA514 final guidance conclusions:

- Most plausible ICER is £55,829 to £68,137 per QALY gained, depending on drug wastage assumptions used
  - Committee acknowledged that although wastage could be minimised, the pharmacists' evidence provided by the company suggested that it could not be eliminated entirely

Company's rapid review submission: updated PAS

- Rapid reviews are for changes in commercial offers and use the major assumptions in previous final guidance – TA514
- Company has proposed an updated PAS

Company's rapid review submission: drug wastage comments

- Half-cycle correction in model already accounts for wastage from terminating treatment mid-cycle
- Previous evidence from 2 NHS tertiary centres suggested wastage is reduced by delaying dispensing of new packs or use of pack splitting
- Patients did not receive maximum dose intensity in trial due largely to planned dose reductions (68% in regorafenib group, 31% in placebo group)

Company's rapid review submission: drug wastage in previous technology appraisals

Regorafenib appraisal	20 previous TAs for oral oncology treatments
Lower bound ICER: relative dose intensity from clinical trial Upper bound ICER: maximum daily dose and all unused medication disposed	16 (80%) used relative dose intensity from clinical trial • 1 of which committee did not accept, but preferred RDI to be increased from 82 to 90%
Costs of treatment for patients who stop treatment during a cycle are included in modelling (half-cycle correction turned off)	These costs not always included

Cost-effectiveness results with updated PAS

Company's ICERs

Upper bound

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (£/QALY)
Placebo + BSC	[redacted]	0.648	-	-	-
Regorafenib +BSC	[redacted]	0.968	[redacted]	0.320	£51,760

Lower bound

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (£/QALY)
Placebo + BSC	[redacted]	0.648	-	-	-
Regorafenib +BSC	[redacted]	0.968	[redacted]	0.320	£44,296

Cost-effectiveness results with updated PAS

Company's ICERs, including ERG correction to upper bound for no. of cycles per year

Upper bound

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (£/QALY)
Placebo + BSC	[redacted]	0.648	-	-	-
Regorafenib +BSC	[redacted]	0.968	[redacted]	0.320	£51,868*

Lower bound

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (£/QALY)
Placebo + BSC	[redacted]	0.648	-	-	-
Regorafenib +BSC	[redacted]	0.968	[redacted]	0.320	£44,296

Key issues for consideration

- What is the most plausible ICER?
- Is regorafenib cost-effective?
  - In the population included in the trial?
  - In the population included in the marketing authorisation?