

Guidance on thiamine replacement in patients at risk of Refeeding Syndrome

Position Statement issued by

British Pharmaceutical Nutrition Group (BPNG), British Association of Parenteral and Enteral Nutrition (BAPEN), Parenteral and Enteral Nutrition Group (PENGE) and Neonatal and Paediatric Pharmacy Group (NPPG) May 2024

This guidance has been issued in view of Medicine Supply Notification (MSN/2024/038) for Pabrinex® (Vitamins B and C) Intravenous and Intramuscular High Potency solution for injection ampoules (03/04/2024). Pabrinex® Intravenous will be out of stock from Summer 2024.

There are no UK licensed alternatives to Pabrinex® IV and IM injections. The Medicines Supply Group work on behalf of the Department of Health and Social Care (DHSC) to ensure continuous supply of medicines in the UK. They are looking at parenteral thiamine preparations to be used once Pabrinex® stock has been exhausted. **All local protocols for refeeding syndrome should be reviewed as a priority to conserve stock for life threatening conditions.** For use of Pabrinex® in alcoholism and treatment of Wernicke's encephalopathy please refer to separate guidance.

Pabrinex® Intravenous contains per dose: thiamine 250mg, riboflavin 4mg, pyridoxine 50mg, nicotinamide 160mg, ascorbic acid 500mg, glucose 1000mg. This guideline focuses on thiamine supplementation as the key co-factor in refeeding syndrome.

Intravenous thiamine/Pabrinex® in prevention of refeeding syndrome should be reserved for those with intestinal failure, where oral/enteral route is unavailable.

Refeeding syndrome

The mechanism for the role of thiamine in refeeding is well recognised.¹ Thiamine is a co-factor in aerobic glucose consumption, and during refeeding there is an increase in utilisation of thiamine. Without replacement this can lead to the development of Wernicke's encephalopathy which can progress to the irreversible Korsakoff's syndrome. Patients with clinical symptoms of Wernicke's should be treated with higher doses of thiamine as per national guidance. Thiamine stores become depleted in patients at high risk of refeeding and exacerbated on the introduction of nutrition support, therefore guidelines recommend starting thiamine prior to introduction of nutrition in adult patients at high or extremely high risk of refeeding syndrome.

National Institute for Health and Care Excellence (NICE)² sets out the following criteria for determining adults at high risk of developing refeeding syndrome:

Patient has 1 or more of the following:

- BMI less than 16 kg/m²
- unintentional weight loss greater than 15% within the last 3 to 6 months
- little or no nutritional intake for more than 10 days
- low levels of potassium, phosphate or magnesium before feeding.

Or patient has 2 or more of the following:

- BMI less than 18.5 kg/m²
- unintentional weight loss greater than 10% within the last 3 to 6 months
- little or no nutritional intake for more than 5 days
- a history of alcohol abuse, or drugs including insulin, chemotherapy, antacids or diuretics.

Those with a BMI < 14 kg/m² with negligible nutrition for more than 15 days are at extremely high risk.

In paediatric patients, practice is variable and evidence remains limited. The current guidance for anorexia nervosa Medical Emergencies in Eating Disorders (MEED) suggests prescribing a complete multivitamin and mineral supplement for malnourished young people is logical and carries minimal risk. It also reports for older adolescents and those with chronic illness, following adult guidelines on prescription of thiamine and phosphate is justifiable. American

Society for Parenteral and Enteral Nutrition (ASPEN) consensus guidelines for refeeding suggests thiamine 2mg/kg to a max of 100–200 mg/day.³ In practice, if IV thiamine is indicated (where the oral or enteral route is not available) a proportion of Pabrinex® is usually prescribed according to the child's age as per the Summary of Product Characteristics for Pabrinex®.

The table below summarises worldwide variation in key guidelines.

Guideline	Recommendations for thiamine supplementation
NICE, Nutrition support for adults, CG32 ²	Providing immediately before and during the first 10 days of feeding: oral thiamine 200-300mg daily, Vitamin B Compound Strong 1-2 tablets, 3 times a day (or full dose daily intravenous vitamin B preparation, if necessary) and a balanced multivitamin or trace element supplement once daily.
ASPEN Consensus Recommendations for Refeeding Syndrome ⁴ (children and adults)	In adults: 100mg before feeding or before initiating glucose containing IV fluids inpatients at risk. 100mg/day for 5–7 days or longer in patients with severe starvation, chronic alcoholism, or other high risk for deficiency and/or signs of thiamine deficiency. In paediatric patients: Thiamine 2mg/kg to a max of 100–200mg/day before feeding commences or before initiating IV fluids containing dextrose in high-risk patients. Continue thiamine supplementation for 5–7 days or longer in patients with severe starvation, chronic alcoholism, or other high risk for deficiency and/or signs of thiamine deficiency.
ESPEN micronutrient guideline ⁵	300mg IV before initiating nutrition therapy, 200-300mg IV daily for at least 3 more days.

In view of more recent guideline and national shortages we advise parenteral thiamine should be used at the **lowest clinically suitable dose and course length**. Thiamine and Vitamin B Compound Strong tablets remain available and should be used as appropriate when clinically indicated as first line choice of vitamin B supplementation. Seek local pharmacy guidance for administration via enteral feeding tubes.

Recommendations

1. Intravenous thiamine replacement should only be used for patients with intestinal failure at high risk or extremely high risk of refeeding syndrome where the oral or enteral route is not available.
2. In adults, where IV thiamine is indicated we recommend 200-300mg (or 1 pair Pabrinex® ampoules) once daily before initiation of nutrition support and continued at this dose for 3 days. This may need to be extended to 5 days for higher-risk patients.
3. In paediatrics, where IV thiamine is indicated we recommend:

Age	Thiamine dose
Under 6 years	100mg thiamine once daily before initiation of nutrition support and continued at this dose for 3 days. This may need to be extended to 5 days for higher-risk patients.
6 - 10 years	150mg thiamine once daily before initiation of nutrition support and continued at this dose for 3 days. This may need to be extended to 5 days for higher-risk patients.
10 years and over	200-300mg thiamine (or 1 pair Pabrinex® ampoules) once daily before initiation of nutrition support and continued at this dose for 3 days. This may need to be extended to 5 days for higher-risk patients.

Patients should continue to receive multi-ingredient micronutrient preparation(s) whilst receiving parenteral nutrition (PN), either alongside every PN infusion or added to the bag.

References

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2. National Institute for Health and Care Excellence. Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition. Clinical guideline [CG32]. <https://www.nice.org.uk/guidance/cg32>. Published 2006 (updated 2017). Updated 2017. Accessed 22/04/2024.
3. The Royal College of Psychiatrists (RCPsych). Medical Emergencies in Eating Disorders: Guidance on Recognition and Management. [https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr233-medical-emergencies-in-eating-disorders-\(meed\)-guidance.pdf?sfvrsn=2d327483_42](https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr233-medical-emergencies-in-eating-disorders-(meed)-guidance.pdf?sfvrsn=2d327483_42). Published 2022. Accessed 22/04/2024.
4. da Silva JSV, Seres DS, Sabino K, et al. ASPEN Consensus Recommendations for Refeeding Syndrome. *Nutrition in Clinical Practice.* 2020;35(2):178-195. doi:<https://doi.org/10.1002/ncp.10474>.
5. Berger MM, Shenkin A, Schweinlin A, et al. ESPEN micronutrient guideline. *Clin Nutr.* 2022;41(6):1357-1424. doi:10.1016/j.clnu.2022.02.015.