

MAPLE SYRUP URINE DISEASE (MSUD)**Priority patient: must not wait in A&E / ED**

Patient Label

If presenting with fever, vomiting, diarrhea or fasting state

Risk of coma, cerebral oedema**Do not wait for signs of decompensation, in all cases initiate management as set out below****1 EMERGENCY WORKUP****Plasma aminoacids (quantitative)** (heparin tube with green stopper; at night or weekend centrifuge and freeze the plasma)+ Tests in line with triggers and/or intercurrent illness. **Serum electrolytes**, urinalysis (ketones).

Do not delay infusion. Normal usual lab test results do not exclude ongoing decompensation.

2 TREATMENT TO BE STARTED URGENTLY, without waiting for lab results

- **NO NATURAL PROTEINS: stop feeding with normal food. Specific low-protein food allowed.**
- Infusion using **10% glucose** with standard electrolyte additions* (never pure 10% glucose)
+ Infusion using a Y-Set of **20% lipids** (e.g. Medialipids®, Intralipids®)
- By peripheral line, flow rate depending on age:

Age	0-24 months	2-4 years	4-14 years	> 14 years / adult	MAX INITIAL RATE
Polyionic 10% glucose* (glucose infusion rate)	6mL/kg/h (10mg/kg/min)	5mL/kg/h (8mg/kg/min)	3.5mL/kg/h (6mg/kg/min)	2.5mL/kg/h (4mg/kg/min)	120mL/h (3L/24h)
Lipids 20%	0.4 mL/kg/h (2g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	0.3mL/kg/h (1.5g/kg/day)	20mL/h (500ml/24h)

*e.g.: Bionolyte®, Glucidion®, etc. if no pre-made solution available, use 10% glucose in water + 4 to 6g/L NaCl (70 mEq/L) + 2g/L KCl (27 mEq/L)

If IV line is impossible => Nasogastric tube or gastrostomy: prepare the IV fluids listed above and pass them through the tube at the same rates.

- If there are no gastrointestinal disorders and if the preparation is available: instead of infusion, **emergency diet** by **continuous** enteral feeding using nasogastric tube or gastrostomy (see diet sheet from parents)
- **Specific amino acids (AA) mixtures or blends for MSUD: MANDATORY**
 - **Give the AA mixture according to the patient's emergency diet sheet.** If the protocol or products are missing: see advice overleaf.
 - **If the patient is vomiting, is incapable of taking the preparation, or if there are signs of severity:** give the AA mixture continuously over 24 hours via NG tube.
- Supplement with **VALINE** (50 mg capsules) and **ISOLEUCINE** (50 mg capsules) if available:
 - VALINE: 100 mg x 4/ day (children), 200mg x 4/day (adults).
 - ISOLEUCINE: 100 mg x 4/ day (children), 200mg x 4/day (adults).
 - **Essential after 24 hours of progress.**
- Treatment of the potential intercurrent infection.

3 SEVERITY SIGNS = Consult / Transfer to Intensive CareSeek referral from **Intensive Care** and the **metabolism clinician** regarding **urgent haemofiltration**, if:

- **Coma**, altered mental status, ataxia or **worsening** of clinical condition.
 - ⇒ **Increase the concentration of the infusion** (risk of cerebral oedema) while maintaining intake of glucose, lipids and sodium [example: 30% glucose in quantity sufficient for same glucose intake as above, NaCl 6 g/L (100meq/L), potassium and calcium according to serum electrolytes + normal saline (NaCl 0.9%) in parallel with glucose solution using a Y-Set to give a total intake of **1.5 L/m² of BSA/day**.
(Body surface area = $(4 \times \text{Weight}(kg) + 7) / (\text{Weight}(kg) + 90)$)]
 - ⇒ **Maintain continuous administration of the AA mixture via NG tube.**
 - ⇒ Continuous haemofiltration for a minimum of 24H.

4 MONITORING

- **Glasgow score** and check for signs of severity every 4 hours.
- **Capillary blood glucose q4h:** target range 1.0-1.80g/L. If blood glucose >2.0g/L and glycosuria, consider insulin 0.01 IU/kg/h with subsequent adjustment every hour.
- Urinalysis (ketones = sign of catabolism) +/- DNPH test if **available** (1mL of urine + 1 mL of DNPH) on every micturition until negative.
- **Plasma aminoacids (quantitative: leucine concentration) to be sampled once daily:** green heparin tube, send urgently to biochemistry by courier if necessary. At night and weekends, centrifuge and freeze the plasma, send urgently in the morning.

