

DISORDERS OF KETOGENESIS

(3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) lyase deficiency/HMG-CoA synthase deficiency)

Label

Priority patient: must not be kept waiting in the emergency department**IN THE EVENT OF VOMITING, DIARRHOEA, FEVER, FASTING = RISK OF HYPOGLYCAEMIA, HYPERAMMONAEMIA, COMA**

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

1 EMERGENCY ASSESSMENT

Capillary blood glucose, venous blood glucose, liver function tests, PT, factor V, blood ammonia, blood gases, serum electrolytes. Treatment must not be delayed.

2 START TREATMENT URGENTLY, without waiting for test results

- **If hypoglycaemia < 60 mg/dL (3.3 mmol/L):** Administer glucose 1 mL/kg as 30% glucose solution (max 30 mL) orally or via enteral tube if the patient is conscious, or 3 mL/kg of 10% glucose IV if unconscious (30% glucose also possible IV).
- Check capillary blood glucose 5 minutes later. If hypoglycaemia persists, administer a second glucose dose and check again 5 min later.
- Start an infusion immediately, even if blood glucose has been corrected: Infuse **10% glucose** with standard electrolyte supplementation* (not 10% glucose alone)

Age	0 - 24 months	2 - 4 years	4 - 14 years	> 14 years/adult	MAX. FLOW RATE
Balanced electrolyte solution 10% glucose	5 mL/kg/h (i.e. 8mg/kg/min)	4 mL/kg/h (7mg/kg/min)	3.5 mL/kg/h (6 mg/kg/min)	2.5 mL/kg/h (4 mg/kg/min)	<u>120 mL/h</u> <u>(3L/24h)</u>

*e.g.: Balanced electrolyte solutions such as Bionolyte, B45, Glucidion. If unavailable: 10% glucose + 4–6 g/L NaCl (70 mEq/L) and 2 g/L KCl (27 mEq/L).

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

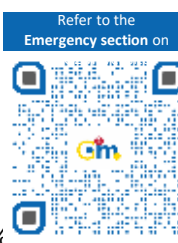
- **Continue** usual oral or IV medication
 - **L-Carnitine/Levocarnil:** usual dose or 100 mg/kg/day IV or in 4 doses/day (max 8 g/day)

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

- Presence of **coma** or **worsening** neurological clinical condition, or **persistence** of neurological signs 3 hours after start of treatment
- Signs of **severe hepatic failure:** PT < 30%, factor V < 50%
- **Hyperammonaemia > 100 µM, clearance treatments:**
 - **Sodium benzoate** by continuous IV infusion Start with a **loading dose** of 250 mg/kg over 2 hours (**max. 8g over 2 hours**), then 250 to 500 mg/kg/24h (**max. 12g/24h**) (give orally or via NG tube if no venous access available). Take ammonia level just before administering the loading dose, without waiting for the result.
- **Severe metabolic acidosis, pH < 7.1**, with hyperlactataemia. Treatment with bicarbonate is not usually necessary.

4 MONITORING

- Vital signs monitor
- Capillary blood glucose every 2 h: If hyperglycaemia is present: adjust carbohydrate intake (maintain at least 50%)
- Assessment: If initial assessment abnormal: monitor electrolytes, pH, blood ammonia and liver function.



PATHOPHYSIOLOGY

HMG-CoA lyase or HMG-CoA synthase deficiencies are **disorders of ketone body synthesis** (disorders of ketogenesis), that mimic **fatty acid oxidation disorders**. Risks: energy deficiency (**metabolic acidosis with hyperlactataemia, hepatic failure, hypoglycaemia**) during fasting episodes, and in HMG-CoA lyase deficiency, an additional toxic risk (intoxication by breakdown products of proteins).

Usual treatment may include (depending on patient):

- **Carnitine** (Levocarnil®) PO, to be given IV if fasting or food intolerance.
- Limiting duration of fasting, with nocturnal enteral nutrition or uncooked cornstarch in some patients.
- In HMG-CoA lyase deficiency: a low-protein diet may be recommended. See the “maintenance diet” sheet and a protein-free carbohydrate “emergency” diet by NG tube or IV in cases of risk of catabolism.

SITUATIONS WITH RISK OF DECOMPENSATION

- Intercurrent infection, fever, anorexia, vomiting, surgery **or any condition involving fasting, calorie deficiency, weight loss or catabolism**.
- **In all these situations, the patient must be hospitalised. This is an emergency:** stabilise the patient in the ED before transfer to hospital ward, and apply the protocol on the previous page. **ACT QUICKLY** to avoid hypoglycaemia and/or severe acidosis and/or hepatic failure (intoxication in HMG-CoA lyase), which can cause severe and irreversible neurological damage.

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

- Signs of **hypoglycaemia, impaired consciousness, vomiting, acidotic dyspnoea**.
- Progression to **coma +/- status epilepticus**
- **Hepatic failure**

GUIDANCE ON PRACTICAL ADMINISTRATION OF TREATMENTS

- 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. 1 g = 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 of sodium per gram of benzoate. Status = hospital preparation.

DRUG CONTRAINDICATIONS/GENERAL ADVICE:

Prohibited: salicylic acid, valproic acid

- All vaccinations are recommended (especially influenza).
- Prolonged fasting contraindicated: never leave patient without carbohydrate intake (infusion or continuous enteral tube feeding) or treatment
- Remember vitamin and trace element supplementation if the patient is on prolonged exclusive parenteral nutrition
- Do not leave the patient without protein intake for more than 3 days

SURGERY:

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

NUMBERS AND MEDICAL SPECIALISTS

On-call telephone numbers for metabolic emergencies:

At night, only 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. Whenever possible, calls should be made before nightfall.

Secretarial issues must be dealt with via the medical secretariat during the week, or by email addressed to the patient’s metabolic medicine specialist.

Certificate issued on

Dr