



Recommendations to achieve appropriate and prioritised use of immunoglobulins in Europe

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SUPPLY Project Factsheet

Why?

European's plasma supply chain faces shortages and high dependence on the American market

EHA's role

WP6 leader: "Demand: Clinical programme on appropriate and prioritised use of PDMPs"



Objectives

- Evaluate current legal framework on plasma collection in the EU;
- Assess current strategies to recruit and retain voluntary non-remunerated plasma donors;
- Develop practical recommendations to improve plasma collection

Timeline

- Start: 1 September 2022
- End: 28 February 2024

Work Package 6 Aim

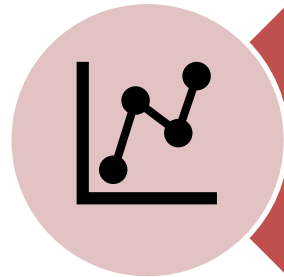
To deliver a set of recommendations on the appropriate use of immunoglobulins (Ig) at baseline and on its prioritisation in times of crisis

(Note: We did not assess the appropriateness of evidence in guidelines)

Overview of methodology



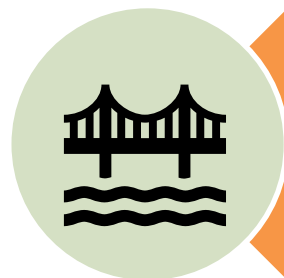
Five recommendations categorized topically



Improved understanding
of Ig usage

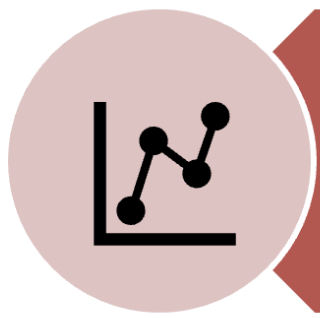


Structured and
harmonised management
plan for shortages



Enhanced collaboration
and linkages

Understand, harmonise, and collaborate!



Improved understanding of Ig usage

Context – Data collection

- Member States exhibit unequal capacities for data collection.
- Need for data on Ig use by indication.

Recommendation

We recommend the creation of a **comprehensive national database** that includes information (at a minimum) on consolidated Ig use at the patient level, discharge summaries with specific indications and clinical efficacy of Ig use.

Concrete actions

Prerequisite:

Establish robust policies and regulations on data jurisdiction, maintenance, and accessibility.

- Identify key stakeholders, determine governance structures and funding mechanisms.

Step 1: Identify and map existing data sources on Ig use within each Member State.

- Utilise registries and databases from existing reference networks and scientific societies.

Step 2: Establish a comprehensive centralised Ig-database and analytics hub.

- At the regional or national level.
- An outline of both a minimum and extensive variables is provided.
- Interconnect aggregated data with the European Health Data Space for optimal analysis.

To improve understanding of Ig usage...and as a prerequisite to harmonisation

Recommendation

We recommend the **sharing of information** in a structured manner, with the aim of maintaining a **consistent set of indications** in all EU Member States.

Concrete actions

- Agree on a limited number of indications, beginning with EMA's authorised indications for Ig
- Include and share data on each MS' approved indications
- MS can decide on which other indication(s) to include



Structured and harmonised management plan for shortages

Context

Existing EU indications and prioritisation plans are not uniform between countries; Member States need to establish a prioritisation plan for shortages.

We recommend the creation of:

1) A harmonised methodology for a prioritisation plan that includes:

- High medical need and unmet medical need;
- Added benefit of Ig, considering alternative treatments;
- Quality of evidence;
- Quality of life for patients, with patient involvement;
- Utilising EMA's authorised indications.



Structured and harmonised management plan for shortages

Context

There is great variability on how things are done (e.g., protocols, practices) and communicated during crisis *and* non-crisis.

