To: Trust Medical Directors
Hospital Chief Pharmacists
Immunoglobulin Assessment Panel
Members

NHS England and NHS Improvement
Skipton House
80 London Road
London
SE1 6LH

10 November 2021

Dear Colleagues,

Guidance on switching immunoglobulin (IG) products for existing patients on long term treatment

Please cascade the enclosed guidance and patient information leaflet to your Trust's clinicians, pharmacists and the Immunoglobulin Assessment Panel (IAP) to support the planned switching of immunoglobulin products.

A Department of Health and Social Care Medicine Supply Notification was issued to Trusts on 19 July identifying growing international demand for IG. Global conditions related to the COVID-19 pandemic have also impacted on the donation of plasma in the US and Europe. The scale of plasma donations shortage globally has been estimated at a 20% reduction in overall donations. In the UK, supply remains challenging and in some regions shortages may still occur.

The MSN outlined at that time which presentations of immunoglobulin are experiencing a decreased volume. While the overall supply situation on IVIg requires careful stewardship, there are currently supplies of subcutaneous immunoglobulin (SCIg) and Facilitated subcutaneous immunoglobulin (fSCIg). Trusts are advised to speak to suppliers on stock levels before commencing treatment.

To support clinicians to switch IG products where clinically safe, clinicians on the Specialised Immunology and Allergy Clinical Reference Group (CRG) have developed guidance (as below) outlining the key principles that should guide switching. This guidance has been supported by the UK Primary Immunodeficiency Network (UKPIN) and the Association of British Neurologists (ABN). These principles were used to guide safe switching in 2017-18 and are being re-issued as a reminder to help with the current exercise.

It is recognised that patients and clinicians may have reservations about switching. However, the scale of the current supply situation is such that action is likely to be required for a proportion of patients.

Yours sincerely,

<Supplier Manager/Local Commissioning Team signature >

Cc: Trust Chief Pharmacist

SRIAP Chair

Specialised Immunology and Allergy Clinical Reference Group (CRG) Guidance

The key principles how outcomes for patients can be safeguarded when switching products

Ensure no adverse clinical outcomes

The overriding principle that should guide switching is to ensure patients are not adversely affected, either in terms of clinical outcomes or product-associated adverse effects.

All IG products have a licence for a common group of indications (across antibody replacement and immunomodulation) that has been obtained following the stringent quality requirements of regulatory agencies. This includes evidence of meeting the minimum requirements for prevention of blood-borne virus transmission. The introduction of rigorous donor plasma screening and nucleic acid testing coupled with anti-viral measures has greatly reduced the risk of Hepatitis C viral transmission by IG to approximately 1:1,000,000 (data extrapolated from blood transfusions). Consequently, Hepatitis PCR testing or storage of serum prior to switching is no longer considered essential, but individual centres may wish to consider doing so if deemed necessary by local protocols.

Notwithstanding, the differences in manufacturing processes and the absence of head-to-head trials comparing products from different manufacturers, the available evidence to date and clinical experience suggests that different IG products are likely to be of equal clinical efficacy.[1]

Ensure that product is well tolerated

While previous experience of switching IG products in response to product withdrawal and adverse effects data suggest that this process can be safely undertaken, a minority of patients may experience mild to moderate infusion-related adverse effects.[2,3]

Analysis of patient experience from 30 immunology centres involving 802 product switches in 2017-18 showed that switching products can be safely undertaken, with no serious adverse reactions, but required considerable staff time and resources.[4]

For this reason, it is essential that patients undergo individual risk assessment and are closely supported during the switching process. For the large numbers of patients on home IG therapy, this may necessitate a visit to hospital where they can be shown the practicalities of using the new product and demonstrate tolerability and safe use. In some cases, therapy will be able to be switched with virtual or phone support at home if clinically considered appropriate by the treating team.

Patients should be given the reassurance of being able to revert to their original product, if it remains available, or another alternative should they experience **serious** adverse reactions on switching. It is essential to emphasise that the standard of care provided to patients will not be diminished by the switch and that patients will continue to be fully supported by their clinical team.

Ensure treating centre capacity is sufficient to safely manage switch process

For major centres it is possible that a significant proportion of the patients may need to be supervised and supported during this process. The process of switching a whole cohort of patients in a single centre may take six months or longer. Depending on the

local supply situation, it may be necessary to switch patients over a shorter time. Local discussions at trust level will be required to determine how best to manage this transition.

Ensure consent

It is important that patient consent is obtained and arrangements for switching are sufficiently flexible to take into account patients' mobility and individual circumstances.

