

Position statement on managing immunoglobulin replacement therapy for primary immunodeficiency (PID) / Inborn Errors of Immunity (IEI) patients during stock shortage

By the Primary Immune Deficiency Working Group (PIDDSA) of the Allergy Society of South Africa (ALLSA) and the Medical Advisory Panel of the Primary Immunodeficiency Network of South Africa (PiNSA)

Summary statement

Immunoglobulin replacement therapy is a life-saving treatment for patients suffering from antibody deficiency secondary to PID/IEI. Most these conditions are prescribed minimum benefits (ICD10 coding D80.1-84.9).

Stock shortage of registered immunoglobulin products occurs in South Africa, leaving PID/IEI patients vulnerable. Immunoglobulin therapy cannot be discontinued by PID/IEI patients during stock shortages.

We strongly call on:

- i) **Doctors, patients and patient support organisations to assist patients with the burdens of frequent, unanticipated product changes**
- ii) **Medical Funders to be responsive to request for short-term use of alternative, usually more expensive products during stock-outs**
- iii) **Suppliers of immunoglobulin to improve the supply chain process and limit stock shortages**

Immunoglobulin therapy cannot be discontinued when stock shortages occur

Replacement immunoglobulin therapy (IRT) is life-saving and cost-effective for patients with hypogammaglobulinemia or functional antibody deficiencies owing to primary genetic immunodeficiencies/IEI. Most patients require 0.4-0.6g/kg/month to provide protective antibody levels and prevent serious bacterial infections. PID/IEI patients are completely reliant on this expensive and logistically challenging therapy. Failure of regular replacement therapy will lead to a dangerous decline in protective antibodies within 1-3 months, given a half-life of approximately 21 days for IgG. A single serious bacterial infection can lead to death or serious morbidity, such as the neurological impairment that may result from bacterial meningitis. ***PID/IEI patients cannot discontinue life-saving IRT during stock shortages***

The route of administration can be changed to ensure Immunoglobulin treatment continues

PID/IEI patients can receive IRT via either an intravenous or subcutaneous routes, with largely equal efficacy but distinct side-effect profiles, pharmacokinetics and administration challenges. Thus, it is reasonable in times of shortage to consider changing the route of administration to ensure that IRT treatment interruptions are limited. ***However, changing the route of administration may NOT be appropriate if the reason for an original change from the intravenous to subcutaneous route was serious side-effects.*** Patients with medical reasons for using the subcutaneous route of administration for IRT must be fully funded and supported to use an alternative available subcutaneous product as this is a PMB condition.

The additional expense of short-term product change must be paid by medical funders when change is forced by stock shortage in PMB conditions

Product change for PID/IEI patients during times of stock shortage in many instances may mean using a more expensive alternative therapy to avoid treatment interruption. It is mandatory that medical funders support the additional expense of short-term product change. It is unacceptable that patients be expected to provide large co-payments to support the use of more expensive alternative products.

Patients should call on treating physicians, patient organisations and medical funders to help ensure treatment interruptions are avoided

Stock shortages and the resultant need for product change is a challenging situation for patients and their treating clinicians. We need to act fast to ensure that antibody levels do not drop dangerously low. We would encourage individual patients to contact treating physicians and vice versa to notify them of available stock and make an immediate plan. Treating clinicians then need to liaise with the patient and funder to ensure continuity of IRT. Patients can also reach out to their patient organisation PINSA to assist them in ensuring continued therapy through direct support and more widespread advocacy.

Available products need to be increased and existing supply chains strengthened

Immunoglobulin therapy is derived from donor plasma through a process of fractionation. It is complex to manufacture and make safe for patient administration; it is expensive and dependent on donor availability. SA has only one fractionator, that provides an intravenous and intramuscular immunoglobulin product. There are two other registered, imported products. Several patients access imported products via section 21 MCC approvals. ***This is a very limited number of products and suppliers by international standards. The consequence of this is inevitable stock shortages, which is a catastrophe for vulnerable patients' dependent on these products.*** All suppliers in SA have experienced stock shortages at some time point. Thus, we call on our local manufacturers to make renewed efforts to ensure that the current problem is resolved and that future problems are avoided. We also call on government to facilitate the registration of new products in the SA market to allow for the unavoidable fluctuations in plasma donation. The current situation is untenable and may cost lives.

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