Best practice guidance

Consensus guidance on the identification and management of Wernicke’s encephalopathy

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Introduction

Wernicke’s encephalopathy (WE) is an acute neuropsychiatric disorder with heterogeneous symptoms caused by thiamine (vitamin B₁) deficiency. Thiamine, one of the first water-soluble vitamins to be discovered, is:
- an essential coenzyme involved in intricate organic pathways within the body that has a central role in cerebral metabolism
- necessary for myelin sheath formation.

Thiamine deficiency was first reported in China over 1000 years ago, where it was and has been linked to the increased popularity of polished white rice. Although WE and Korsakoff’s syndrome were first described in the late 19th century, decades elapsed before these conditions were directly linked to their true cause—thiamine deficiency. Wernicke’s encephalopathy and Korsakoff’s syndrome can be considered acute and chronic sequelae of thiamine deficiency, respectively. Wernicke’s encephalopathy occurs early in the disease course and is characterised by non-inflammatory brain lesions. Without intervention, WE can eventually evolve into Korsakoff’s syndrome, which is associated with more permanent neurological damage and memory loss.

Wernicke’s encephalopathy is most commonly observed in patients with alcohol dependency, with a prevalence of up to 14% in patients with chronic alcoholism compared with between 0.4% and 2% in the general population. It requires urgent intervention as a medical emergency because failure to treat WE can lead to substantial morbidity and mortality. Conversely, prompt treatment can reverse the early symptoms of WE and reduce the risk of a patient developing Korsakoff’s syndrome.

The brain relies heavily on thiamine to function effectively; however, its absorption from the gastrointestinal tract can be reduced by up to 70% in people who misuse alcohol. Alcohol also increases the body’s demands for thiamine because this vitamin is required for alcohol metabolism and alcohol abuse impairs thiamine storage in the liver. As a result of impaired enteric absorption in patients with alcohol dependency, oral supplementation of thiamine does not increase thiamine levels in the cerebrospinal fluid; therefore, it is inadequate for correcting acute thiamine deficiency and preventing permanent brain damage in patients with WE. Thus, the cornerstone of treatment for WE is parenterally administered thiamine, which, at a concentration high enough, can be effectively transported across the blood–brain barrier.

Rationale for development

Wernicke’s encephalopathy is difficult to diagnose because the classic triad of signs (ophthalmoplegia, ataxia, and changes in mental status) occurs in around only 10–16% of patients. Additionally, symptoms may be overlooked because of their similarity to the effects of acute alcohol intoxication or mistaken for other neurological disorders or head trauma. The potential for poor identification and subsequent lack of treatment is evidenced by studies showing that WE is first diagnosed postmortem in over 80% of patients.

Current NICE guidance covers the use of thiamine in people at high risk of developing WE or with suspected WE and its prophylactic use in harmful or dependent drinkers. However, there is no UK guidance on the identification of WE in acute settings and a lack of consensus on treatment pathways. Therefore, there is a clear need for comprehensive guidance that compiles best practice for the identification and management of WE in an acute hospital setting into a single document. This consensus guideline focuses principally on the identification and management of alcohol-induced WE, including a care pathway (Figure 1, p.3), and represents the output of a consensus discussion.

Identification of WE

The diagnostic sensitivity of WE increases from around 23% when using the classic triad of signs to approximately 85% with the use of Caine’s criteria. These diagnostic criteria have also been adopted by the European Federation of Neurological Societies (EFNS) guideline.
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Risk of WE

- People at risk of WE include those with:
  - Malnutrition
  - Liver disease or an alcohol-related emergency
  - A current or previous alcohol-related admission to the emergency department

RISK OF WE

Parenteral thiamine for ≤3 days while in hospital

Emergency attendees
- Acute medical + surgical units
- Elective admission
- General medical + surgical wards
- Focus on at-risk groups
- Consider referral to geriatric medicine + geriatric medicine + surgical units

Diagnosis

Suspected or confirmed WE:
- Caine's criteria met
- Other diagnoses excluded

SUSPECTED WE

Review at day 3—is there an ongoing need for parenteral thiamine?

CONFIRMED WE

Review at day 5—is there continued clinical improvement?

Parenteral thiamine 2–3 pairs tds

One-off dose of 2 pairs of parenteral thiamine

Has the patient been discharged?

