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Patients with primary immunodeficiency should have access to safe, efficacious, and high-quality immunoglobulin therapies

Primary immunodeficiencies (PIDs) are a large group of more than 480 rare and chronic genetic disorders in which the immune system does not work adequately or at all. People with PIDs are prone to severe and recurrent infections, autoimmune diseases and dysregulated inflammation. When PIDs are left underdiagnosed or are misdiagnosed, the defective immune system leads to illness, disability, permanent organ damage and even death. Around 60% of patients with a PID need immunoglobulin replacement therapies (Igs) throughout their lives to keep the levels of antibodies within a suitable threshold to fight life-impairing or life-threatening infections. Patients with PIDs do not have any alternative treatment options.

Immunoglobulin replacement therapies are plasma-derived medicinal products that require healthy donors to give their plasma either through plasmapheresis or from a blood donation for the development of these medicines. Because Ig treatment products are sourced from human blood, it is very important to ensure that products being considered for use are safe and free from infection from blood-borne pathogens. The combination of appropriate donor selection procedures, screening with the current generation of standard serological tests and the fractionation of the medicines by today's manufacturing processes with attention to good manufacturing practices ensure that Igs are good and safe therapeutic products. Ig therapies are prepared from large pools of plasma obtained from thousands of healthy donors, safeguarding the diversity of the immunoglobulin repertoire that far exceeds that of an individual, providing the patient with a wide spectrum of antibodies to specific pathogens that are found in the general population.

A robust regulatory framework is therefore crucial. As such, it is a key element that national regulatory agencies, responsible for the licensing, regulation and control of medicinal products ensure that the medicinal products under their jurisdiction comply with the level of safety, efficacy and quality necessary to be put into the market. To properly assess a product, national regulatory authorities must have information on:

- the safety and the quality of the plasma raw material: the safety of the raw material can only be ensured by the fractionator through the use of suppliers that exclude high-risk donors and use good quality viral screening tests.
- the manufacturing process, including: manufacturing steps and related controls; viral inactivation and/or removal steps, process consistency and batch release specification.
- on the final product, including: the potency of the product and shelf life, other markets where the product is available, a product history and the clinical studies demonstrating the product's efficacy.

The reality of the resources available to different countries in terms of regulatory capacity in the area of plasma-derived medicinal products varies greatly. Notwithstanding the differences, regulatory agencies in countries with no established arrangements for regulation of plasma products should ensure the safety and quality of plasma products by:

- Forming alliances with similarly placed national regulatory authorities.
- Working directly with manufacturers, not through brokers or agents.
- Considering products licensed through established national regulatory authorities first.

- Establishing arrangements for pre-selection and audit of suppliers.
- Focusing on evidence of plasma quality and secure manufacturing rather than on testing finished product.
- Consulting with independent institutions and experts.

In addition, immunoglobulins are biological drugs, whose properties are dependent on the individual manufacturing processes used to generate them. As such, immunoglobulins cannot be considered as generic drugs, the properties of which can be transposed between one brand of product and another. With biologicals, “the process is the product” and each product needs to be trialed for its effects on patients before it is approved for general marketing.

Igs are life-saving products for patients with PIDs and many other conditions. It is therefore crucial that these essential medicines follow stringent manufacturing process and a solid regulatory oversight that takes into account and uses well-established regulatory principles to ensure that they are safe, efficacious and of good quality for the patients they are meant to treat. An IPOPI Guide for users, assessors and funders on the safety and efficacy of immunoglobulin therapies for primary immunodeficiencies is available on the IPOPI website here.