Tyrosinemia type 1

Label

Acute risk in cases of non-compliance with Nitisone treatment (Orfadin®)
Outside of this situation: no acute risk in treated patients.

1 PATHOPHYSIOLOGY

This pathology DOES NOT present a risk of coma nor acute metabolic decompensation in correctly treated patients.
It is a deficiency of an enzyme on the tyrosine degradation pathway, with hepatic toxicity (liver failure, cirrhosis, long-term risk of hepato-cellular carcinoma) and renal toxicity (proximal tubulopathy). The diagnosis is made in the first months of life following liver failure or earlier via neonatal screening.
This disease requires:

- **An essential medicinal treatment: NTBC or Orfadin (Nitisinone) at a dose of 1 to 2mg/kg/d orally.**
- A strict low-protein diet with controlled intake of tyrosine and amino acid substitutes. This type of diet totally excludes meat, fish and eggs, and any other protein-rich foods.

It is important to follow this diet, including in cases of hospitalisation, but there is no risk of acute decompensation in the case of an isolated error, or interruption to the diet.
- 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) provided by the family, or, if by bottle: 65 g malto-dextrin + 20 ml oil + 350 ml measured water (choose the volume you want to give); or PFD1® / Energivit® / Duocal ®: 1 measuring spoon per 30 mL of water (0.7 Kcal/ml)

2 IN CASE OF HOSPITALISATION OR INTERCURRENT PATHOLOGY

Provide treatment for the pathology that caused the patient to be admitted to A&E or hospital, as for all other patients, with no need for metabolic expertise.
It is vital to ensure that the Orfadin® treatment is taken regularly, with no recent interruptions, and to continue it (if doubts as to compliance: measure NTBC, Succinylacetone and urinary D-Ala - see methods overleaf).

In cases of interruption to Orfadin treatment, rare but serious risk of acute “pseudo-porphyric” crisis. The initial symptomatology is insidious, often starting a few weeks after stopping the treatment, sometimes triggered by a banal infectious episode: asthenia, agitation and psychosis, anorexia, vomiting, abdominal pains with hyponatremia and sometimes self-mutilation, HBP, tachycardia. Following this, the clinical picture also includes painful paresthesias and ascending motor polyneuropathy of “pseudo-Guillain-Barre” type with hyperextension, paralysis of the extremities (tetraparesia) and the diaphragm (respiratory paralysis), convulsions then death by asphyxia. These symptoms regress in a few weeks after retaking NTBC. This situation requires artificial ventilation, analgesia (morphine), correction of the hyponatremia, and an energy supply (glucose perfusion), beta-blockers, clonazepam, diazepam. A treatment by heme arginate (Normosang) should be considered (contact the French porphyria centre (https://www.porphyrie.net/contact/). See the detailed emergency protocol for porphyria when treating an acute porphyria attack.

3 DRUG CONTRAINDICATIONS / GENERAL ADVICE:

- Aspirin and NSAID are contraindicated. All other treatments can be given.
- All vaccinations are recommended.
- In case of surgery: no particular precautions to be taken. No contraindication to anaesthetics, excluding an acute pseudo-porphyria attack (see above).

NEVER STOP THE NTBC (Orfadin) TREATMENT, INCLUDING IN CASES OF INDUCED FASTING. This treatment is only available orally, no IV form is available.

SAMPLE METHODS AND SAMPLE DISPATCH TO MEASURE NTBC, Succinylacetone and urinary D-ALA

- Blood sample to measure NTBC:
    - Lithium heparin tube (green) 3ml. Centrifuge, aliquote the plasma in 2 tubes then freeze at -20°C. Dispatch the frozen plasma to the laboratory.
    - With the request, give details of the time the orfadin treatment was taken, the dosage and the time the sample was taken.
- Urinary sample for succinylacetone and D-ALA:
    - Urines over 12 hrs if possible, or 10ml sample. Freeze at -20°C. Dispatch the frozen urine to the laboratory.

Contact details for Bicêtre laboratory:
Laboratory of Biochemistry level 3
Hôpital Bicêtre – APHP-Université Paris Saclay
78 rue du général Leclerc
94275 Le Kremlin-Bicêtre
Tel: 01 45 21 26 05 / Fax: 01 45 21 35 74

Consult the **Emergency page** on

REFERENCE 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 clinical state or test results are worrying. As far as possible make calls 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