Yes

Yes

No

No

If not at risk consider need for oral thiamine (possibly in referral letter to GP)

CONFIRMED WE

Continue parenteral thiamine until no further clinical improvement

SUSPECTED WE

Switch to oral thiamine (50–100 mg tds)

Emergency presentation to ED (e.g. neurological, alcohol-related, medical emergency, trauma, or septicemia)

Referral to GP to consider oral thiamine and multivitamins

Figure 1: Care pathway for WE
Caine’s criteria apply not only to patients with alcohol dependency but also to any patient with suspected WE, although some symptoms may be more prominent in alcohol-dependent versus non-alcohol dependent patients.

Key clinical indicators, such as the early and late signs and symptoms of thiamine deficiency (see Box 1, above) as outlined by Thomson et al., may also aid healthcare professionals in the recognition of potential cases of WE.

**Box 1: Clinical indicators of thiamine deficiency**

<table>
<thead>
<tr>
<th>Early signs and symptoms</th>
<th>Later signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of appetite</td>
<td>Classic triad:</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>- oculomotor abnormalities</td>
</tr>
<tr>
<td>Fatigue, weakness, apathy</td>
<td>- cerebellar dysfunction (ataxia)</td>
</tr>
<tr>
<td>Giddiness, diplopia</td>
<td>- confusion</td>
</tr>
<tr>
<td>Insomnia, anxiety, difficulty concentrating</td>
<td>- Quiet global confusion with disorientation in time/place</td>
</tr>
<tr>
<td>Memory loss.</td>
<td>- Confabulation/hallucination</td>
</tr>
<tr>
<td></td>
<td>- Onset of coma.</td>
</tr>
</tbody>
</table>

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**Consensus recommendations—diagnosis of WE:**

Diagnosis of WE should be based on Caine’s criteria, which state that a patient must demonstrate any two of the following four signs:

- dietary deficiencies:
  - for example, significant weight loss over a short period of time, poor diet, or evidence of malnourishment
- eye signs:
  - ophthalmoplegia, nystagmus, or gaze palsy
- cerebellar dysfunction:
  - ataxia, abnormal past pointing, or dysdiadochokinesia
- altered mental state (e.g. disorientation, confusion) or mild memory impairment.

Other clinical indicators of thiamine deficiency may also point towards a diagnosis of WE.

**Assessment of risk of WE**

In up to 90% of patients with acute thiamine deficiency the development of WE is directly linked to alcohol consumption. Key risk factors include chronic misuse of alcohol, poor diet, or malnourishment, and decompensated liver disease. When looking for signs of malnourishment, it is important for clinicians to be vigilant for specific vulnerable populations (e.g. people of no fixed abode).

Although WE is most commonly observed in alcohol-dependent patients, it can also occur in patients with other predisposing conditions (Box 2, p.5). Given the increasing uptake of weight-loss surgery, special mention must be given to the long-lasting risk of WE after bariatric surgery.

**Screening for alcohol use disorders**

Effective assessment of patients’ alcohol use using validated alcohol screening tools is key to evaluating their risk of WE and constitutes clinical best practice for all patients presenting to hospital, be it via an emergency or elective route. This is particularly important in patients with an alcohol-related emergency department (ED) admission, decompensated liver disease, or evidence of malnutrition.

It is particularly important not to overlook any non-emergency medical presentations outside of the acute medicine setting in which alcohol may have played a significant role (Box 3, p.5). This includes patients presenting to general medical or surgical wards with cancers linked to chronic alcohol consumption, which is associated with risk of WE.
A validated alcohol questionnaire should be used for screening alcohol use—in most cases, AUDIT should be used, but an abbreviated version (Alcohol use disorders identification test – consumption [AUDIT-C]; Alcohol use disorders identification test – primary care; car, relax, alone, forget, friends, trouble [CRAFFT]; Single alcohol screening question [SASQ]; or the fast alcohol screening test [FAST]) can be used if time is limited.

Screening should examine the amount and frequency of alcohol consumption and patients’ dependence because alcohol intake directly affects thiamine concentration. Any person drinking above low-risk levels (e.g. above 14 units/week), whether dependent or not, is exposed to the risk of health problems (injury/liver disease/cancer/alcohol-related brain injury including WE).

Patients defined as at higher risk by Public Health England criteria and dependent by the World Health Organization (WHO) should be considered at high risk of WE (see Table 1, p.6).

**Box 2: Non-alcohol related causes of WE**
- Cancer
- Gastrointestinal surgery
- Hyperemesis gravidarum
- Starvation/fasting
- Gastrointestinal tract diseases
- AIDS
- Malnutrition
- Dialysis and renal disease
- Parenteral nutrition
- Persistent or recurrent vomiting
- Anorexia nervosa
- Stem cell/bone marrow transplantation.