PATHOPHYSIOLOGY:

Maple Urine Syrup Disease is caused by a deficit in the catabolism of branched chain aminoacids, including leucine, which are contained in every natural protein. Excess leucine causes endogenous intoxication associated with gastrointestinal and neurological disorders which can lead to coma with functional and life-threatening consequences for the patient.

The standard treatment consists of:

- A strict low-protein diet: completely excludes meat, fish and eggs, with other foodstuffs being allowed only in carefully measured amounts. See "maintenance diet" sheet.
- A formula of amino acids specific for MSUD is **ESSENTIAL** for patient survival. Must never be interrupted, especially in situations of metabolic decompensation.
- +/- Valine and isoleucine supplements for some patients (mandatory for all patients during metabolic decompensation).
- Regular monitoring of leucine levels (target range between 1 and 5 mg/dL or 100 to 400 µmol/L).

ADVICE FOR PREPARATION OF THE AMINOACIDS MIXTURE FOR MSUD AND THE DIET:

According to the specific "emergency diet" sheet for each patient, if the products have been taken with them.

If the patient's AA mixture is not available, after reading the composition of the product:

- Mixtures or blends of AAs in powder for MSUD (MSUD express[®], MSUD 2 secunda[®], etc.): **check that it really is a mixture for MSUD and not for some other disease.**
- **1,5 to 2g of protein equivalents/kg/day** (! not 2g/kg of powder), divided into administrations every 4 to 6h.
- Dilute **15g of protein equivalents in 100 mL** of mineral water (warning: does not equal to 15g of powder).
- For liquid AA blends (e.g. MSUD cooler[®]): no dilution needed.
- Do not hesitate to contact the metabolism clinician to check the prescription.

- If exceptionally a feeding bottle / meal is missed during a hospital stay: give an emergency, protein-free meal (low-protein pasta, low-protein bread with butter and jam) or, if by bottle: PFD1[®] / Energivit[®]: 1 measuring spoon per 30 mL of water (0.7 kcal/mL)

- If the composition of the ongoing emergency diet is unknown: prepare an isocaloric solution with [100g PFD1[®] or Energivit[®] or Duocal[®] + 430mL water] or [80g maltodextrin + 20mL oil + 425 mL water]: equivalent preparations of 500mL = 500kcal, adjust total intake according to the patient's needs. Review during working hours with a dietician, especially for calcium and electrolytes (Na, K etc.) intake.

CIRCUMSTANCES WITH RISK OF DECOMPENSATION:

- Intercurrent infectious disease, fever, anorexia, vomiting, surgery, excess protein intake, **or any fasting state, insufficient caloric intake, weight loss or catabolic state.**
- **In all these situations, the patient must be kept in hospital** because coma can occur very rapidly. **They represent an emergency:** do the workup on the patient in A&E before admitting them to the ward. **ACT QUICKLY** to prevent cerebral oedema and its neurological sequelae.

CLINICAL SIGNS OF DECOMPENSATION: Do not wait for these signs!

- Acute neurological disorders (altered mental status, confusion, drowsiness, balance disorder, ataxia, behavioural change, tremors, abnormal movements, etc.).
- Or gastrointestinal signs (vomiting, anorexia, nausea, etc.).
- **Will progress to coma +/- seizures and death, or serious neurological sequelae if treatment is not started rapidly.**

DRUG CONTRAINDICATIONS / GENERAL ADVICE:

No drugs are contraindicated. Corticosteroid therapy: consider the need if duration > 3 days. Use hydrocortisone if necessary in intensive care.

- All vaccinations are recommended (particularly influenza).
- **Prolonged fasting is contraindicated**, never leave the patient without a supply of carbohydrate (infusion or continuous enteral feeding). **The oral aminoacid mixture must be reintroduced as soon as possible.**
- **Do not leave the patient without proteins for more than 3 days.** Do not forget vitamins and trace elements when intake is exclusively parenteral. The emergency treatment will be reassessed with the metabolism clinician during the day.
- **In case of admission to hospital** (or attendance at A&E): patients must take with them their usual treatments and the special products that they have in order to prepare an emergency diet.

SURGERY under General Anaesthesia:

WARNING: never leave the patient fasting without an infusion. Implement the emergency protocol with infusion as above, in preparation for surgery.

REFERENCE PHYSICIANS 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 clinical state or test results are worrying. As far as possible make calls before night-time.

Secretarial issues must be dealt with the outpatient office during the week or by email addressed to the patient's referring metabolic physician.

Certificate issued on :

Dr