Phenobarbital: Pediatric drug information  Lexicomp®

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(For additional information see "Phenobarbital: Drug information" and see "Phenobarbital: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

**Brand Names: Canada**  Phenobarb

**Therapeutic Category**  Anticonvulsant, Barbiturate; Barbiturate; Hypnotic; Sedative

**Dosing: Neonatal**

**Status epilepticus; neonatal seizures:** Limited data available: IV: Initial: 15-20 mg/kg as a single dose; may repeat doses of 5-10 mg/kg every 15-20 minutes as needed (maximum total dose: 40 mg/kg) (Cloherty, 2012; Gilman, 1989; Lockman, 1979; Painter, 1978; Painter, 1981). **Note:** Additional respiratory support may be required, especially when maximizing loading dose (Hegenbarth, 2008).

**Seizures, maintenance therapy:** Oral, IV: 3-4 mg/kg/day given once daily; maintenance dose usually starts 12-24 hours after loading dose; assess serum concentrations; increase to 5 mg/kg/day if needed (usually by second week of therapy) (Bourgeois, 1995; Cloherty, 2012; Kleigman, 2011)

**Neonatal abstinence syndrome** (AAP, 1998; Burgos, 2009; Hudak, 2012): Limited data available:

- **Loading dose (optional):** IV, Oral: 16 mg/kg
  - IV: Administer as a single dose; follow with maintenance dose 12-24 hours after loading dose
  - Oral: Administer divided into 2 doses and administered every 4-6 hours; follow with maintenance dose 12-24 hours after loading dose

- **Maintenance dose:** Oral, IV: Initial: 5 mg/kg/day divided every 12 hours; adjust dose according to abstinence scores and serum concentrations; usual required dose: 2-8 mg/kg/day. After patient is stabilized, decrease phenobarbital dose 20% every other day or such that drug concentration decreases by 10% to 20% per day (AAP, 1998; Burgos, 2009; Finnegan, 1979).

- **Neuroprotectant following anoxic injury (with or without cooling):** Limited data available: IV: 40 mg/kg once; if introducing therapeutic hypothermia, administer prior to cooling (Hall, 1998; Meyn, 2010).

**Dosing: Usual**

(For additional information see "Phenobarbital: Drug information")

**Pediatric:**

**Status epilepticus:** Infants, Children, and Adolescents: IV: Initial: 15-20 mg/kg; maximum dose: 1000 mg; may repeat once after 10-15 minutes if needed; maximum total dose: 40 mg/kg; repeat doses administered sooner than 10-15 minutes may not allow adequate time for peak CNS concentrations to be achieved and may lead to CNS depression (Brophy, 2012; Hegenbarth, 2008).
Note: Additional respiratory support may be required particularly when maximizing loading dose or if concurrent sedative therapy.

Seizures, maintenance therapy: Note: Maintenance dose usually starts 12 hours after loading dose:

Manufacturer's labeling: Infants, Children, and Adolescents: Oral: 3-6 mg/kg/day

Alternate dosing: Limited data available (Geurin, 2006; Kliegman, 2011):

Initial: Oral, IV:

Infants and Children ≤5 years: 3-5 mg/kg/day in 1-2 divided doses
Children >5 years: 2-3 mg/kg/day in 1-2 divided doses
Adolescents: 1-3 mg/kg/day in 1-2 divided doses (Nelson, 1996)

Usual dosing range: Note: Dosage should be individualized based upon clinical response and serum concentration; once daily doses usually administered at bedtime in children and adolescents. Some centers have used:

Infants: 5-6 mg/kg/day in 1-2 divided doses
Children:

1-5 years: 6-8 mg/kg/day in 1-2 divided doses
5-12 years: 4-6 mg/kg/day in 1-2 divided doses
Adolescents: 1-3 mg/kg/day in 1-2 divided doses

Sedation: Note: Newer, shorter-acting agents may be preferable.

Manufacturer's labeling: Children and Adolescents: Oral: 2 mg/kg/dose 3 times daily; maximum dose: 40 mg

Alternate dosing: Limited data available: Infants and Children: IM, Oral: 2-3 mg/kg/day in divided doses every 8-12 hours (Nelson, 1996)

Insomnia (hypnotic): Limited data available; shorter-acting agents may be preferable: Infants and Children: IM, Oral: 2-3 mg/kg/dose; may repeat dose as needed after 12-24 hours (Nelson, 1996); some centers have used: IM, IV: 3-5 mg/kg at bedtime

Hyperbilirubinemia: Limited data available: Infants and Children: Oral: Usual range: 3-8 mg/kg/day in 2-3 divided doses; doses up to 10 mg/kg/day in divided doses have been used in case reports (Cies, 2007; Nelson, 1996); for the treatment of hyperbilirubinemia in Crigler-Najjar Syndrome, a dose of 5 mg/kg/day has been used to reduce serum bilirubin concentrations (Kliegman, 2011); not recommended for management of biliary cirrhosis due to sedation and other adverse effects (Lindor-AASLD, 2009)

