

Phenobarbital (Phenobarbitone) (red)

Introduction

SPECIALIST PALLIATIVE CARE INVOLVEMENT ESSENTIAL

Description:

Phenobarbital is classed as a sedative anti-epileptic that has an overall effect of depressing the central nervous system. This is achieved by a dual action of prolonging the opening of chloride channels on GABA receptor complex and inhibiting glutamate transmission at non- NMDA receptor channels.

High doses of Phenobarbital can result in general anaesthesia.

Preparations


Phenobarbital sodium 200mg/ml injection: 1ml ampoules: Excipients include propylene glycol 90%

This formulation is classified as Controlled Drug Schedule 3.

Indications

Licensed indications - all forms of epilepsy except typical absence seizures and status epilepticus.

In palliative care phenobarbital may be considered by specialist palliative care practitioners for:

1. Controlling seizures in patients who are unable to swallow and for whom a benzodiazepine (midazolam/clonazepam) is either ineffective or inappropriate. **Unlicensed use when administered by CSCI.**
2. Patients with terminal agitation who have not responded to the combined use of a benzodiazepine (midazolam/ clonazepam) and an anti-psychotic (levomepromazine/  haloperidol). **Unlicensed use.**

Cautions

Avoid subcutaneous bolus injections; the solution has a high pH 10-11 that can cause tissue necrosis. For IV administration dilute with 10 times own volume with water for injection (WFI).

Avoid sudden withdrawal.

In mild/moderate renal and hepatic impairment, use lowest effective dose and monitor for adverse effects.

Use with caution in elderly patients.

Contraindications

- Severe hepatic and renal impairment
- Acute intermittent porphyria
- Severe respiratory depression

These are not absolute contraindications if the patient is in the last days of life. Careful titration is however necessary.

Important drug interactions

Phenobarbital is metabolised by CYP2C19. CYP2C19 Inhibitors **may enhance** the effect of Phenobarbital

Examples of CYP2C19 inhibitors:


Fluconazole Fluoxetine

Omeprazole Lansoprazole

Phenobarbital induces various cytochrome P450 enzymes (CYP1A2, CYP2B6, CYP2C8/9, CYP2C19 and CYP3A4) that can cause many clinically significant drug interactions. As enzyme induction may take up to two weeks to develop, dose adjustments of concurrently administered drugs, that are predominantly metabolised by the cytochrome pathway or undergo glucuronidation, may be necessary.

Phenobarbital **may decrease** the effect of the following: The list is not exhaustive,

Clonazepam Corticosteroids: - (dexamethasone, methylprednisolone, prednisolone)

 Haloperidol Fentanyl

Methadone Metronidazole

Mirtazepine Oxycodone

Phenytoin Tricyclics

Valproate Paracetamol

Be aware of the potential for interactions: doses may need to be adjusted

Side effects

Drowsiness, lethargy, ataxia, confusion, respiratory depression, paradoxical excitement, irritability, restlessness, delirium

Skin reactions (common if given by continuous subcutaneous infusion (CSCI); undiluted Phenobarbital injection is very alkaline)

Dose and Administration

Terminal refractory agitation: (Generally third line with specialist palliative care input)

Initial dose 100 to 200mg IM (undiluted) or IV (diluted with 10 times own volume) injection.

Continue treatment with 200 to 600mg via CSCI over 24hours. Final volume of CSCI recommended to be at least 10 times the Phenobarbital volume. See Further information section below for advice on administering doses above 440mg/day to take account of volume issues.

[SEE GUIDELINE FOR TREATING AGITATION](#)

Epilepsy:

Initial dose (if necessary) 100mg by IV injection, dilute 0.5ml Phenobarbital with 5ml WFI

Continue treatment with 200 to 400mg (i.e total volume 11 to 22ml after dilution with 10 times own volume) via CSCI over 24hours.

Status epilepticus:

10mg/kg by IV injection at a rate of not more than 100mg/min. Ensure dilution with 10 times own volume of WFI. Maximum dose: 1 gram

[SEE GUIDELINE FOR TREATING SEIZURES](#)

Practice Points

- Specialist input recommended
- Dilute each 200mg (1ml) Phenobarbital ampoule with at least 10ml WFI to minimise skin reactions when administering dose by subcutaneous or intravenous injection.
- Diluent: Water for injection, but Sodium Chloride 0.9% may also be used.
- May be given undiluted by the IM route
- Avoid SC bolus injections; CSCI usually well tolerated if diluted appropriately
- Phenobarbital is incompatible with most drugs when mixed in CSCI. Generally best to administer via a separate CSCI or seek specialist pharmacy advice.
- This formulation is classified as Controlled Drug Schedule 3. Phenobarbital does not legally require safe custody in a locked cabinet or a record to be kept in the CD register
- CD prescription requirements apply

Patient and carer advice points

Report any signs of skin reactions

Further Information

The requirement to dilute with 10 times own volume presents potential difficulty when administering higher doses. Approximately 440mg (i.e. 22ml) can be administered in a 30ml BD Plastipak® leurlock syringe using a T34 syringe pump in a lockbox. Up to 600mg (i.e. 33ml) can be administered in a 50ml BD Plastipak® leurlock syringe but the T34 lockbox cannot accommodate the larger syringe. The following options may be considered depending on your area's preferred choice (Please see local guidance);

1. Divide the daily dose between 2 pumps to administer over 24hrs
2. Administer via two 12hourly infusions (medical physics may be required to reset the pump)
3. Administer using a non-ambulatory volumetric pump

There are anecdotal reports of more concentrated solutions being administered subcutaneously with minimal adverse effect. This practice should only be considered in exceptional circumstances where further dilution is impractical and the increased risk of skin reactions is accepted.

References

1. Palliative Care Formulary 4th Edition
2. The Syringe Driver 3rd Edition