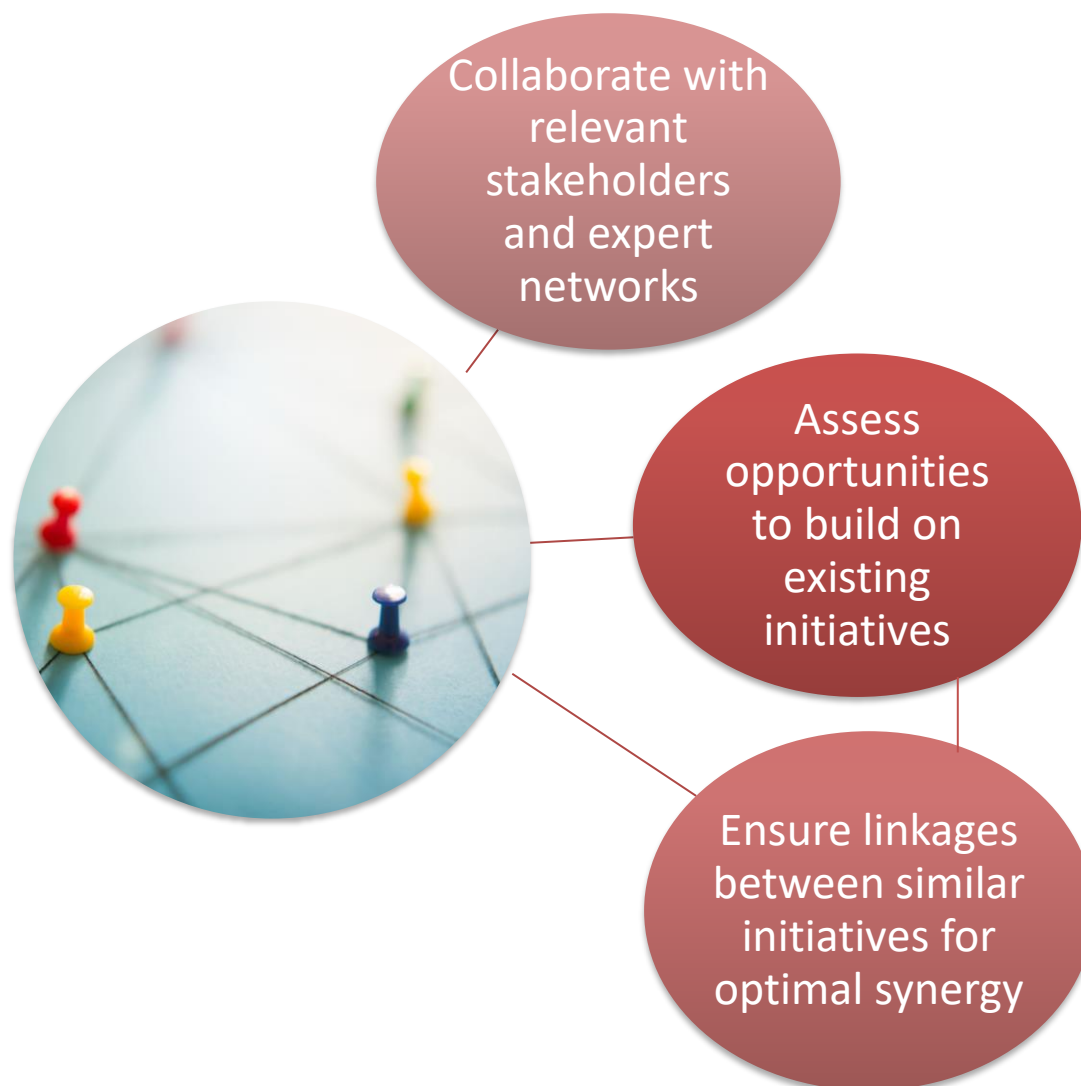
2) A harmonised **management plan** that includes:

- Include a system of checkpoints (e.g., UK's "Commissioning Criteria Policy for the use of therapeutic immunoglobulin England").
- Align with treatment recommendations and guidelines from scientific societies.
- A coordinated communication and shortage awareness system should be set in place at the EU level.

❖ A systematic method of monitoring and assessment to measure (long-term) adherence.



Enhanced collaboration and linkages



We recommend the inclusion of patients and patient advocacy groups in all discussions regarding the therapeutic value of current and future Ig use

- Green Paper on the “Appropriate use of immunoglobulins” by Vintura
- EMA Single Point of Contact (SPOC) Working Party
- Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network (CHESSMEN) project
 - “Next step” of our work

Key points and next steps

01

Three key words:

“Understand”

“Harmonise”

“Collaborate”

02

Demand may be expected to increase due to Latent Therapeutic Demand

03

Further work is required to making these into actual Ig management strategies

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Thank you



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Brief Summary of WP6 Recommendations

Improved Understanding of Ig Usage:

- Create a comprehensive national database in each Member State.
- Include, at a minimum, information on Ig use at a granular patient level.
- Share information in a structured manner to establish consistent indications across all EU Member States (prerequisite to harmonise Ig usage).

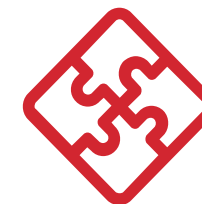
Structured Management Plan for Shortages:

- Develop a harmonised European prioritisation plan methodology.
- Utilise a common backbone adaptable to each country's organization, epidemiology, and resources.
- Implement a harmonised approach for managing Ig use across Europe.
- Establish Europe-wide communication and shortage awareness systems.

