National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

ERG report

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196) [ID696]

You are asked to check the ERG report from Southampton Health Technology Assessment Centre to ensure there are no factual inaccuracies contained within it.

If you do identify any factual inaccuracies you must inform NICE by **5pm** on **Thursday 17 April 2014** using the below proforma comments table. All factual errors will be highlighted in a report and presented to the Appraisal Committee and will subsequently be published on the NICE website with the Evaluation report.

The proforma document should act as a method of detailing any inaccuracies found and how and why they should be corrected.

Issue 1

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
pg 63. "The manufacturer's response does not appear to address this question."	Please delete this statement.	We feel that our answer to B9 fully addressed the question: "The HR of 0.111 is valid for the treatment period (first 12 months /36 months) of patients at high risk of recurrence (~Miettinen risk criteria), and used in cost – effectiveness calculations. This HR was derived from the primary analysis sample updated with the retrospective data of 36 high risk patients (n=103 and n=98 on imatinib and on placebo, respectively), truncated at 12 months for the imatinib arm to estimate RFS compared to placebo (see more on the method in 7.3.2 of the MS)."	No factual inaccuracy. The ERG requested the manufacturer to indicate whether the difference between reported hazard ratios - 0.265 (95% CI 0.148 to 0.477) in the clinical effectiveness section and 0.111 (95% CI 0.043 to 0.281) applied in the model – arose due to truncating the data at 12 months or due to re-classification of patients. The manufacturer's response does not address this question.

Issue 2

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
pg 64. "The values estimated for HR1 and HR2 were 0.519 (95% CI 0.297 to 0.906) and **0.633** (95% CI 0.392 to	The values estimated for HR1 and HR2 were 0.519 (95% CI 0.297 to 0.906) and **0.663** (95% CI 0.392 to 1.123).	This is a typo; we provided the correct number.	This has been changed to 0.663.

1.123)."			

Issue 3

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
pg 69. "The calculation is based on a reported value of 44% (which does not agree with the value for imatinib once daily reported by Verweij and colleagues) and yields an estimated value of 0.034 (monthly rate (mr) = -1/2*ln(0.44), converted to a monthly transition probability as **1-exp(-mr))**."	"The calculation is based on a reported value of 44% (which does not agree with the value for imatinib once daily reported by Verweij and colleagues) and yields an estimated value of 0.034 (monthly rate (mr) = -1/2*ln(0.44), converted to a monthly transition probability as **1-exp(-mr^(1/12)**)).	We think there is an error in the reported formula.	Agree, the formulae we presented are inconsistent with the text. Page 69 of the ERG has been updated. The first formula (-1/2 * ln(0.44)) would convert the proportion to an **annual rate** (0.410). The second formula (1-exp(-mr)) would convert the annual rate to an annual probability. The correct formula to convert the annual rate to a monthly probability would be (1-exp(-r/t)) where *r* is annual rate and *t* – (1-exp(-0.410/12) = 0.034). The proposed amendment is not correct.

Issue 4

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
pg 89. "Worksheet	Please delete.	The name of the parameters	Not a factual inaccuracy.

Costs_QALYs_noNo tx: No recur and no treatment health state costs, the duration is incorrect (see MS Table B-31) £102 0 - 2 years, £94.83 2 - 4 years, £51 4 - 6 years, £29 6+ years."		used in our excel formula was misleading, but there was no calculation error in the model.	No change necessary. As stated there is an error in the model for the medical cost using a duration that differs from reported in MS Table B-31.

Issue 5

Description of problem	Description of proposed amendment	Justification for amendment	
pg90 "The ERG has not been able to ascertain the specific reasons for the differences between the results, however it notes that the approach taken to model RFS and the HRs used has changed between the appraisals."	Please add a statement that we now have patient level data for two RCTs, with follow up out to five years whereas, previously, this was not available.	Please note that the data available in the previous appraisal related only to the ACOSOG trial. The ICERs for 3 years of treatment versus no treatment were entirely modelled on extrapolations from the 1-year data, whereas now we have additional information from the SSG trial. It should also be noted that, at that time, we had not been given access to patient-level data and so were reliant on digitised estimations of the data.	This is not a factual inaccuracy. No change necessary.

		This analysis has used patient-level data from both the ACOSOG and SSG studies.	

Issue 6

Description of problem	Description of proposed amendment	Justification for amendment	
In various places across the document, the EORTC study is noted as 62064, when it should be 62024.	Change all mentions of 62064 to 62024	The EORTC study number which is currently listed relates to a different study (non GIST), which could be confusing.	Amended accordingly (ERG report pages 7, 8 and 12)