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Expanding horizons for patients with Pompe disease: Using data to guide clinical practice

Practice aid for the management of people living with Pompe disease

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Real-world data highlight ongoing unmet needs in Pompe disease

Unmet needs in Pompe disease: Insights from RWE

Diagnostic delays and initial misdiagnoses persist

Swedish RWE in 14 patients with LOPD reported:[1]

Median time from:

- Symptom onset to diagnosis: **5.4 years**
- Diagnosis to ERT initiation: **1.5 years**

Diagnoses prior to LOPD diagnosis:

- **71%** Symptoms, signs and abnormal clinical/laboratory findings not classified elsewhere
- **53%** Endocrine, nutritional and metabolic diseases
- **53%** Nervous system diseases
- **41%** Respiratory system diseases

Healthcare needs and disease burden are complex

US RWE highlights disease burden in ERT-treated patients:[2]

12-month cumulative incidence of comorbidities, %

	IOPD (n=50)	LOPD (n=55)
Respiratory	85	79
Ambulatory	57	54
GI	68	33
CV	17	29

Cumulative incidence of most comorbidities, notably respiratory infections, increased over time

Treatment burden remains a challenge

US RWE highlights ERT-related treatment burden in Pompe disease:[2,3]

- Outpatient visits and ERT prescription costs were key contributors to the economic burden of treatment[3]
- Healthcare resource utilization and medical visits were substantial, adding to the burden of treatment[3]
- New treatments are needed to help reduce medical visits, resource use and healthcare costs[3]

Supportive service use (occupational, speech and physical therapy) increased over time in IOPD and LOPD[2]

Pompe disease patient registries (e.g. NCT06121011, NCT00231400)[4–7] may help to address current knowledge and data gaps

Current ERT options for Pompe disease are expanding

ERT

ALG

Contraindications:[8] Life-threatening hypersensitivity (anaphylactic reaction) to active substance or any of the excipients when rechallenge was unsuccessful

Long-term ERT in adult and paediatric patients of all ages with a confirmed diagnosis of Pompe disease[8]*	**Precautions:** IARs, immunogenicity, immunomodulation, anaphylactic/hypersensitivity reactions, IMRs
For use in patients with Pompe disease[9]*	**Warning:** Anaphylactic/severe allergic reactions/IMRs, acute cardiorespiratory failure, cardiac arrhythmias/sudden cardiac death during GA, risk of Ab development

AVA

Contraindications:[10] Life-threatening hypersensitivity (anaphylactic reaction) to active substance or any of the excipients when rechallenge was unsuccessful

Long-term ERT for the treatment of patients with Pompe disease[10]*	**Precautions:** Anaphylactic/hypersensitivity reactions, IARs, immunogenicity, acute cardiorespiratory failure, cardiac arrhythmia/sudden death during GA for central venous catheter placement
Treatment of patients aged ≥1 year with LOPD[11]*	**Warning:** Hypersensitivity reactions (including anaphylaxis), IARs, risk of acute cardiorespiratory failure in susceptible patients

CIPA

Contraindications:[12,13] Life-threatening hypersensitivity (including anaphylaxis) to active substance or any of the excipients when rechallenge was unsuccessful,[12] pregnancy[13]

Long-term ERT in combination with MIG in adults with LOPD[12]*	**Precautions:** Anaphylaxis and IARs, risk of acute cardiorespiratory failure in susceptible patients, immune complex-related reactions, sodium content
In combination with MIG for treatment of adults with LOPD weighing ≥40 kg and not improving on current ERT[13]*	**Warning:** Hypersensitivity reactions (including anaphylaxis), IARs, risk of acute cardiorespiratory failure in susceptible patients

Enzyme stabilizer

MIG

Contraindications:[14,15] Hypersensitivity to the active substance or to any of the excipients, contraindication to CIPA,[14] pregnancy[15]

Enzyme stabilizer of CIPA, long-term ERT in adults with LOPD[14]*	**Precautions:** Adverse drug reactions may occur upon the use of MIG in combination with CIPA
Enzyme stabilizer indicated with CIPA for treatment of adults with LOPD weighing ≥40 kg and not improving on current ERT[15]*	**Warning:** Embryo-foetal toxicity, must be administered with CIPA – refer to CIPA PI for description of additional risks