Enhanced Collaboration and Linkages:

- Assess opportunities to build on existing initiatives.
- Collaborate with relevant stakeholders and expert networks, including patient representatives.
- Ensure linkages between similar initiatives for optimal synergy.

Doctors' Survey Results



Clinical prescription behaviour

- From 2017-2021, majority of respondents did not change their prescription behaviour for Ig use; Ig usage stayed the same

Shortages and mitigating measures

- From 2019-2021, shortages were increasingly present overall, especially from Italy and Spain
- Top mitigating measures were: i) lowering dose or longer time interval between doses, ii) substitution with other drugs or products, iii) change brand, iv) delay of treatment (combination thereof)

Prioritisation strategies

- Majority of respondents followed some type of guidelines (international, national, or local priority protocols) followed by their own clinical expertise



Expert Interview Results

Pre-existing Ig approval process for off-label usage

- Yes (respondents from the UK, France, and Portugal)
- No (respondents from the Netherlands, Denmark, Italy)

Guidance documents

- International, national, hospital protocols, published papers, consensus documents, clinical expertise, and/or combination thereof
- Variability of protocols for the same speciality throughout the same country, e.g., haematologists in CAR-T and cellular therapies

Shortages during COVID-19 and mitigating measures

- Different scenarios in these countries; the pandemic exacerbated existing shortages
- Mitigating measures included: switching to SCIg; “every drop counts”; creating an internal hospital system for Ig monitoring; using more PLEX and steroids as first line treatment (neurology)
- Spain’s shortage scenario was most extreme



Grey literature results

Comparison of:

- Guidelines used (national vs EU),
- Ig clinical indications,
- Ig national managements plans,
- Prioritisation plans,
- Databases,
- Shortage awareness measures.

Focused on the five biggest Ig markets: **France, Italy, Spain, Germany, and the UK**

Data availability was very different from one country to another!

Comparison of prioritisation plans

Fair match between these plans.

➤ 5 indications are the most prioritised in all 3 plans

➤ 4 are the most prioritised in 2 plans

Need for harmonisation

Indications	France ⁷⁰	UK ⁷¹	Spain ⁷²
Immunodeficiencies			
Primary Immunodeficiencies	X	X	X
Thymoma with immunodeficiency		X	
Specific antibody deficiency		X	
Haematology/Immunology			
Idiopathic thrombocytopenic purpura (ITP)	X	X	X
Low serum IgG concentrations after HSCT due to neoplasia		X In PID	X
Acquired von Willebrand disease (vWD)	X		
Erythroblastopenia (= red cell aplasia) associated with chronic parvovirus B19 infection	X		
Haemolytic disease of the newborn		X	
Alloimmune thrombocytopenia (foetal-maternal / neonatal)	X	X	X
Internal medicine			
Kawasaki disease	X	X	X
Infectious Diseases**			
Measles (if subjects at risk)	X		
Transplant (solid organ)			
Antibody Mediated Rejection (AMR)	X		
Cytomegalovirus-induced pneumonitis			X
Neurology			
Dermatomyositis			X
Demyelinating neuropathy associated with paraproteins		X	X
Chronic inflammatory demyelinating polyneuropathy (CIDP)		X	X
Guillain-Barré syndrome	X	X	X
Dermatology			
Toxic epidermal necrolysis		X	X
Stevens-Johnson syndrome			
Total (nb)	9	12	11

