Expert peer review on application for Human normal immunoglobulin (Additional dosage) -- Adults and Children

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes   No (if no, please provide reference and information)
      All studies which were used to support the Marketing Authorization Application in the European Union are included.

   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      The clinical efficacy of immunoglobulin replacement therapy in primary immunodeficiencies is well established. Studies with the new formulation support this observation. A superiority of the new formulation (20% IG) versus the established formulations (15% or 16% IG) is not shown.

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes   No (if no, please provide reference and information)
      All studies which were used to support the Marketing Authorization Application in the European Union are included.

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      Although there are no studies comparing new and old formulations head by head, there is the impression that there is no change in the spectrum and the frequency of adverse reactions.

   c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
   a. Have all relevant data on cost provided
      Yes   No (if no, please provide reference and information)
      There are no data on costs and the cost effectiveness of the new formulation versus the old formulations.

   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      While the cost effectiveness of immunoglobulin replacement therapy in patients with primary immunodeficiency is undisputed the cost effectiveness of subcutaneous administration versus the
intravenous administration is less well established, not to speak about relative cost effectiveness between different formulations of subcutaneous immunoglobulins (SCIGs). An advantage of the administration of SCIGs seems to be a more stable Ig concentration in plasma between administrations on the cost of more frequent administrations. That this translates in a better protection against infections seems not to be demonstrated by clinical data.

c. Please provide any additional relevant information with reference

A soft factor for SCIG is home treatment while the new formulation may lead to shorter infusion times (theoretically reduction by 25% compared to a 15% formulation) or less parallel infusion sites.

d. Is the product available in several low and middle income countries?

Approved in Argentina, applied for authorization in Brazil, Mexico and Peru.

4. Assessment of public health need

a. Please provide the public health need for this product (1-2 sentences)

There is a public health need for IVIG and SCIG, not specifically for a 20% formulation. However, there is also no convincing argument for exclusion of the 20% formulation.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

Not checked.

5. Are there special requirements for use or training needed for safe/effective use?

If yes, please provide details in 1-2 sentences

Yes, as for SCIGs listed in EML

6. Is the proposed product registered by a stringent regulatory authority?

   Yes   No

   FDA and EMA

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

This reviewer supports the proposal by the coordinator QSM to replace the listing of specific Ig concentrations by the range which is proposed in the draft European Pharmacopeia monograph (“protein concentration not less than 100g/l and not more than 220g/l”). However, as there is no obvious need to rush I propose to postpone the decision until the draft monograph is finalized and approved and until the applicant has demonstrated that the cost effectiveness of a treatment with 20% SCIG is equivalent to the cost effectiveness of a treatment with 15% or 16% SCIG.