Sedative/hypnotic withdrawal; prevention; conversion of PENTobarbital to PHENobarbital (PENTobarbital infusion, a total cumulative PENTobarbital dose ≥25 mg/kg or duration ≥5-7 days): Limited data available: Infants, Children, and Adolescents: The following approach transitioning from PENTobarbital to PHENobarbital has been described: Discontinue PENTobarbital infusion, administer half of the PHENobarbital IV loading dose (see table) over 1 hour followed 6 hours later by the remaining half of PHENobarbital loading dose IV (over 1 hour). Begin IV maintenance PHENobarbital dose 6 hours after loading dose completed; the maintenance
PHENobarbital dose should be $1/3$ of the initial loading dose and given every 12 hours. Once patient is stabilized, may switch to oral therapy and begin tapering 10% to 20% weekly (Tobias, 2000; Tobias, 2000a). **Note:** This conversion method is based on preliminary data in mechanically ventilated patients. Closely monitor respiratory status and evaluate patient for withdrawal symptoms.

<table>
<thead>
<tr>
<th>PENTobarbital Infusion Rate (mg/kg/hour)</th>
<th>PHENobarbital IV Loading Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 2</td>
<td>8</td>
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<tr>
<td>2 to 3</td>
<td>15</td>
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<td>3 to 4</td>
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**Adult:**

**Sedation:** Oral, IM: 30-120 mg/day in 2-3 divided doses

**Preoperative sedation:** IM: 100-200 mg 1-1.5 hours before procedure

**Anticonvulsant/status epilepticus:**

Loading dose: IV: 10-20 mg/kg (maximum rate: ≤60 mg/minute in patients ≥60 kg); may repeat dose in 20-minute intervals as needed; maximum total dose: 30 mg/kg

Maintenance dose: Oral, IV: 1-3 mg/kg/day in divided doses or 50-100 mg 2-3 times/day

**Dosing adjustment in renal impairment:** No specific dosage adjustment provided in manufacturer's labeling; reduced doses are recommended. The following guidelines have been used by some clinicians (Aronoff, 2007):

**Infants, Children, and Adolescents:** **Note:** Renally adjusted dose recommendations are based on doses of 3-7 mg/kg/day every 12-24 hours

GFR ≥10 mL/minute/1.73 m²: No adjustment necessary

GFR <10 mL/minute/1.73 m²: Decrease normal dose by 50% and administer every 24 hours

Intermittent hemodialysis (moderately dialyzable (20% to 50%)): Supplemental dose may be needed during and after dialysis depending on individual seizure threshold

Peritoneal dialysis (PD): 40% to 50% removed; amount varies depending on number of cycles

Continuous renal replacement therapy (CRRT): Monitor serum concentrations; a case report suggests that clearance and volume of distribution increased with CVVH; more frequent and higher dosing may be necessary in some cases (Pasko, 2004)

**Adults:**

CrCl ≥10 mL/minute: No dosage adjustment necessary.

CrCl <10 mL/minute: Administer every 12-16 hours.

Hemodialysis (moderately dialyzable (20% to 50%)): Administer dose before dialysis and 50% of dose after dialysis.
Peritoneal dialysis: Administer 50% of normal dose.

CRRT: Administer normal dose and monitor levels.

**Dosing adjustment in hepatic impairment:** No specific dosage adjustment provided in manufacturer’s labeling; reduced doses are recommended. Phenobarbital exposure is increased with hepatic impairment; use with caution.

**Dosage Forms**  Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

- **Elixir, Oral:**
  - Generic: 20 mg/5 mL (473 mL)

- **Solution, Oral:**
  - Generic: 20 mg/5 mL (473 mL)

- **Solution, Injection, as sodium:**
  - Generic: 65 mg/mL (1 mL); 130 mg/mL (1 mL)

- **Tablet, Oral:**
  - Generic: 15 mg, 16.2 mg, 30 mg, 32.4 mg, 60 mg, 64.8 mg, 97.2 mg, 100 mg

**Generic Availability (US)**  Yes

**Controlled Substance**  C-IV

**Administration**

- **Oral:** Administer elixir or solution with water, milk, or juice

  Parenteral: Do not inject IV faster than 1 mg/kg/minute with a maximum of 30 mg/minute for infants and children and 60 mg/minute for adults ≥60 kg. Neonatal studies that used a loading dose of 40 mg/kg for perinatal asphyxia infused the dose over 60 minutes (Hall, 1998). Do not administer intra-arterially. Avoid extravasation; SubQ administration is not recommended. For IM administration, inject deep into muscle; do not exceed 5 mL per injection site (adults) due to potential for tissue irritation.

**Storage/Stability**

- **Oral:** Store between 20°C and 25°C (68°F and 77°F). Protect from light.

  Injection: Store between 20°C and 25°C (68°F and 77°F); excursions are permitted to 15°C to 30°C (59°F to 86°F).

