PPTA
Plasma Protein Therapeutics Association

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Comments on the advice to the Commissioners and Commissioning Bodies

Dear Dr. Ewart, Dear Mr. Qualie, Dear Dr. O'Shaughnessy,

In October 2011, the UK Department of Health issued a document entitled "Commissioning Immunoglobulin: Advice to the Commissioners and Commissioning Bodies" which comments on the Second Edition Update: Clinical Guidelines for Immunoglobulin use.

Several new documents are introduced to contribute to the value of the Demand Management Plan. The Second Edition Update[i] now requires efficacy outcomes to be measured in all indications (except those patients with primary immunodeficiency) as stated in the document. We believe that improvement of documenting clinical outcomes will contribute to the existing clinical data to support the current clinical evidence for the use of immunoglobulin in different indications.

The statement in the comment document[ii] to the Second Edition Update, page 4, section 4,: "*All immunoglobulin products are considered generic and therefore the commissioners insist that, when prescribers begin treatment on a new patient, the product with the lowest acquisition cost should be used unless compelling reasons for using the alternative have been specified as part of the IAP's approval*", implies that Ig products are generic and clinically interchangeable.

We believe that it is necessary to clarify the position regarding the desirability to maintain chronic patients, and those patients already being treated with immunoglobulin, on their existing treatment. An additional sentence, when this publication is reprinted, sooner if possible should be added after the above quoted paragraph to say, *"Existing patients already being treated with immunoglobulin, and particularly chronic patients, should only be switched to an alternative immunoglobulin in exceptional circumstance and then, following initial infusion with a different immunoglobulin, careful monitoring."*

Returning to the "generic" consideration, PPTA has serious concerns regarding the message this sends to the prescribing clinicians and the patients who are dependent on these therapies[iii]. It is also counter to regulatory principles for the assessment and approval of therapeutic claims for Ig products.

Medicinal therapies are broadly categorized as pharmaceuticals and biologics. Both types are generally composed of a molecule – the active ingredient (AI), which is responsible for the therapeutic action – and a number of additives or excipients which have no therapeutic action but are included in order to assist stability, solubility, etc., of the AI. In pharmaceuticals, the AI is derived from chemical synthesis using fully specified ingredients, to result in molecules that are generally small and well-characterized. These constitute the majority of drugs in medicinal practice.

In biologics, the AI is derived from a biological source (e.g. blood, tissue, cell culture, etc.). Biological AIs are isolated using complex processes that can have important effects on the properties of the AI. Not only the AI, but also the excipients and impurities, can vary between the same biologic produced by different manufacturers, leading to the different safety and efficacy profiles. IgG therapies approved by the major regulatory agencies for marketing are all safe and efficacious, but being different products they show differences in relative efficacy in different patients and different adverse event profiles. It is for these reasons that the modern concept of Ig therapy, like much of modern medicine, hinges on individualised treatment tailored to the specific needs and features of each individual patient. Clearly, the lowest common denominator policy proposed by the Department of Health runs counter to this important therapeutic principle.

Knowledge of the particular features of each preparation that might precipitate adverse events in patients at risk, such as the type of excipient and the protein concentration, is important for treating clinicians so as to be able to choose the most appropriate therapy. We are apprehensive that short sighted policies attempting to

cut costs at the expense of good care will result in increased patient morbidity and hence, increased medical costs.

To summarise, all immunoglobulin products are different, product characteristics are reflected in the coreSPC for the specific products. The safe and effective use of IGIV requires attention to numerous issues that relate to both the product and the patient is also stated by many physicians.

We propose that, to ensure optimal safety and efficacy issues when prescribing immunoglobulin it is of extreme importance that physicians have the opportunity to choose between products, which cannot be guaranteed when the lowest acquisition cost should be used in purchasing immunoglobulin products. The choice of product should be made by the physician and not by the product purchase process of the hospital pharmacy. Monitoring safety and efficacy as mentioned in the Second Update advice to commissioners should not be influenced by cost drivers limiting physicians choice.

We would like you to consider this when you review the current published statement as mentioned in the third paragraph of this letter.

Sincerely Yours,

Charles Waller
PPTA, Vice-President Europe

[i] Department of Health, 2011. *Clinical guidelines for immunoglobulin use: update to second edition.*

[ii] Department of Health, 2011. *Commissioning Immunoglobulin: Advice to commissioners and commissioning bodies. Comment on second update: Clinical guidelines Immunoglobulin use*.

[iii] International Patient Organization for Primary Immunodeficiency (IPOPI), 2012, *Access to Immunoglobulin Therapies for patients living with a Primary Immunodeficiency*. Position statement, 8 May 2012.

Immune Deficiency Foundation (IDF), 2011, *IDF Medical Advisory Committee Resolution on Product Choice for Immunoglobulin Replacement Therapy .* Resolution, 19 January 2011.