ERT home infusion

EMA SmPCs:[8,10,12]

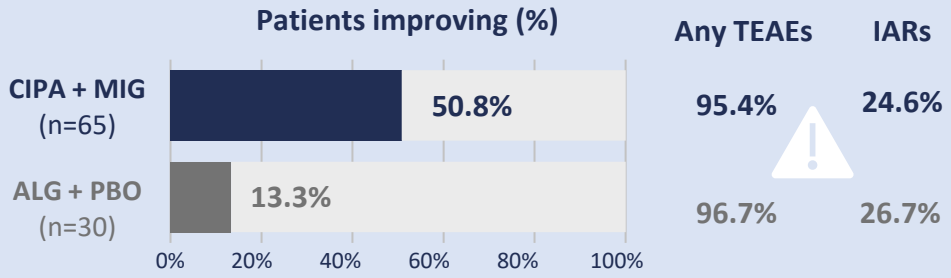
Infusion of ERT at home may be considered for patients who are tolerating their infusions well and have no history of moderate or severe IARs for a few months. The decision to have a patient move to home infusion should be made after evaluation and upon recommendation by the treating physician

*Confirmed diagnosis of Pompe disease (GAA deficiency).

Clinical trials and RWE show ERT switching is a feasible option in Pompe disease

PROPEL study: Switching from AVA + PBO to CIPA + MIG in patients with LOPD showed clinically meaningful improvements[16]

Overall proportion of patients with clinically relevant improvement or worsening in 6MWD and/or FVC after switching ERT, with similar safety profiles



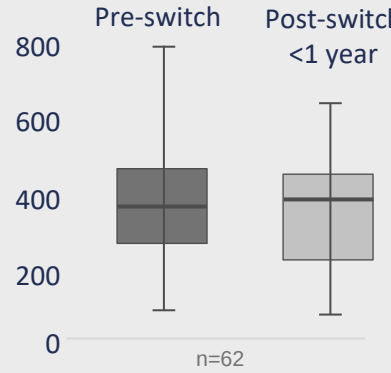
Nearly **4**× as many patients who switched to CIPA + MIG **improved** in 6MWD and/or FVC vs those remaining on ALG

Pompe Registry (NCT00231400): Motor and respiratory outcomes were stable in patients with LOPD switching from ALG to AVA[6]

Mean change in pulmonary measures between visits (pre- and post-ERT switch)

% pred. FVC	1.2%
% pred. FEV_1	1.4%

6MWD at last assessment, m



In addition to current and emerging therapies, a need for a multidisciplinary, holistic approach to the care of patients with Pompe disease remains[17]

- Patients living with Pompe disease should undergo periodic evaluation and examinations to explore heart, respiratory and muscle function[18]
- Follow-up programmes should be tailored to individual patient needs and adjusted to the stage of disease[18]

General evaluation[18]

Evaluate growth parameters at regular intervals in infants and children (every 3–6 months, depending on age/clinical forms)

Musculoskeletal and functional tests[18]

Perform motor and functional assessments every 3–6 months for children aged <5 years, every 6–12 months for older children and adults

MDT considerations[18]

- Antibody/biochemical status
- Auditory function
- Anaesthesiology evaluation
- Behaviour/cognitive function
- Bone density
- Cardiology
- GI function
- Neuromuscular evaluation
- Quality of life
- Respiratory function

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Abbreviations and references

Abbreviations

6MWD, 6-minute walk test distance; Ab, antibody; ALG, alglucosidase alfa; AVA, avalglucosidase alfa; CIPA, cipaglucosidase alfa; CV, cardiovascular; EMA, European Medicines Agency; ERT, enzyme replacement therapy; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GA, general anaesthetic; GAA, acid alpha glucosidase; GI, gastrointestinal; IAR, infusion-associated reaction; IMR, immune-mediated reaction; IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; MDT, multidisciplinary team; MIG, miglustat; PBO, placebo; PI, prescribing information; pred., predicted; RWE, real-world evidence; SmPC, summary of product characteristics; TEAE, treatment-emergent adverse event.

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