It is hoped that this advice, in addition to the patient information leaflet, will facilitate switching of IG products where this is required for individual patients.

Further questions

Should you have any queries on the above or wish to receive a copy of the patient information leaflet, please do not hesitate to contact:

Dr Siraj Misbah
Consultant Immunologist and Chair, Programme of Care for Blood and Infection
Email: Siraj.Misbah@ouh.nhs.uk

or

Dr Tomaz Garcez
Consultant Immunologist and Chair, Specialised Immunology and Allergy Clinical Reference Group
Email: Tomaz.Garcez@mft.nhs.uk

References

[1] Misbah SA. *Should therapeutic immunoglobulin be considered a generic product: An evidence-based approach*. J Allergy Clin Immunol Pract 2013; 1: 567-72

[2] Ameratunga R, Sinclair J, Kolbe J. *Increased risk of adverse events when changing immunoglobulin preparations*. Clin Exp Immunol 2004;136: 111-3

[3] Aghamohammadi A et al. *Adverse reactions of prophylactic intravenous immunoglobulin infusions in Iranian patients with primary immunodeficiency*. Ann Allergy Asthma Immunol 2004; 92: 60 -4

[4] Bethune C, Herriot R. *Switching immunoglobulin products, what are the implications? Result of 2018 census of immunology centres*. Clin Med (Lond). 2019 May;19(3):201-204.

The following products are impacted

Strength	Product	Level of supply shortage*
10% IVIg	Gamunex (10%)	Severe
10% IVIg	Privigen	Severe
5% IVIg	FlebogammaDIF (5%)	Moderate
SCIg	Hizentra	Severe
SCIg	Hizentra PFS	Minimal

*Minimal <10% normal stock levels; moderate 10-30%; severe over 30%

(The listed items have been updated from the July MSN and are correct at 5 November 2021)

Alternative products that should be considered for switching

Strength	Product
10% IVIg	Intratect (10%)
10% IVIg	Iqymune
10% IVIg	Kiovig
10% IVIg	Panzyga
fSCIg	HyQvia
SCIg	Cutaquig
SCIg	Cuvitru
SCIg	Gammanorm

(The listed items have been updated from the July MSN and are correct at 5 November 2021)

Other products where stock levels should require no switching

Strength	Product
10% IVIg	Octagam 10%
10% IVIg	Gammaplex (10%)
5% IVIg	Octagam 5%
5% IVIg	Gammaplex (5%)
5% IVIg	Gammagard
5% IVIg	Intratect (5%)
SCIg	Subgam

(The listed items have been updated from the July MSN and are correct at 5 November 2021)

Department of Health & Social Care

NHS

Medicine Supply Notification

Reference: MSN/2021/035

Human normal immunoglobulin

Tier 2- medium impact*

Date of issue: 19/07/2021

Summary

- There is a decreased volume of some presentations of immunoglobulin (see annex) leading to a shortfall of 3% to 14% when compared to predicted volumes available for use in the UK until December 2021. This is due to a global decrease in plasma collections.
- Trust level allocations have now been cascaded to all trusts in England and volumes agreed with suppliers.
- Trusts are advised to assess patients who require long term immunoglobulin therapies and use allocations to minimise the need to switch between presentations and brands.
- NHS England and NHS Improvement's (NHSEI) Commercial Medicines Unit (CMU) has sourced additional 10% intravenous immunoglobulin (IVIg) (Panzyga®) which should be used to supplement a deficit in available 5% and 10% presentations. This stock should be used as first line treatment for any indicated acute conditions and for long term conditions if it's the only available product.
- Panzyga® stock has been allocated to each of the regions and will be assigned to Trusts with the most significant deficits by the Regional Pharmacy Procurement Specialists (RPPS). Patients receiving homecare intravenous or subcutaneous immunoglobulin should move to deliveries every four weeks with immediate effect.
- RPPSs will support mutual aid across trusts based on local stock holding, if required.

Actions Required

Trust pharmacy procurement and clinical teams should:

- review stock holding of all immunoglobulins and ensure brand specific stock is prioritised for use in established patients requiring long term treatment;
- ensure local physical and pharmacy stock control systems for immunoglobulin stocks are accurate and complete including ***all*** home care stock issues and that the Rx-info monthly Define extract is in place to support national allocations by CMU;
- ensure that all Sub Regional Immunoglobulin Assessment Panels (SRIAPs) and trusts use the immunoglobulin e-referral system for all new immunoglobulin requests;
- ensure all immunoglobulin use is in accordance with the latest national commissioning criteria and is tracked on the national reporting database MDSAS;
- utilise available stock of Panzyga® to treat patients who require acute immunoglobulin treatment for supported indications;
- continue to place orders for all NHSEI CMU agreed volumes of immunoglobulins; and
- engage with the Sub Regional Immunoglobulin Assessment Panels (SRIAPs) to ensure optimal use of immunoglobulins (see supporting information).

