PPTA
Plasma Protein Therapeutics Association

11TH IPOPI PID Forum

Access to Paediatric Medicines:

The Case of PIDs
Towards the Revision of Paediatric Regulation

Industry perspective

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PPTA - Who we are and what we do

PPTA

- International trade association and standards-setting organization
- Represents private plasma donation centers and manufacturers of plasma-derived and recombinant plasma protein therapies (PPTs)

Mission

- To promote availability of and access to safe and effective PPTs for all patients in the world

Global Members

- Biotest, BPL, CSL Behring, Grifols, Kedrion and Shire
- Provide over 60% PPTs manufactured globally
- Cover over 60% of world's need for source plasma and majority of world's safe and effective PPTs, including **Immunoglobulins**

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PPTA Manufacturers

Biotest

Plasma derived therapies;
Manufacturing site in Germany;
15 Collection centers

GRIFOLS

Plasma derived therapies;
Manufacturing sites in Spain and USA;
196 Collection centers

bpl
Bio Products Laboratory
a commitment for life

Plasma derived therapies;
Manufacturing site in UK;
44 Collection centers

KEDRION

Plasma derived therapies;
Manufacturing sites in Italy, Hungary and USA;
19 Collection centers

CSL Behring

Plasma derived therapies and Recombinant therapies;
Manufacturing sites in USA, Australia, Germany, Switzerland;
194 Collection centers

Shire

Plasma derived therapies and Recombinant therapies;
Manufacturing sites in USA, Austria, Belgium, Switzerland, and Italy;
107 Collection centers

emergent
biosolutions™

Plasma derived therapies;
Manufacturing site in Canada;

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Ig therapy in PID – general concepts

- **PID: Human normal Immunoglobulin**
  - **Absolute PID priority medicine, no alternative**
  - 'Essential Medicine' according to WHO
- **Long-term/ lifelong treatment needed**
- **Not interchangeable and not generic**
  - Efficacy, patient outcomes and side-effects depend on product and patient/ genetics
- Different treatment modalities provide **some flexibility**
- **Steady increase in clinical need** over past 20 years

Current regulatory requirements

1. **General framework: EU Paediatric Regulation**
   - Requirements, provisions and incentives to facilitate paediatric medicines development and accessibility

2. **Practical guidelines: EMA Guidelines on**

- **Clinical investigation for IVIg, 3rd revision, 2016 (draft)**
  - Requirements for biological data, clinical trial conduct and patient management
- **Core summary of product characteristics (SPC) for IVIg and SCIg, 2015**
  - Product characteristics, posology, treatment modalities

Current regulatory challenges

- **Low patient numbers**
  - Fully powered efficacy studies difficult, very long timelines for completion (if at all) esp. neonates and some genetic populations
  - Companies have to perform similar studies with similar protocols investigating similar issues…
- **Trials and product development are GLOBAL**
  - Regulatory approaches and requirements differ globally
  - Example: PK data in children_ Are they **REALLY needed?**
  - Result: More time needed to complete trials in EU vs. USA
- **Patient recruitment is LOCAL**
  - **Informed Consent:** Different provisions, requirements and expertise by **NATIONAL** Ethics Committees

Current regulatory challenges

Practical example: EMA guideline on clinical investigation for IVIg –Pharmacokinetic (PK) parameter requirement:

- 40 PID patients/ 50% (20) children or adolescents
- Ig assessed prior to each infusion for 6 months, starting after 5-6 administrations

Issue: IS THIS REALLY NEEDED IN PAEDIATRIC POPULATION?

- Additional trips for parents and children with no real benefit - no treatment given; parents need to take extra time off work
- PK of Igs known and studied for ~30 years, 'scientific' reason is questionable…
- No PK requirement by FDA: **Medicines in EU available 1-2 years later than in USA**

Recommendations

1. Utilisation of real-life setting complimentary to trials, common scientific approach for global trial conduct and collaboration of all stakeholders

2. Globally ALIGNED regulatory approach

3. Early industry-regulator dialogue on key scientific data
   - Assessment of which parameters are REALLY needed
   - Innovative clinical trial designs to be considered

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Recommendations (1)

1. Utilisation of real-life settings and enhancement of collaborative global trial conduct

- **Use of registries**: real-life data, complimentary to trials
- **Use of big data** and real world evidence to assess efficacy (EMA/FDA)
- **Use of existing networks, public funding** (EU Rare Disease init.)
- **Global collaboration:** Industry, patients, clinicians, academia, regulators
- **Use of experience** from other successful international approaches (Juvenile Arthritis/ PRINTO)

2. Globally ALIGNED regulatory approach

- **Increased regulatory collaboration** (FDA-EMA paediatric cluster)
- **Scientific alignment needed** for increased efficacy and shorter times for trials (i.e.: R1 ICH E11 addendum)
- **Informed Consent**: National alignment/ consistent requirements

Recommendations (2)

3. Early scientific/ regulator-Industry dialogue to determine CRITICAL SCIENITIFIC parameters

- **Better utilization of existing data and use of new approaches**
  - PK modelling
  - Extrapolation of adult-based results
  - Alternative approaches for small populations
  - Collaboration with parents and patients on feasibility so paediatric studies are completed

- **Innovative clinical trial designs**
  - Better design ‘Master Protocols’ (draw on experience from other successful small population trials, i.e. ‘Umbrella’, ‘Basket’ and ‘Platform’)
  - Enriched trial design approaches, n-of-1 trials, etc., …

Final thoughts

Availability of Igs in EU

- Majority plasma for Ig products sourced from USA
- Igs are a PRIORITY medicine for PID – no other medicines available
- Clinical need increasing over past 20 years and rising

➢ **Europe needs to collect more plasma to cover increase in clinical need for Igs**

Thank you

Questions?

Comments?

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