**Consensus recommendations—drinking behaviour**
- All patients presenting to hospital should ideally be assessed for quantity of alcohol use and level of dependence using validated alcohol screening tools
- Certain medical presentations should trigger a higher index of suspicion for screening alcohol use (Box 2)
- As part of the clinical assessment, it is important to classify drinking behaviour as abstinent, low-risk, hazardous, harmful, or dependent; the AUDIT-C criteria are recommended for use in this risk stratification.

**Box 3: ‘Pitfall’ medical presentations at assessment of WE risk**
- Alcohol-associated cancers:
  - breast
  - upper gastrointestinal
  - colorectal
  - hepatocellular carcinoma
  - ear, nose, and throat
  - orofacial/maxillofacial
- Previous orthopaedic treatment
- Advanced age
- Dementia
- Previous bariatric surgery.

**Consensus recommendations—screening for WE**
- Recommended assessments for WE include history taking, clinical examination, basic cognitive screening, laboratory investigations, and radiological tests where indicated
- Cognitive screening should focus on orientation to time and place, concentration, and short-term memory (Box 4)
- Advanced thiamine assessments are unnecessary; however, testing of magnesium levels may be informative
- Clinicians should maintain a low threshold for performing a CT scan of the head to exclude other organic causes of confusion.
Standardised laboratory tests are also indicated to eliminate other potential causes of confusion. This panel should include:

- glucose
- urea and electrolytes
- liver function tests
- ammonia
- international normalised ratio
- full blood count
- magnesium
- phosphate levels.

Measurement of magnesium levels may also be useful because of the direct impact of this cofactor on the therapeutic efficacy of parenteral thiamine and high prevalence of hypomagnesaemia in patients who misuse alcohol.16

When assessing the confused, inebriated patient, it is always important to consider multiple possible causes; hence, computed tomography (CT) scanning of the head may be warranted to rule out other organic pathologies such as a subdural bleed or tumour. A magnetic resonance imaging (MRI) scan may be considered if there are diagnostic difficulties because it may show the classic lesions of WE.

Criteria for initiation of treatment

The only licensed treatment option for WE in the UK and the Republic of Ireland is Pabrinex® (vitamins B & C [high

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**Box 4: Initial basic screening of cognitive function**

- **Orientation to time and place:**
  - Do you know what day/date/month/year/ season it is?
  - Do you know the name of this ward/floor/ building/nearest town/county/country?

- **Concentration:**
  - Serial sevens test or spelling ‘world’ backwards

- **Short-term memory:**
  - Three words, 2-minute recall – e.g. apple, table, penny
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potency). The solution for infusion, which is also referred to as parenteral thiamine in this consensus document—is indicated in adults and children for rapid treatment of severe depletion or malabsorption of the water-soluble vitamins B and C, particularly in alcoholism.21,22

In the hospital setting, including acute medical units and emergency departments (EDs), clinicians should maintain a high index of suspicion for WE and a low threshold for treatment. These treatment criteria are recommended because they most closely mirror current clinical practice in the acute setting and are closely aligned with NICE guidance.12

In the hospital setting, parenteral thiamine should be started immediately in the following groups:

■ any patient at risk of WE (e.g. dependent drinkers who are malnourished or at risk of malnourishment or who have decompensated liver disease) or with suspected WE
■ all alcohol-dependent patients requiring hospital admission—even if apparently well-nourished
■ all dependent drinkers who attend the ED and are malnourished or who have decompensated liver disease but who do not require admission—this group should be followed up with oral thiamine.

From a practical perspective, it is better to administer parenteral thiamine to all patients with alcohol dependence, even the small fraction who appear well nourished, given that the majority of these patients are likely to be thiamine-deficient. Attendance at the ED also provides a useful opportunity to 'top-up' thiamine levels prior to discharge in people who misuse alcohol, even if the patient is not being admitted (the full course of parenteral thiamine will not be completed in this situation). Ideally, this intervention should be followed up with ongoing oral thiamine prescribed by the patient’s GP.

Consensus recommendations—treatment initiation:

■ In the acute hospital setting, there should be a high index of suspicion for WE and a low threshold for treatment
■ Initiation of parenteral thiamine is recommended in the following patients:
  ▪ all dependent drinkers
  ▪ all harmful or hazardous drinkers with either malnutrition or decompensated liver disease
  ▪ all cases or suspected cases of WE
  ▪ anyone at risk of WE (e.g. dependent drinkers, all harmful or hazardous drinkers with either malnutrition or decompensated liver disease)
  ▪ all harmful or dependent drinkers who present to the ED with malnourishment or decompensated liver disease
■ Treatment should be initiated immediately.

