EMERGENCY CERTIFICATES - G2M NETWORK

V2 – Sept 2024

ORGANIC ACIDURIAS = METHYLMALONIC ACIDURIA (MMA) OR PROPIONIC ACIDURIA (PA)

PRIORITY PATIENT: MUST NOT BE KEPT WAITING IN THE EMERGENCY DEPARTMENT

In the event of vomiting, diarrhoea, fever or fasting
= Risk of hyperammonaemic coma, ketoacidosis and stroke-like episode

Label

Do not wait for signs of decompensation; always initiate the following management protocol:

1 EMERGENCY ASSESSMENT

Phone call only if the emergency certificate is not understood.

Urine dipstick/capillary ketonaemia (positive if >1+ or 0.8 mmol/L), **blood gases, lactate, electrolytes, bicarbonate, blood glucose, calcium, blood ammonia, uric acid, creatinine**, liver function tests, **prothrombin time**, lipase.
CBC (including platelets) Infection screen. ECG (risk of prolonged QT interval). Do not delay infusion.
If possible: plasma MMA and amino acid chromatography, urinary organic acid chromatography; send during working hours (see overleaf for technical details).

2 START TREATMENT URGENTLY, without waiting for test results

A- Emergency infusion or Emergency enteral nutrition

- NO IV amino acids or oral proteins: **stop feeding or use a specific low-protein diet.**
- If **dehydrated**, **rehydrate** with Ringer's lactate or 0.9% sodium chloride **10 mL/kg** (maximum 500 mL) if there are no cardiac signs. reassess and repeat if needed. Then adjust the infusion volumes below.
- Infuse **10% glucose** with standard electrolyte supplementation* (not 10% glucose alone)
- + Y-site infusion of **20% lipids** (e.g. Medialipids, Intralipids) via a peripheral line:
- **The carbohydrate intakes below are for guidance; adapt infusion volume to hydration status.**

Age	0 - 24 months	2 - 4 years	4 - 14 years	> 14 years/adult	MAX. FLOW RATE
10% glucose + electrolytes	5 mL/kg/h (8 mg/kg/min)	4.2 mL/kg/h (7mg/kg/min)	3.5 mL/kg/h (6 mg/kg/min)	2.5 mL/kg/h (4 mg/kg/min)	120 mL/h (3L/24h)
20% lipids	0.4 mL/kg/h (2 g/kg/d)	0.3 mL/kg/h (1.5 g/kg/d)	0.3 mL/kg/h (1.5 g/kg/d)	0.3 mL/kg/h (1.5 g/kg/d)	20ml/h (500ml/24h)

e.g.: Balanced electrolyte solution such as Bionolyte, B45, Glucidion. If unavailable: 10% glucose + 4 g/L NaCl (70 mEq/L) and 2 g/L KCl (27 mEq/L)

If IV infusion is not possible **=>** Nasogastric tube: prepare the above IV solutions and administer via the tube at the same rates

- **Emergency diet**: in the absence of gastrointestinal issues and if preparation is available: instead of infusion, **continuous** enteral feeding through a nasogastric tube or gastrostomy (preparation known to parents according to the dietary sheet).

B. Medicinal clearance treatments

- **L-carnitine (Levocarnil): double the patient's usual dose, max 200 mg/kg/day (not exceeding 12 g/24h),** orally every 6–8 hours or continuous IV if vomiting.
- If **blood ammonia >100 µmol/L** in children/adults or **>150 µmol/L** in newborns:
  - Check and, without waiting for results, give: **Carbaglu®** (N-carbamylglutamate): oral loading dose of 50–100 mg/kg, then maintenance dose of 50 mg/kg every 6 hours orally or via NG tube (max 8g/24h)
  - If unavailable: **Sodium benzoate** continuous IV (oral if no IV access): Start with a **loading dose** of 250 mg/kg over 2 hours (max 6g/2h), then 250 mg/kg/24h (max 12g/24h).
- **For B12-responsive MMA:** give vitamin **B12 1 mg/day IM or IV daily** (instead of usual oral or spaced IM B12 therapy)