*Classification of Tiers can be found at the following link: **A Guide to Managing Medicines Supply and Shortages.**

Supporting Information

SRIAPs are established across England to support local hospitals to manage the use of immunoglobulins. They provide effective clinical stewardship of immunoglobulin that supports and facilitate robust decision making and governance applied to the prescribing of immunoglobulin.

SRIAPs will continue to support stewardship by ensuring the following actions are taken to enable the management of supply and demand:

- Review the appropriateness, dose and frequency of immunoglobulin in all existing and new patients.
- Ensure use of immunoglobulin is in line with the NHSEI Commissioning Criteria for the use of Therapeutic Immunoglobulin in Immunology, Haematology, Neurology and specific Infectious Diseases (2018 guidance) For all other indications refer to the Clinical Guidelines for Immunoglobulin Use (2011 guidance).
- Ensure that all immunoglobulin products which are included within the NHSEI CMU framework are considered, including HyQvia which although currently restricted until further notice can be used where clinically indicated.
- Review which patients could be moved from intravenous to subcutaneous treatment if clinically appropriate.
- Ensure providers submit complete and accurate data to the MDSAS national immunoglobulin database to support accurate monitoring of use.
- Use in those grey indications which are presumed to be immune-mediated disorders with little or no evidence of efficacy (right hand side of grey indications table in the 2011 Clinical Guideline) is not routinely commissioned. An Individual Funding Request (IFR) form should be completed by the prescribing clinician and submitted to the SRIAP for review. However, at this time it is unlikely to take priority for use of immunoglobulin over routinely commissioned indications.
- Use of the immunoglobulin e-referral system supports trusts and SRIAPs to manage immunoglobulin more effectively, including adherence to commissioning criteria and recording appropriate usage data. The system is being further developed to support on-going review of existing patients. Should providers require assistance in either using the system or moving onto the system- please contact support@mdsas.com
- Alternative available treatments to immunoglobulin need to be considered such as: plasma exchange (PLEX) for use in autoimmune encephalitis, Guillain-Barre syndrome (GBS) and myasthenic crises along with steroids and rituximab where appropriate.

Enquiries

Enquiries from NHS Trusts and NHS foundation trusts in England should in the first instance be directed to your Regional Pharmacy Procurement Specialist, who will escalate to national teams if required.

REGION	Full Name	Email
East Midlands	Andi Swain	andi.swain@nhs.net
East of England	James Kent	james.kent@.nhs.net
London	Jackie Eastwood	jacqueline.eastwood@lpp.nhs.uk
North East	David Cook Umair Hamid	david.cook20@nhs.net umair.hamid2@nhs.net
North West	Glenn Harley	Glenn.Harley@liverpoolft.nhs.uk
South Central	Alison Ashman	Alison.Ashman@berkshire.nhs.uk
South East Coast	Richard Bateman	richard.bateman2@nhs.net
South West	Danny Palmer	Danny.Palmer@UHBristol.nhs.uk
West Midlands	Diptyka Hart	Diptyka.Hart@uhb.nhs.uk
Yorkshire & Humber	David Allwood	davidallwood@nhs.net

All other organisations should send enquiries about this notice to the DHSC Medicine Supply Team quoting reference number MSN/2021/035.

Email: DHSCmedicinesupplyteam@dhsc.gov.uk

Scotland
nss.nhssmedicineshortages@nhs.scot

Wales
MedicinesShortages@gov.wales

Northern Ireland
RPHPS.Admin@northerntrust.hscni.net

Annex - Product details

The following products are affected:

Strength	Product
10% IVIg	Gamunex (10%)
10% IVIg	Octagam 10%
10% IVIg	Privigen
5% IVIg	FlebogammaDIF (5%)
5% IVIg	Gammaplex (5%)
5% IVIg	Intratect (5%)
SCIg	Hizentra
SCIg	Hizentra PFS

Alternative products:

10% IVIg	Gammaplex (10%)
10% IVIg	Intratect (10%)
10% IVIg	Iqymune
10% IVIg	Kiovig
10% IVIg	Panzyga
5% IVIg	Gammagard
5% IVIg	Octagam 5%
fSCIg	HyQvia
SCIg	Cutaquig
SCIg	Cuvitru
SCIg	Gammanorm
SCIg	Subgam