Consensus recommendations—thiamine administration:

■ Parenteral thiamine is the only recommended treatment option for suspected WE
■ Dosing of two to three pairs of Pabrinex (vitamins B and C [high potency]) solution for infusion three times a day for 3–5 days is recommended for all patients undergoing admission to hospital; the same dose should be employed for both prophylaxis and treatment (i.e. for suspected and confirmed WE)
■ For at-risk patients who are not admitted to hospital, a one-off dose of two pairs of Pabrinex solution for infusion should be given
■ Parenteral thiamine should be administered in 100 ml of 0.9% sodium chloride or 5% dextrose over 30 minutes
■ Administration of thiamine is preferentially by IV infusion; however, IM injection is a potential alternative in certain situations.*

*Pabrinex IM injection is licensed for use in the UK at one pair twice daily for up to 7 days, and is not licensed for use in the Republic of Ireland.

WE=Wernicke’s encephalopathy; IV=intravenous; IM=intramuscular

For rapid therapy of severe depletion of thiamine, particularly in alcoholism, which can lead to WE, the recommended dose of Pabrinex solution for infusion is two to three pairs given three times a day.21 In confirmed or suspected WE (unless WE has been excluded), NICE recommends giving parental thiamine for a minimum duration of 5 days.22 In practice, patients are usually administered two pairs three times a day.

Treatment

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In severe cases of established WE, patients with severe malnutrition, or where clinicians have significant concerns, the higher parenteral thiamine dose of three pairs three times a day may be considered.

Parenteral thiamine should be administered in 50–100 ml of 0.9% sodium chloride or 5% dextrose over 30 minutes. The same dose of parenteral thiamine should be used for both prophylaxis and treatment. This recommendation for uniform dosing is based on the recognition that many clinicians already adopt the practical approach of using the same dose of parenteral thiamine for suspected, confirmed, and 'at-risk' cases of WE because of the complexities involved in making an accurate diagnosis of WE.

For patients at risk of WE but not undergoing admission to hospital, a one-off dose of two pairs of Pabrinex is recommended as a valuable opportunity to ‘top-up’ thiamine levels.

It is preferable to give thiamine via intravenous (IV) infusion; however, intramuscular (IM) injection is a potential alternative administration route in situations where an infusion is not practical. For example, infusion may be challenging for very confused or agitated patients. The recommended adult dose of IM is one pair twice daily for up to 7 days.

Duration of treatment

Patients with suspected WE should be treated with parenteral thiamine and undergo review, with cognitive reassessment, after 3 days. Treatment should be continued for up to 5 days to attain maximal improvement. If no improvement occurs after 5 days, then a full formal assessment should be performed to rule out other possible aetiologies. In practice, it may be preferable to prescribe all patients a full 5-day course of parenteral thiamine but reassess at day 3 and continue or cease treatment as required.

Consensus recommendations—treatment duration

- For confirmed WE, 5 days of parenteral thiamine treatment is recommended
- For suspected WE, 3–5 days of parenteral thiamine treatment is recommended, with review at day 3.

Consensus recommendations—follow-up treatment

- It may be appropriate to explore methods for ongoing delivery of parenteral thiamine outside the acute setting to allow treatment to continue and be completed in the community when required
- Follow-up treatment with oral thiamine (50–100 mg three times per day for ≥6 weeks) should be offered to any patient who has received parenteral thiamine.

Ensuring treatment continuation

For patients moving from hospital to complete their detox in a community setting (e.g. a detox centre or ambulatory care), it would be advantageous to have processes in place for continuing and completing parenteral thiamine therapy on site. This is recognised as predominately a commissioning issue and therefore beyond the scope of this guideline. However, the perceived risk of anaphylaxis with parenteral thiamine, which has represented a stumbling block to community usage in the past, appears overstated. In reality, evidence suggests that thiamine is generally well tolerated, with a risk of anaphylaxis of around four in one million administrations of IV thiamine and one in five million administrations of IM thiamine). Indeed, the EFNS guideline states that: ‘because a delay in treatment may cause irreversible brain damage and is life-threatening we recommend to start treatment immediately, even in the absence of facilities for resuscitation.’

