

Homocystinuria (CBS deficiency)

Treatment recommendations for pregnant and postpartum women:
INCREASED RISK of venous or arterial thrombosis due to combination of pro-thrombotic states: pregnancy, labour, postpartum and hyperhomocysteinaemia.

1 GENERAL TREATMENT

❑ B6-responsive CBS deficiency:

- **Preconception consultation (Obstetrician, Anaesthetist, Haemostasis specialist, Metabolic doctor).**
- **Preconception** metabolic work-up and quarterly monitoring: Total homocysteine (Hcyt), plasma amino acid chromatography (pAAC), methionine (Met), vitamins B9 and B12.
- Hcyt if possible close to normal in preconception (discuss compliance).
- Maintain vitamin B6 at minimum effective dose.
- Identical treatment to the general population in the absence of serious previous cerebrovascular event.
- If serious previous cerebrovascular event:
 - Prophylaxis for a thrombotic risk considered to be high:
 - LMWH 100 IU/kg/24h in one intake
 - from the start of pregnancy and up to 6 weeks postpartum
 - if treatment by AVK before the pregnancy: switch to LMWH at curative dose

❑ B6 non-responsive or partially responsive CBS deficiency:

- **Preconception consultation (Obstetrician, Anaesthetist, Haemostasis specialist, Metabolic doctor).**
- **Preconception** metabolic work-up and **monthly monitoring**: Hcyt, pAAC, Met, B9, B12.
- **Preconception** nutritional assessment (in the context of the low-protein, methionine-controlled diet with amino acid mixture substitutes without methionine) and at least three-monthly monitoring.
- Adjust the diet over the course of the pregnancy, particularly after the middle of the 2nd trimester: the methionine tolerance increases (because of the needs of the foetus) and the intake should be increased (the normal methionine tolerance is often doubled).
- Maintain the usual treatment by betaine, B6. Supplement with B9, B12 and trace elements in function to the nutritional assessment.
- Thrombophylaxis (see paragraph 2).

2 Thromboprophylaxis during pregnancy and postpartum

For B6 non-responsive or partially responsive CBS deficiency

1. If serious previous cerebrovascular event*:
 - Prophylaxis for a thrombotic risk considered to be high:
 - LMWH 100 IU/kg/24h in one intake
 - from the start of pregnancy and up to 6 weeks postpartum
 - if treatment by AVK before the pregnancy: switch to LMWH at curative dose
 - Platelet aggregation inhibitor 100mg/day in the evening, from the start of pregnancy and until 35 WA.
2. In the absence of a serious previous cerebrovascular event:
 - Prophylaxis to support the pregnancy:
 - LMWH starting from the 3rd trimester and up until 6 weeks postpartum.
 - Platelet aggregation inhibitor 100mg/day in the evening, from the start of pregnancy and until 35 WA.

* **serious previous cerebrovascular event:** venous (deep vein thrombosis, pulmonary embolism, cerebral thrombophlebitis, etc.) or arterial (embolic phenomenon or in situ thrombosis).

Consult the
Emergency page on



3 Procedure to follow when planning the labour

Preventing the risk of thrombosis for B6 non-responsive or partially responsive CBS deficiency:

1. Inform the referring metabolic doctor of the birth if the date is scheduled.
2. Inform the anaesthetist of the ongoing anticoagulant treatment and the latest metabolic work-up (conducted monthly).
3. In the birthing room or operating theatre: take samples for Hcyt, pAAC (Met).
4. Infusion: the day before, starting from the start of fasting if the birth is scheduled, otherwise from when the patient is admitted: **10% serum glucose** with standard electrolyte additions (not pure 10% glucose) with provision of 2 to 2.5 L/m²/d (hyperhydration to limit the risk of thrombosis), for example: 10% glucose + 4 to 6g/L of NaCl (70 to 105meq/L) and 2g/L of KCl (27meq/L).
5. Contraindication for Nitrous oxide (e.g. as MEOPA): contraindicated in CBS deficiency.
6. Continue Thromboprophylaxis following paragraph 2. Maintain the anticoagulation up until 6 weeks postpartum.
7. Return to usual pre-pregnancy low-protein diet: adjust this diet in line with the Hcyt results to be measured on D3.
8. Plan Hcyt at one month and three months after the birth, and in cases of a thrombotic event.

References:

- Bates et al. American Society of Haematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy. *Blood Adv.* 2018 Nov 27;2(22):3317-3359.
- Kernan et al. American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2014 Jul;45(7):2160-236

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