The guideline comes down in favour of episodic treatment. However, the evidence base presented seems to lack any data on the effectiveness or side effects of episodic treatment. The trials quoted provide data on the effectiveness and safety of a single treatment course and similar data on regular maintenance treatment. However, none of the trials presented provide any information on the effectiveness or safety of the recommended episodic treatment or how it may compare with placebo, with one-off treatment or with maintenance treatment. I am therefore rather confused by the lack of an evidence-base for the recommended episodic treatment. Concerns are mentioned that episodic treatment may lose its efficacy due to the development of antibodies to the treatment and that this might also result in increased incidence of side effects.

The guidelines must therefore address the fact that they are recommending a treatment for which they are not presenting any evidence of efficacy or safety. This is essential if these guidelines are to be considered to be in any way evidence-based. If the Review Committee really thinks that episodic treatment is the most appropriate treatment then they do have to provide the basis upon which they have concluded that it is effective and safe and superior to the other treatment options.

Reviewer 1.

1. Whether you consider that all the relevant evidence has been taken into account.

*The evidence presented appears to have been taken into account.*
2. Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence.

   This a complicated area but as far as it seems practicable, it appears that the summaries are reasonable interpretations.

3. Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.

   From the evidence provided, the provisional recommendations do sound suitable.

7 October 2008