All patients treated with parenteral thiamine should receive follow-up treatment with oral thiamine at a dose of 50–100 mg three times per day. This oral thiamine prescription should be reviewed after 6 weeks and continued for as long as the patient continues to drink or remains in an at-risk group.

Monitoring and review

At all times, right from the outset of the treatment pathway, it is important to assess patients’ mental capacity and, if necessary, consider detention under the Mental Health Act or Mental Capacity Act.

Patients with suspected WE should be reviewed daily to assess improvement in their cognitive function and coordination. It is also important to remain vigilant for any signs of clinical deterioration suggestive of a different underlying diagnosis. If a patient shows continuing
neurocognitive improvement after 5 days of parenteral thiamine therapy, consideration should be given to continuing this treatment.

Incomplete recovery of cognitive function

Any patient who appears to have residual cognitive deficits when the confusion resolves should undergo assessment by the following clinical specialties:

- psychiatry—to assess mental capacity and assist with monitoring of cognitive function and mental state:
  - consider formal cognitive testing using the Montreal Cognitive Assessment, Addenbrooke’s Cognitive Examination, Frontal Assessment Battery, or Mini Mental State Examination if cognitive impairment persists
- occupational therapy—to evaluate functional ability and capacity to live at home alone
- social work—to assess funding of care, support package requirements, and alternative placement options (if unable to return home)
- neuropsychology—to provide more in-depth cognitive testing in complex cases and assess rehabilitation potential.

In practice, psychiatrists are often asked to make a formal diagnosis of Korsakoff’s syndrome and exclude other conditions. However, confirmation of a definitive diagnosis of Korsakoff’s syndrome may require a longer period of assessment.

Discharge pathways

Dependent on the individual patient assessment, options after discharge include: neurorehabilitation; a return home with support from social work or family; or residential care. There is substantial evidence to suggest that patients with Korsakoff’s syndrome can improve over a sufficiently long period with dedicated, specialist neurocognitive rehabilitation. All patients discharged after treatment for alcohol-related WE require follow up from addiction services and relapse prevention work.

Conclusion

Wernicke’s encephalopathy is a serious, acute neuropsychiatric syndrome most commonly seen in patients with alcohol dependence, especially those with

**Consensus recommendations—assessment of mental capacity**

- It is important to assess patients’ mental capacity and consider detention under the Mental Health/Mental Capacity Acts where required
- Patients with suspected WE should be reviewed daily for improvements in cognitive function and coordination and for deterioration requiring consideration of alternative diagnoses
- If continued neurocognitive improvement is evident on day 5 of treatment, consideration can be given to continuing parenteral thiamine.

**Consensus recommendations—residual cognitive defects**:

- If clinical improvement abates and the patient has residual cognitive deficits, specialist assessment for suspected Korsakoff’s syndrome is required (including an MRI), followed by referral to a neurocognitive rehabilitation centre
- A multidisciplinary care review should be conducted involving the patient and their family, with input from the following clinical specialities:
  - psychiatry
  - occupational therapy
  - social work
  - neuropsychology.

**Consensus recommendations—discharge**

- The discharge pathway for an individual patient will depend on the outcomes of multidisciplinary assessment
- The follow up of patients successfully treated with parenteral thiamine for WE should include assertive outreach and follow up from alcohol recovery services.
Concurrent malnourishment. The syndrome is difficult to diagnose because the classic triad of symptoms is rarely present. The consequences of neither identifying nor treating WE are significant: patients with Korsakoff’s syndrome may require care for the rest of their lives. Parenteral thiamine, when given early, helps to manage the acute and chronic consequences of thiamine deficiency.

Conflicts of interest

Mark Buchanan (chair)—has received consultancy fees from Kyowa Kirin Ltd.

Adrian Brown—has received consultancy fees from Kyowa Kirin Ltd.

Malcolm Cameron—has received consultancy fees from Kyowa Kirin Ltd.

Stephen Stewart—has received funding from Kyowa Kirin Ltd to run a liver health day for hospital staff and has also received consultancy fees from Kyowa Kirin Ltd.

