4.6.3 Uncertainties surrounding the reliability of the clinical effectiveness

The main uncertainties in the clinical evidence primarily relate to duration of treatment and generalizability to the UK population. Further details are provided below.

Duration of treatment

The duration of treatment of vedolizumab in the GEMINI II trial was 52 weeks, followed by enrolment in the ongoing GEMINI LTS study. As a result, the long-term efficacy and safety of vedolizumab is unknown and the optimum duration of therapy remains unclear. There are no data on strategies for withdrawal of the drug in those on maintenance therapies or with respect to how to predict instances in which this can be successfully achieved. The SmPC for vedolizumab[9,10] recommends monitoring and reporting of any suspected adverse reactions after authorisation especially for new onset or worsening of neurological signs and symptoms.

Generalizability to the population of England and Wales

In GEMINI II,[11] at induction phase, patients were predominantly white (89.2%) with a mean age of 36.1 years. The mean body weight was 69.8kg and 46.6% were male. The mean duration of disease was 9 years, patients had a mean CDAI score of 324, and the mean faecal calprotectin score was 1,254. In GEMINI IIII,[12] most patients were white (90%). The mean age was 37.9 years, mean body weight was 70.4kg and 43% were male. Median duration of disease was 8.4 years in the vedolizumab group and 8 years in the placebo group. Patients in the vedolizumab group had a mean CDAI score of 301.3, and 313.9 in the placebo group. Median faecal calprotectin score was 1148.1 in the vedolizumab group, and 1426.5 in the placebo group. It should be noted that the faecal calprotectin in the GEMINI trials was deemed to be high, indicating that patients may had had significant active inflammation. Although information on the number of UK-based study sites was not available, it appears that very few were used and very few UK patients included in either GEMINI II[11] or GEMINI III.[12] In comparison, a large number of study sites were US-based. In the US, patients were required to have failed either an immunomodulator (6-MP or azathioprine) and or an anti-TNF-α agent, whilst outside of the US, failing corticosteroids alone was sufficient for study entry. It is unclear to the ERG how the different criteria might have impacted on the study results. The trials also assess response in the induction phase earlier than would be done in the UK, at six weeks. As such, the population entering the maintenance phase in GEMINI II is not fully representative of the UK spectrum, as patients who take longer to respond are excluded. This could conceivably lead to an overestimation of maintenance treatment effect, if these patients are also less likely to maintain a response when in remission.