C- Other treatments:

- **Continue** usual maintenance treatments, including any **ammonia scavengers** (Carbaglu®, sodium benzoate)
- **STOP amino acid** supplementation (AA mixtures, valine, isoleucine).
- Treat any infectious cause

3 SIGNS OF SERIOUS ILLNESS = Specialist opinion/transfer to intensive care

- **Coma** or **no neurological improvement** 3 hours after starting treatment
- **Haemodynamic failure**, arrhythmia (risk of QTc prolongation or heart failure in PA)
- **Severe hyperammonaemia** (Infant > 200 µmol/L; Child/Adult > 150 µmol/L)
- **Ketoacidosis and severe lactic acidosis with pH < 7.10**
  - Consider emergency haemodialysis
  - **Insert a central line to deliver a concentrated infusion** (risk of cerebral oedema) while maintaining carbohydrate, lipid and sodium intake [example: 30% glucose (enough to provide the same carbohydrate intake as above), NaCl 6 g/L (100 mEq/L), potassium and calcium according to electrolytes + 0.9% sodium chloride in Y with glucose infusion, for a total of **1.5 L/m²/day** *(Body surface area = (4W + 7)/(W + 90)].*

4 MONITORING

- **Vital signs monitor with ECG every 24h** - Echocardiography during working hours if propionic acidaemia with severe decompensation.
- Urine dipstick at each void and/or capillary ketonaemia (positive if > 1+ or 0.8 mmol/L).
- Repeat blood tests (blood glucose, blood gases with lactate, electrolytes, urea, creatinine, Ca, NH_3, PT): at 4 h if pH < 7.1 and/or NH_3 > 100 µmol/L (then reassess), at 6–12 h if pH >7.1 and NH_3 <100 µmol/L. Adapt according to context (vomiting, fever).
- Capillary blood glucose every 4 hours: target 1–1.8 g/L. If BG > 2 g/L and glycosuria is present, consider insulin 0.01 IU/kg/h, adjusted hourly. Consider reducing sugar intake (25–50%) if hyperglycaemia persists despite insulin therapy at 0.05 IU/kg/h, and/or if hyperlactataemia > 5 mmol/L occurs

ORGANIC ACIDURIAS = METHYLMALONIC ACIDURIA (MMA) OR PROPIONIC ACIDURIA (PA)

PHYSIOPATHOLOGY:

Organic acidurias (MMA, PA) expose patients to endogenous intoxication, with **ketoacidosis, lactic acidosis, and hyperammonaemia** due to breakdown of certain amino acids and other molecules such as odd-chain fatty acids. The usual treatment is (depending on the patient):

- Oral L-carnitine (Levocarnil®).
- Limiting fasting with nocturnal enteral feeding in children.
- Extremely strict low-protein diet: This diet excludes meat, fish and eggs entirely; other foods are allowed in strictly weighed quantities. See "maintenance diet" sheet
- Some patients are on ammonia scavengers: Carbaglu® or sodium benzoate

These patients are at risk of **hypocalcaemia**, **acute pancreatitis** and **pancytopaenia** in cases of severe decompensation.
Patients with **propionic acidaemia** are at risk of cardiomyopathy with **arrhythmia** and **QT prolongation.**
Patients with **methylmalonic acidaemia** are at risk of **renal failure** and tubulopathy.

SITUATIONS WITH RISK OF DECOMPENSATION:

- Intercurrent infection, fever, anorexia, vomiting, surgery, excessive protein intake, **any state of fasting, calorie deficiency, weight loss or catabolism.**
- **In all these situations, the patient must be kept in hospital,** as acidosis and hyperammonaemia can worsen very quickly. **This is an emergency:** manage the patient in the ED before inpatient admission. **RAPID ACTION** prevents severe acidosis and multi-organ failure.