References

12. NICE. Alcohol-use disorders: diagnosis and management of physical complications. NICE Clinical Guideline 100. NICE, 2010. Available at: www.nice.org.uk/cg100
**For the United Kingdom:**

**PABRINEX® Intravenous High Potency (IVHP), Concentrate for Solution for Infusion**

**Prescribing Information.** Please refer to the full Summary of Product Characteristics before prescribing.

**Name:** PABRINEX® Intravenous High Potency (IVHP), Concentrate for Solution for Infusion. **Active Ingredients:** Pabrinex IVHP is presented as a pair of (two) 5ml ampoules (labelled No. 1 and No. 2). Each No. 1 ampoule contains thiamine hydrochloride 250mg, riboflavin 4mg and pyridoxine hydrochloride 50mg. Each No. 2 ampoule contains ascorbic acid 500mg, nicotinamide 160mg and glucose (as monohydrate) 1000mg. **Indications:** Rapid therapy of severe depletion or malabsorption of the water-soluble vitamins B and C, particularly in alcoholism. **Dosage and Administration:** Before administration ensure both the Summary of Product Characteristics and ampoule labels refer to INTRAVENOUS infusion. **Adverse Effects:** Hypersensitivity (including anaphylaxis, rash and urticaria), paraesthesia, hypotension, and injection site reactions. Prescribers should consult the summary of product characteristics for further details of side-effects. **Contraindications:** Known hypersensitivity to any of the active substances or excipients. **Precautions:** Potentially serious allergic reactions such as anaphylactic shock may occur rarely, during or shortly after administration of Pabrinex IVHP. Symptoms such as sneezing or mild asthma are warning signs that further injections may give rise to anaphylactic shock. Facilities for treating anaphylactic reactions should be available whenever Pabrinex IVHP is administered. To minimise risk, infuse over 30 minutes. **Interactions:** The content of pyridoxine may interfere with the effects of concurrent levodopa therapy. **Pregnancy and Lactation:** No adverse effects have been noted during pregnancy or lactation at recommended doses when used as clinically indicated. The potential risk for humans is unknown. **Legal category:** POM. **Marketing Authorisation Holder:** Kyowa Kirin Limited, Galabank Business Park, Galashiels, TD1 1QH, UK. **Marketing Authorisation Number:** Pabrinex IVHP: PL 16508/0049. **NHS price:** Pabrinex IVHP as 5 pairs of 5 ml ampoules: £16.23; Pabrinex IVHP as 10 pairs of 5 ml ampoules: £22.53. **Date of prescribing information:** June 2018. *Pabrinex is a registered trade mark. UK/PAB/0276*

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**For the Republic of Ireland:**

**PABRINEX® Intramuscular High Potency (IMHP) solution for injection.**

**Prescribing Information.** Please refer to the full Summary of Product Characteristics before prescribing.

**Name:** PABRINEX® Intramuscular High Potency solution for injection. **Active Ingredients:** Pabrinex IMHP is presented as a pair of (two) ampoules (5ml ampoules labelled No. 1 and 2ml ampoules labelled No. 2). The contents of a pair of ampoules (7ml) are mixed immediately prior to use. Each No. 1 ampoule contains: thiamine hydrochloride 250mg, riboflavin 4mg and pyridoxine hydrochloride 50mg. Each No. 2 ampoule contains ascorbic acid 500mg and nicotinamide 160mg. **Indications:** Rapid therapy of severe depletion or malabsorption of the water-soluble vitamins B and C, particularly in alcoholism. **Dosage and Administration:** Before administration ensure both the Summary of Product Characteristics and ampoule labels refer to INTRAMUSCULAR injection. **Adulst:** The contents of one pair of ampoules (total 7ml) should be drawn up into a syringe to mix just before use and injected slowly, high into the gluteal muscle 5cm below the iliac crest, twice daily for up to 7 days. **Elderly:** As for adults. **Children:** Pabrinex IMHP is rarely indicated for administration to children; for further information refer to full SmPC. **Adverse Effects:** Hypersensitivity (including anaphylaxis, rash and urticaria), paraesthesia, hypotension, and injection site reactions. Prescribers should consult the summary of product characteristics for further details of side-effects. **Contraindications:** Known hypersensitivity to any of the active constituents or excipients. **Precautions:** Potentially serious allergic adverse reactions such as anaphylactic shock may occur rarely, during, or shortly after administration. Symptoms such as sneezing or mild asthma are warning signs that further injections may give rise to anaphylactic shock. Facilities for treating anaphylactic reactions should be available whenever Pabrinex IMHP is administered. Known hypersensitivity to any of the active substances or excipients. **Legal category:** POM. **Marketing Authorisation Holder:** Kyowa Kirin Limited, Galabank Business Park, Galashiels, TD1 1QH, UK. **Marketing Authorisation Number:** Pabrinex IMHP: PA 2288/001/001. **NHS price:** Pabrinex IMHP as 10 pairs of ampoules: £22.53. **Date of prescribing information:** December 2017. *Pabrinex is a registered trade mark.*

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