

Section 7

Managing immunoglobulin stock shortages

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Failure of regular IRT will lead to a dangerous decline in protective antibodies within one to three months, given the half-life of approximately 21 days for IgG. A single serious bacterial infection can lead to death or serious morbidity, such as neurological impairment from meningitis.

IRT preparations are a finite source.

South Africa has only one fractionator, the National Bioproducts Institute (NBI), that have an IV and IM Ig product currently registered.

Other available products are imported, with currently only one other IV and one SC product registered in South Africa at the time of this guideline development. Other IV and SC products can be access on an individual patient basis via section 21 (South African Health Products Regulatory Authority (SAPHRA) approval.)

The major consequence is stock shortages, a catastrophe for vulnerable patients, dependent on these products.

Patients, physicians, and funders need to have a plan for inevitable supply shortages. We would encourage individual patients to contact treating physicians and vice versa, to notify them of available stock and make an immediate plan.

Treating physicians need to liaise with the patient and funder to ensure continuity of IRT. The best alternative product for the patient needs to consider the specific medical indication including guideline-based indications for SCIg, licensing and cost.

Patients receiving SCIg for a specific medical indication e.g., debilitating side effects from IVIg, should receive an alternative SCIg preparation without funding penalty as per the Regulation 15I(c) of the Medical Schemes Act 131 of 1998. Regulatory bodies, such as SAHPRA, need to be alerted as specific products may need approval via section 21 on an individual patient basis.

Long-term management of IRT preparations requires improved data monitoring and determination of the latent therapeutic demand (LTD). This is difficult to achieve without good country-specific epidemiology data and treatment guidelines.

A recent modeling study from the American Immunodeficiency Network, estimated that the mean (SD) LTD for all PIDs is 105.1 \pm 88.5g per 1000 population, with CVID contributing the most.^[1] Every effort should be made to model local data to aid accurate forecasting.

Other useful approaches include reservation of stock based on registry patient location across the country.

The limited natures of registered products and dependence on plasma donation will mean inevitable stock shortages for South African patients.

The following are suggested measures that can be taken by patients and providers to mitigate the associated risk:

- Product dose adjustment: during stock shortages, patients and physicians should discuss the lowest dose necessary to maintain IgG levels >4g/L necessary to prevent serious bacterial infections. Absolute dose reduction or dose interval lengthening are options

- Contacting larger distribution pharmacies outside of your particular area where there may be product still available
- Commencement or initiation of antibiotic prophylaxis may offer some protection against increased infections
- All PID patients should be vigilant about infection control measures e.g., hand washing, caution with raw food and unfamiliar water sources; additional measures such as limiting air-travel and use of respiratory masks may be required with decreased IgG titers.

References

1. **Stonebraker JS, Farrgia A, Gathmann B, et al.** Modeling primary immunodeficiency disease epidemiology and its treatment to estimate latent therapeutic demand for immunoglobulin. *J Clin Immunol*, 2014 Feb;34(2):233-44.

UPDATED DECEMBER 2021