1. Executive summary

Imatinib therapy is a proven and effective treatment for metastatic/unresectable gastrointestinal stromal tumours (GISTs), which was originally appraised and approved for use by NICE in this patient group in England and Wales in October 2004 (NICE TA86). These current recommendations endorse the use of 400mg imatinib as first-line treatment for people with KIT (CD117)-positive unresectable and/or KIT (CD117)-positive metastatic GISTs. Within these recommendations an increase in the dose of imatinib is not recommended for patients receiving imatinib who develop progressive disease after initially responding.

The scope for this part-review of TA86 is limited to the treatment of GISTs that have progressed on imatinib 400 mg/day, and to appraise the clinical and cost-effectiveness of imatinib at escalated doses of 600mg or 800mg. The scope of the appraisal is to compare such an approach to sunitinib and/or best supportive care (BSC).

However, the evidence base for sunitinib relates to its use after failure of imatinib dose-escalation, and there are currently no head-to-head trial data comparing imatinib and sunitinib. The possibility of conducting an indirect comparative analysis is severely limited because the patient populations in the imatinib and sunitinib trials are different in that approximately 80% of patients in the pivotal sunitinib trial[1] had failed imatinib dose escalation up to 800mg before entering the study. Sunitinib thus represents a third line treatment, rather than second line as per the scope of this evaluation. This makes it difficult, if not impossible, to conduct a robust and plausible indirect comparison of the two technologies.

Since the publication of TA86, clinical practice has evolved to consider dose escalation to a daily dose of 600mg or 800mg, when patients progress on the standard daily dose of 400mg. Such clinical practice is also reflected within UK National GIST Guidelines, which recommend dose escalation of imatinib to 800mg/day in the event of tumour progression[2]. These recommendations have been based on the clinical data available demonstrating that approximately one-third of patients achieve a response (partial response or stable disease) with imatinib 800mg/day[3,4]. It is further recommended by these guidelines that changing treatment to sunitinib should only be considered after patients have shown progression on imatinib dose escalation.

In summary, clinical practice has evolved to include imatinib dose escalation for patients whose disease progresses, to the benefit of patients. Furthermore this clinical experience has resulted in inclusion of imatinib dose escalation in the UK National GIST Guidelines. However, due to the limited amount of data available from the key clinical studies and the paucity of data comparing imatinib dose-escalation to sunitinib and BSC, we are unable to submit a sufficiently robust economic analysis which meets the scope of this appraisal.