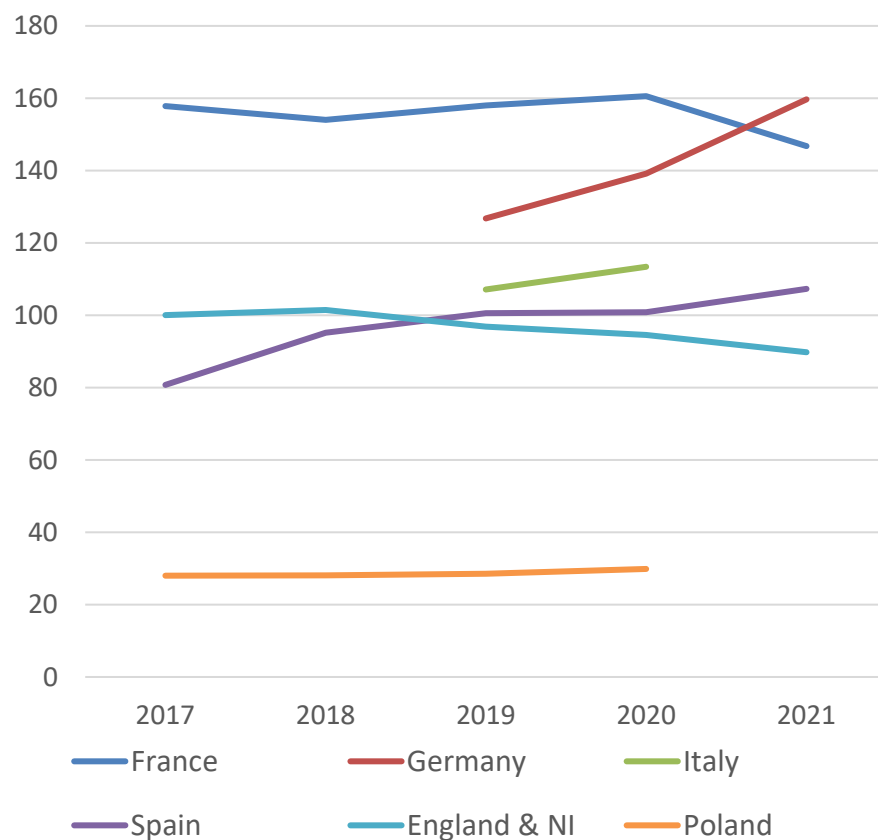




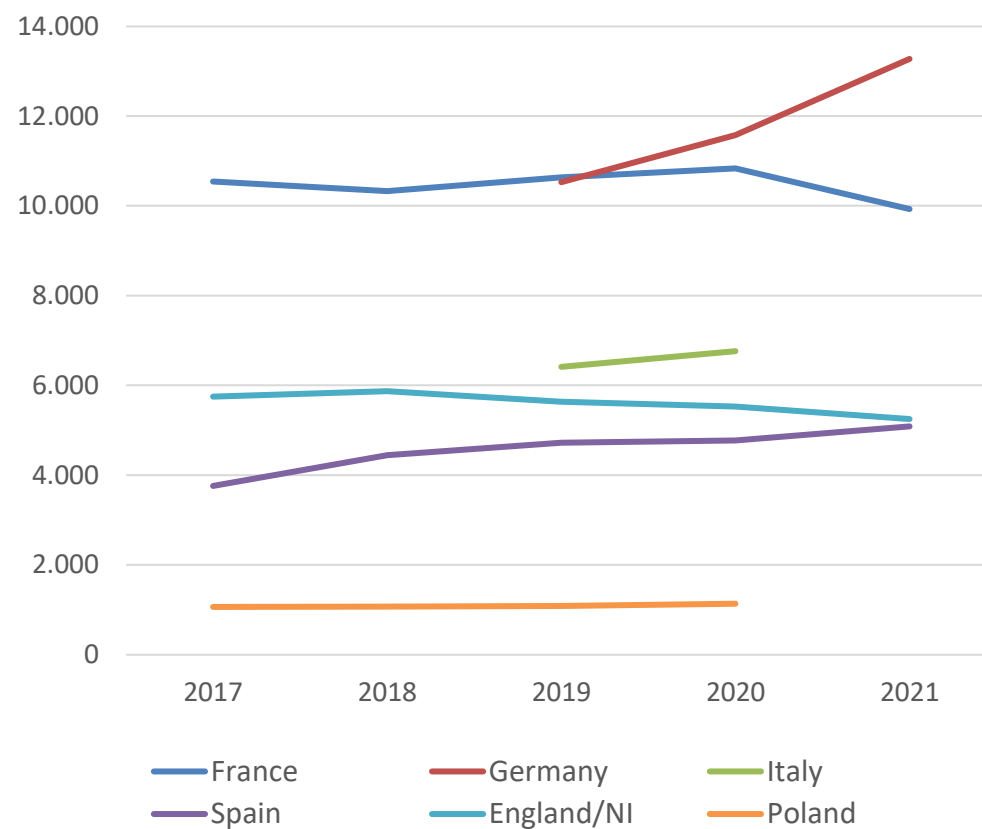
General overview of Ig use

England + NI (2021)	Spain (2021)	Italy (2020)	France (2021)	Germany (2021)
90 grams	107.89 grams	113.4 grams	148.3 grams	159.6 grams

Ig consumption per capita (g/1000)



Total Ig national consumption (kg)



EHA's stance on the proposed SoHO regulation

EHA welcomes the European Commission's proposed SoHO Regulation, particularly its emphasis on:

- strengthening patient and donor safety,
- improved coordination and oversight including quality standards and guidelines (set by expert bodies)
- risk-based authorization
- evidence-based benefit assessment of SoHOs, and access to plasma.