8 March 2018, reviewed in April 2026

IPOPI POSITION STATEMENT

Access to immunoglobulin therapies for patients living with immunodeficiencies

This statement outlines IPOPI's position on the critical importance of ensuring access to the most appropriate immunoglobulin (Ig) therapy for patients living with immunodeficiencies. This includes primarily patients living with a primary immunodeficiencies (PIDs) and associated conditions but also for certain secondary immunodeficiencies (SIDs). IPOPI emphasizes that treatment decisions regarding Ig therapy should always be based on a doctor-patient shared decision-making process. IPOPI is concerned by recent developments in several countries that may restrict access to the most suitable Ig therapy for individual patients or compel PID patients to switch between Ig therapies for non-clinical reasons.

A significant number of immunodeficient patients depend on Ig therapies, which are life-saving biological therapies derived from human plasma. Ig therapy is the most important treatment for a majority of PIDs, as it helps to protect patients against a range of infections and to reduce autoimmune symptoms. It is used to treat various PIDs, including but not limited to common variable immunodeficiency (CVID), X-linked agammaglobulinaemia (XLA), X-linked hyper-immunoglobulin M (Hyper-IgM) syndrome, Ataxia Telangiectasia (AT), Wiskott-Aldrich syndrome (WAS), severe combined immunodeficiency (SCID) and other combined immunodeficiencies. For these patients, Ig therapy is a life-long, life-saving treatment which must be administered regularly and for which there is no alternative treatment. Ig therapy is also increasingly used to treat patients living with certain SIDs. While some SID patients will require Ig therapy[i], others will not. Ig therapy is primarily used for SID patients with severe antibody failure due to underlying diseases or medical treatments[ii]. In some instances, Ig therapy for SID may also only be required on a short-term basis until the immune system recovers[iii].

Ig therapies are not generic medicines. Each Ig therapy is a unique biological medicinal product and as such Ig therapies are not interchangeable. Unlike chemically-based pharmaceuticals, biological medicinal products are composed of an active ingredient derived from a biological source (human plasma in the case of Ig therapies). The active ingredients are isolated using complex processes that will have an impact on the properties of the final product. It is well established that the differences in the processes used to manufacture the products will affect individual patients' tolerability, risk of adverse events, infusion rate, and potential efficacy. Factors such as the volume load, the type and concentration of the excipients used in the preparation, the protein concentration, the osmolarity, the pH and the formulation (liquid or lyophilised) will all affect individual patient's tolerability to a given therapy[iv].

These variations alter the final product and some Ig therapies may cause specific anaphylactic reactions in patients and a personal approach should be taken in order to provide for their specific needs. There are several publications outlining the fact that Ig therapies are not interchangeable and that patients experience adverse reactions when they change from one immunoglobulin product to another[v,vi,vii,viii,ixx]. In addition, the mode of administration can also have an impact on how well an individual patient will tolerate a particular Ig therapy. Whilst some patients may tolerate an intravenous product but not a subcutaneous product, others may not and vice versa[xi]. Calls for individualization of patient treatment in PID highlight the

importance of patient input into decision-making when choosing the most appropriate therapy[xiixiii].

It should also be noted that the impact of a poorly tolerated Ig therapy will not only affect the patient's health but will bring about significant unnecessary budgetary consequences as the patient will more likely require additional treatments (i.e. antihistamines, extended treatment, hospital visits etc); thus the importance of ensuring patients get the most suitable therapy to their individual conditions and tolerability profile. This also ensures that the patient has a better quality of life, less episodes of ill health and less additional medication.

Importantly, the World Health Organisation has acknowledged the need for patients with PIDs to have continued access to the treatment that is better adapted to their needs and has included immunoglobulins in the List of Essential Medicines for adults[xiv] and paediatric populations[xv]. Moreover, in a recent meeting of the Wildbad Kreuth III organised by the Council of Europe's European Directorate for the Quality of Medicines & Health Care, with expert nominees from 36 Council of Europe member states, together with representatives from observer countries and regulatory agencies (such as the EMA and FDA) agreed on a consensus statement that recognised, amongst other items, that "*Ig products differ from one another*[xvi]". It has also been recognised that "*the efficacy and side effects […] may differ from product to product, and even from batch to batch (e.g. TEE and hemolysis)*[xvii]". These side effects have been further developed in the medical literature and encompass, amongst others: anaphylactic reactions, thrombosis, aseptic meningitis, stroke, seizure, loss of consciousness, and acute respiratory distress syndrome[xviii].

IPOPI strongly recommends that necessary measures should be taken at national level to ensure PID patients can have continuous and equal access to the Ig therapy that suits them best. Hospitals, pharmacists, health insurances should provide the widest range possible of safe effective Ig therapies, for both intravenous and subcutaneous administration routes, including also a choice in dosage and concentration. Access to Ig therapies for PID patients, including the selection of the most appropriate Ig therapy for an individual patient, should always be achieved through a doctor-patient shared decision-making process and not dictated by financial considerations. Prescribing physicians and other healthcare professionals should always have the flexibility to choose the most appropriate therapy for their patients.

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