Comments on ACD – Fingolimod for the treatment of highly active relapsing-remitting Multiple Sclerosis

3.8 (page 10 of 48)
The model is based on a Markov cohort approach and estimates disease progression through 21 disability states that are defined by EDSS score (ranging from 0 to 10) and account for disability for patients with relapsing–remitting multiple sclerosis (10 states), patients with secondary progressive multiple sclerosis (10 states) and death. *In each cycle of the model, a patient with relapsing–remitting multiple sclerosis can progress to a worse EDSS state or remain in the same state.*
Comment – patients with RRMS can experience a significantly worsening EDSS score during relapse and can return a much improved EDSS over time. This time span is not predictable.

3.8 (page 10 of 48)
People with an EDSS score greater than 6, or with secondary progressive multiple sclerosis, are assumed to receive best supportive care.
Comment - people with an EDSS greater than 6 cannot be assumed to only receive best supportive care as it may be a transitory score

3.20 (page 15 of 48)
The ERG also noted that the results from the manufacturer's mixed treatment comparisons did not yield clear differences between the beta interferons in patients with relapsing– remitting multiple sclerosis in terms of disease progression and annualised relapse rates. It cautioned that a comparison solely with Avonex could underestimate the ICER of fingolimod and *therefore reasoned that a comparison with best supportive care would have been more appropriate.*
Comment – a comparison with Tysabri would be more appropriate and BSC only appropriate at end stage MS when all other treatment options are inappropriate

4.3 (page 24 of 48)
The Committee heard from the clinical specialists that after a suboptimal response to the first disease-modifying treatment used, clinicians are likely to either offer a different beta interferon or glatiramer acetate, or offer the patient a higher dose of beta interferon (such as Rebif-44). *The Committee also heard that clinicians are generally reluctant to stop treatment altogether after a suboptimal response.*
Comment – this clinical decision is made as suboptimal response does not necessarily represent treatment failure and discontinuation of treatment could

initiate potential deterioration in disease. In this case scenario BSC would still not represent the most effective care choice.

4.18 (page 33 of 48)
The Committee heard from the *ERG that its clinical advisers had estimated that approximately one-third of people with relapsing–remitting multiple sclerosis whose disease has a suboptimal response to beta-interferon treatment will receive best supportive care in the UK. The Committee heard from the clinical specialists at the meeting that this estimate was likely to be correct.*
Comment - The notes do not identify the clinical specialists but I do not remember agreeing with this estimate and I have added additional comment below. My Neurologist colleagues would not concur with this estimate on use of best supportive care in place of disease modifying therapy either.

The Committee therefore considered that best supportive care should be included as a comparator, together with a mix of beta interferons (with the proportions for the beta interferons determined based on market share data from the Prescriptions Pricing Authority). The Committee estimated that the ICER for fingolimod compared with a
comparator made up of equal proportions of best supportive care, Avonex and Rebif-44 using the manufacturer's revised model, would be approximately £40,000 per QALY gained (patient access scheme included). The Committee concluded this to be a starting point for its decision, and noted that using a probabilistic analysis (see section 4.9) and the following, more plausible assumptions, would increase this ICER:
Comment - this is a misunderstanding of the supposition made by the clinical experts that roughly a third of patients who might be considered eligible for disease modifying treatment will defer that treatment option and take a "watchful wait" position (this could be possibly considered BSC). It is highly unlikely that as much as a third of the suboptimal response group will actively receive *only* BSC as treatment of choice. Discontinuation of treatment is a rare decision as it risks an unknown outcome in terms of disease activity. This is a choice likely to be made only when someone is in the end stage of their MS.

Submitted by Victoria Matthews
MS Specialist Nurse
January 5th 2012