Label

Pompe disease (early infantile-onset form)

1 TESTS and/or TREATMENT TO BE INITIATED IN AN EMERGENCY:

There are no specific emergency tests or treatments for Pompe disease. Emergency management is symptomatic and depends on the patient's clinical condition, taking into account the specific risks of this disorder and any necessary treatment (see section 3).
In the event of restrictive respiratory failure (of neuromuscular origin), signs of severity include desaturation and/or hypercapnia. In the event of respiratory decompensation, the administration of high-concentration O_2 must be accompanied by non-invasive ventilation.

2 POSSIBLE COMPLICATIONS ASSOCIATED WITH POMPE DISEASE (cross out all situations that do not apply to the patient)

1/ IMMUNOMODULATION:

Due to the possibility of developing antibodies against enzyme replacement therapy (ERT), some patients receive immunotherapy (usually methotrexate and rituximab), with regular infusions of pooled intravenous immunoglobulin (IVIg) to reduce the risk of infection.
In the event of fever, the therapeutic approach is the same as for any other child (except if the child has an implantable port, see point 2). An infectious episode does not contraindicate IVIg infusion. On the contrary, it may be advisable to bring forward the infusion, which should be discussed with the referring doctor during working hours.

2/ IMPLANTABLE PORT (IP) or PORT-A-CATH (PAC):

Some patients have a central line (PAC) for enzyme replacement therapy. If a fever develops, a catheter-related infection must be ruled out and the patient should be advised to go to A&E for an **infectious work-up**: CBC, CRP, PCT, blood cultures from PAC and peripheral sites +/- other infectious samples depending on the clinic. If a PAC infection is suspected, **anti-staphylococcal antibiotic treatment** should be promptly initiated (in accordance with the local protocol, e.g.: vancomycin IV: loading dose of 15 mg/kg over 60 min, then maintenance dose of 45 mg/kg/day continuously +/- gentamicin IV: 8 mg/kg/day in a single infusion over 30 min +/- local antibiotic lock).

3/ HEART FAILURE and/or ARRHYTHMIA:

Patients with the infantile form of Pompe disease are typically diagnosed with hypertrophic cardiomyopathy, sometimes associated with heart failure. They may also have cardiac conduction disorders (e.g. short PR interval, apparent WPW syndrome, etc.) with a risk of arrhythmia. Symptomatic cardiological treatment may be required (diuretics, β-blockers, +/- ACE inhibitors). ERT leads to the progressive resolution of cardiac signs, but as long as cardiac involvement persists, these patients remain at risk of heart failure and/or arrhythmia.
In case of uncertainty, **assess for signs of heart failure**; perform **a chest X-ray, ECG and BNP assay** (an **NT-proBNP** test is preferred, if available); **+/- echocardiography** depending on the results of the previous criteria (diastolic heart failure, with systolic function generally preserved).
For infusions, the flow rate should be adjusted according to cardiac function and haemodynamics. Care should be taken to avoid rapid filling.

4/ RESPIRATORY FAILURE AND MYOPATHY:

Pompe disease can lead to progressive myopathy, resulting in chronic restrictive respiratory failure with possible acute decompensation. **Caution: in the event of respiratory decompensation, signs of respiratory distress may be completely absent.** Depending on the severity of muscle involvement, warning signs may include isolated tachypnoea, orthopnoea or signs of hypercapnia (morning headache, profuse sweating, confusion, drowsiness, etc.).
In the presence of respiratory signs, a **blood gas analysis** should **always** be performed (to check for hypercapnic acidosis), as well as a chest X-ray. **Desaturation occurs very late in restrictive respiratory failure.**
If fever is present, antibiotic treatment should be readily prescribed and cytobacteriogical testing of sputum performed (for children over 6 years of age).
For patients on chronic non-invasive ventilation, ensure NIV is started as soon as possible in case of decompensation, with the option of adding O_2 to the machine. Avoid administrating high-flow oxygen alone without ventilation.

