hills@who.int 1st May 2007

Dr Sue Hill
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Health Technology & Pharmaceuticals
World Health Organization
CH-1211 Geneva 27

Dear Dr Hill,

Subject: Application for addition of subcutaneous immunoglobulins in section 11.2. human normal immunoglobulin method of WHO list of essential medicines for children

I am writing on behalf of the Primary Immune Deficiency [PID] committee of the International Union of Immunological Societies. We are delighted about the decision of the World Health Organisation (WHO) to create a list of essential medicines for children. The need to consider paediatric medicines separately is absolutely crucial to avoid any problems resulting from the absence of suitably adapted medicinal products for the paediatric population, such as suitable formulations and routes of administration.

We are also pleased that polyvalent human immunoglobulins have been included in the draft list of Essential Medicines List for Children, available on the WHO website. Many primary immunodeficiencies, life-long conditions treated with polyvalent human immunoglobulins, have their onset during childhood, so a proportion of the patients most in need of treatment with polyvalent human immunoglobulins are indeed children. With proper treatment these children will be enabled to live normal lives, avoiding life-threatening infections.

However we notice that whilst the intravenous and intramuscular modes of administration are included in the draft list for children, the subcutaneous mode of administration is not. Subcutaneous immunoglobulins [SCIg] are particularly used in and often preferred by paediatric PID patients and their medical advisers. This straightforward mode of administration offers advantages such as less cost, increased freedom of movement, more patient independence and the ability of parents/carers to administer their treatment at home or in local centres safely and easily. This makes SCIg particularly suitable for use in developing countries. Such products are only suitable for PID patients, since the limited amount given by this route is only appropriate for replacement therapy and not for immune modulation.

I enclose the formal submission for subcutaneous polyvalent immunoglobulins. The following factors summarise why subcutaneous administration should be added to the intravenous and intramuscular modes of administration of human normal immunoglobulins:

1) International Availability

Subcutaneous immunoglobulins are distributed and used worldwide – list attached to application.

2) Summary of comparative effectiveness in a variety of clinical settings

The effectiveness of subcutaneous immunoglobulins has been widely demonstrated – list attached to application.

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3) Summary of comparative evidence on safety

The safety of subcutaneous immunoglobulins has been widely demonstrated.

Attached is a table of publications demonstrating the excellent safety record of subcutaneous immunoglobulins given by rapid infusion since their introduction in the early 1990s. Whereas previous intramuscular preparations contained mercury as a preservative, this is not the case for these subcutaneous preparations.

4) Summary of Quality of life evidence

Attached is the data collected so far on the improved quality of life for children and adults. Supplementary data is available, though not yet published – see appendices.

5) Summary of the regulatory status of the medicine

The European Medicines Agency (EMEA) lists the therapeutic indications for the intravenous preparation of Polyvalent Human Immunoglobulins in its document CPMP/BPWG/282/00 (25 July 2002) 'Core SPC for Human Normal Immunoglobulin for Subcutaneous and Intramuscular Use' – this is also attached to application.

6) Other factors: other available and relevant information such as availability of pharmacopoeial standards, which pertain to subcutaneous immunoglobulins as well as the intravenous preparations, were included in our recent joint submission with the International Patient Organisation for Primary Immunodeficiencies (IPOPI) concerning the inclusion of polyvalent human immunoglobulins in WHO's List of Essential Medicines, - available on the WHO website at:
http://mednet3.who.int/EML/expcom/expcom15/reinstatement.htm

In conclusion, subcutaneous immunoglobulins are widely (and increasingly) used effectively and safely in the treatment of primary immune deficiencies, particularly in paediatric patients, though also in adult populations. The International Union of Immunological Societies (IUIS) therefore respectfully requests that subcutaneous administration be added to the WHO List of Essential Medicines for Children under section 11.2, complementary list, human normal immunoglobulin.

This will complete the proposed section, ensuring that the subcutaneous route of administration will also be considered as essential by all national authorities and other stakeholders seeking guidance from the new WHO list of essential medicines for children in their own countries.

Lastly, we would like to suggest the attached (adapted) text for the WHO Model Formulary (attached and embedded in the application).

I hope that our request for the addition of the subcutaneous method of administration of polyvalent human immunoglobulins in the new WHO list of essential medicines for children will be welcomed and endorsed by the WHO Expert Committee, for the sake of the paediatric population in need of this easily administered form of protective immunoglobulins.

Thank you for your consideration.

Yours sincerely,

Dr Helen Chapel on behalf of the International Union of Immunological Societies