CLINICAL SIGNS OF DECOMPENSATION: Do not wait for these signs to appear.

- **Metabolic acidosis with acidotic polypnoea**
- **Acute neurological disorders** (impaired alertness, confusion, drowsiness, impaired balance, hallucinations, behavioural disorders, tremors, abnormal movements, etc.), transient blindness.
- **Digestive signs** (vomiting, anorexia, nausea, etc.), dehydration, **pancreatitis.**
- Arrhythmia, **haemodynamic failure.**
- **Pancytopaenia, hypocalcaemia.**

DRUG CONTRAINDICATIONS/GENERAL ADVICE/SURGERY:

Prohibited: valproic acid (Depakene®, etc.) Corticosteroid therapy: weigh up the indication if duration > 3 days. No restriction on the use of HSHC if resuscitation is required. For PA: **caution with drugs that prolong the QT interval**

- All vaccinations are recommended (particularly influenza).
- Prolonged fasting contraindicated, never leave the patient without carbohydrate intake (infusion or continuous enteral tube feeding) or carnitine.
- **Do not leave the patient without protein for more than 3 days.** Remember vitamin and trace element supplementation if the patient is on exclusive parenteral nutrition. Emergency treatment must be reviewed with the metabolic specialist during the day.
- **In the event of hospitalisation** (or emergency consultation): patients must bring their usual treatments and any special products they have with them to prepare an emergency diet.

SURGERY with General Anaesthesia:

CAUTION: never leave the patient fasting without an infusion. Apply the emergency protocol with the above infusion in preparation for surgery.

GUIDANCE ON PRACTICAL ADMINISTRATION OF TREATMENTS/SAMPLES:

- LEVOCARNIL IV (1 g amp. = 5 mL), to be administered either undiluted or diluted in saline, via a Y-site infusion.
- LEVOCARNIL PO (1 g amp. = 10 mL), in 3 to 4 oral doses/day.
- SODIUM BENZOATE IV: [Sodium benzoate AP-HP 1 g–10 mL]; ampoule 1 g = 10 mL, to be diluted volume for volume in 10% glucose. Contains 7 mEq sodium per gram of benzoate. Status = hospital preparation.
- Carglumic acid (CARBAGLU®) 1 tablet = 200 mg. PO or via gastric tube diluted in 10 mL water. No temporary authorisation (ATU) required, available from hospital pharmacy.
- VITAMIN B12 (Cyanocobalamin or Hydroxocobalamin): 1 mg IM. May be given IV diluted in at least 20 mL (slow IV infusion over 1 hour).

Biochemical samples: Plasma MMA (methylmalonic acid) and AAC (amino acid chromatography): heparin tube with green cap. At night and weekends, centrifuge and freeze plasma. Urinary OAC (organic acid chromatography): 1 void. Send to specialised biochemistry laboratory during working hours.

GUIDANCE ON DIET:

- If, exceptionally, a feed/meal is missed during hospitalisation: give an emergency protein-free meal (low-protein pasta, low-protein bread with butter and jam) or, for infants: PFD1®/Energivit®: 1 measuring spoon per 30 mL water (0.7 kcal/mL).
- If the composition of the continuous emergency diet is unknown: prepare an isocaloric solution with [100 g PFD1®, Energivit® or Duocal® + 430 mL water] or [80 g maltodextrin + 20 mL oil + 425 mL water]: equivalent preparations 500 mL = 500 kcal. Adjust total intake to the patient's needs. To be reviewed with a dietitian during working hours, particularly for calcium and electrolyte intake (Na, K, etc.).

REFERRING PHYSICIANS AND NUMBERS:

At night, only medical teams may call in emergencies and only if the emergency certificate is not understood or if the clinical condition or test results are concerning. Whenever possible, calls should be made before nightfall.
Administrative questions should be addressed to the medical secretariat during the week or by email to the patient's referring metabolic specialist. Certificate issued on Dr