View the **Emergency page** on the G2M website

3 PATHOPHYSIOLOGY:

Pompe disease (PD), also known as glycogen storage disease type II, is an autosomal recessive lysosomal storage disorder caused by a deficiency of acid alpha-glucosidase (GAA), also called acid maltase. This deficiency leads to the accumulation of glycogen in most tissues, but symptoms primarily result from skeletal muscle involvement and, in paediatric forms, cardiac involvement.

PD has a broad clinical spectrum, ranging from the infantile-onset form, which develops within the first few months of life, characterised by hypotonia and **severe cardiomyopathy**, to the late-onset or adult form, which presents as **progressive muscular and respiratory impairment**.

Enzyme replacement therapy (ERT) is the standard treatment for Pompe disease (Myozyme® or Nexviadyme®, administered every 1 or 2 weeks). ERT is a long-term treatment and is never administered on an emergency basis (except when initiated at diagnosis for paediatric forms). While this treatment improves cardiac involvement, the muscular impairment may worsen gradually (progressive myopathy with **restrictive respiratory failure**). Some patients may also develop neurogenic involvement. Some patients develop antibodies against ERT and may require immunosuppressive therapy in the paediatric forms (either prophylactically or after the antibodies appear).

Depending on the form of PD, ERT may not be indicated.

4 DRUG CONTRAINDICATIONS/GENERAL ADVICE:

- No drug contraindications
- All vaccines should be given, including influenza, COVID and reinforced pneumococcal vaccination. Live vaccines are contraindicated in patients undergoing immunomodulation, and the vaccination schedule should be reviewed with the referring doctor.
- No specific diet is recommended.
- Muscle involvement is chronic, high CPK is habitual but moderate, the same applies for high transaminases. There are no episodes of acute rhabdomyolysis.
- An ERT infusion may be cancelled or postponed if the situation makes its administration impossible.
- **Patients in palliative care/limitation of treatment/end-of-life support:**
  - Some patients have very severe and progressive disease, requiring a limitation of non-beneficial invasive therapies
  - These patients are usually managed in collaboration with a comfort/palliative care team.
  - ERT infusions may be stopped (lack of benefit, infusion-related reactions, etc.).
  - Appropriate and optimal analgesia must be provided, particularly to limit respiratory deterioration.
  - Some patients have a medical information sheet for the emergency team regarding what to do in the event of acute deterioration (agreed care plan).

SURGERY or Anaesthesia:

- The risk of respiratory and/or cardiac decompensation must be considered before any surgical procedure. A preoperative reassessment should be carried out with the referring specialist. Local or loco-regional anaesthesia should be favoured.
- In the case of general anaesthesia, long half-life neuromuscular blocking agents should be avoided. If neuromuscular blockers are essential, non-depolarising agents should be used, and neuromuscular blockade should be carefully monitored. Suxamethonium chloride (succinylcholine) is contraindicated, (it is a depolarising agent that induces muscle contraction and may cause rhabdomyolysis and hyperkalaemia). Halogenated compounds should also be avoided (risk of malignant hyperthermia).
- In the case of hypertrophic cardiomyopathy, additional anaesthetic precautions include: Avoiding myocardial depressant agents such as propofol and sevoflurane, and prioritising midazolam and ketamine. Avoiding hypovolaemia at induction. Fundamental haemodynamic monitoring.
- Intubation may be difficult due to macroglossia. Mask ventilation may also be complicated by upper airway obstruction and risk of obstruction after extubation.
- After surgery: Close monitoring of respiratory function is required, with a frequent indication for prolonged ventilation. After extubation, in the absence of specific complications, usual NIV should then be resumed.
- Optimal analgesia must be provided to prevent respiratory deterioration due to pain (e.g. epidural in combination with general anaesthesia for abdominal surgery to prevent worsening of diaphragmatic paresis).
- For elective surgery, discuss hospitalisation in an appropriate monitoring environment (e.g., intensive care unit) in advance.

REFERRING DOCTORS AND CONTACT DETAILS

On-call telephone numbers for metabolic emergencies of:

At night, only the medical teams can call in emergency situations and only if the emergency certificate has not been understood or if the patient's clinical condition or test results are concerning. Where possible, calls should be made before night time.

Secretarial issues must be dealt with via the medical secretariat during the week or by email addressed to the patient's referring metabolic doctor.

Certificate issued on Dr