**Use**

- **Oral:** Management of generalized tonic-clonic and partial seizures [FDA approved in pediatric patients (age not specified) and adults]; sedation (tablets: FDA approved in children and adults; elixir, oral solution: FDA approved in adults); insomnia (hypnotic) (FDA approved in adults)

  Parenteral: Treatment of generalized tonic-clonic seizures including status epilepticus and cortical focal seizures (FDA approved in adults); sedation (FDA approved in adults)
Phenobarbital has also been used in neonatal and febrile seizures (treatment and prevention); prevention and treatment of neonatal hyperbilirubinemia; hyperbilirubinemia associated with chronic cholestasis; management of sedative/hypnotic withdrawal; management of neonatal abstinence syndrome

Medication Safety Issues

Sound-alike/look-alike issues:

PHENobarbital may be confused with PENTobarbital, Phenergan, phenytoin

Geriatric Patients: High-Risk Medication:

Beers Criteria: Phenobarbital is identified in the Beers Criteria as a potentially inappropriate medication to be avoided in patients 65 years and older (independent of diagnosis or condition) due to its high rate of physical dependence, tolerance to sleep benefits, and increased risk of overdose at low dosages (Beers Criteria [AGS 2015]).

Pharmacy Quality Alliance (PQA): Phenobarbital is identified as a high-risk medication in patients 65 years and older on the PQA’s, Use of High-Risk Medications in the Elderly (HRM) performance measure, a safety measure used by the Centers for Medicare and Medicaid Services (CMS) for Medicare plans.

Adverse Reactions

Cardiovascular: Bradycardia, hypotension, syncope, thrombophlebitis (IV)

Central nervous system: Agitation, anxiety, ataxia, central nervous system stimulation, central nervous system depression, confusion, dizziness, drowsiness, hallucination, hangover effect, headache, impaired judgement, insomnia, lethargy, nervousness, nightmares

Dermatologic: Exfoliative dermatitis, skin rash, Stevens-Johnson syndrome

Gastrointestinal: Constipation, nausea, vomiting

Genitourinary: Oliguria

Hematologic & oncologic: Agranulocytosis, thrombocytopenia, megaloblastic anemia

Local: Pain at injection site

Neuromuscular & skeletal: Hyperkinesia, laryngospasm

Respiratory: Apnea (especially with rapid IV use), hypoventilation, respiratory depression

Contraindications  Hypersensitivity to phenobarbital, barbiturates or any component of the formulation; marked hepatic impairment; dyspnea or airway obstruction; porphyria (manifest and latent); intra-arterial administration, subcutaneous administration (not recommended); use in patients with a history of sedative/hypnotic addiction; nephritic patients (large doses)

Additional contraindications: IV only: Intra-arterial or subcutaneous administration; use in patients with a history of sedative/hypnotic addiction; nephritic patients (large doses)

Warnings/Precautions
Concern related to adverse effects:

- CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving).
- Hypersensitivity: Exfoliative dermatitis and Stevens-Johnson syndrome, possibly fatal, may occur; discontinue if dermatological reactions occur.
- Paradoxical stimulatory response: May cause paradoxical responses, including agitation and hyperactivity, particularly in patients with acute or chronic pain and pediatric patients.
- Respiratory depression: May cause respiratory depression particularly when administered intravenously; use with caution patients with respiratory disease, including status asthmaticus.

Disease-related concerns:

- Anemia: Use with caution in patients with severe anemia.
- Cardiac disease: Use with caution in patients with cardiac disease and in hemodynamically unstable patients (hypotension or shock).
- Depression: Use with caution in patients with depression or suicidal tendencies.
- Drug abuse: Use with caution in patients with a history of drug abuse; potential for drug dependency exists. Tolerance, psychological and physical dependence may occur with prolonged use.
- Hepatic impairment: Use with caution in patients with hepatic impairment. Avoid use in patients showing the premonitory signs of hepatic coma.
- Hyperthyroidism: Use with caution in patients with hyperthyroidism.
- Renal impairment: Use with caution in patients with renal impairment.

Concurrent drug therapy issues:

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

- Debilitated patients: Use with caution in patients who are debilitated.
- Fever: Use with caution in patients with a fever.
- Pediatric: Phenobarbital has been associated with cognitive deficits in children receiving therapy for complicated febrile seizures.

Dosage form specific issues:

- Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasing syndrome”) in neonates; the “gasing syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension
and cardiovascular collapse (AAP 1997; CDC 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors 2001); avoid or use dosage forms containing benzyl alcohol with caution in neonates See manufacturer’s labeling.

- Injection: Do not administer intra-arterially or subcutaneously. Avoid perivascular extravasation. Too rapid administration may cause severe respiratory depression, apnea, laryngospasm, hypertension or vasodilation with fall in blood pressure. Phenobarbital IV may require ≥15 minutes before reaching peak concentrations in the brain; injecting phenobarbital until the convulsions stop may lead to severe barbiturate induced depression. Intramuscular (IM) injection should be confined to a total volume of 5 mL and made in a large muscle in order to avoid possible tissue irritation. Discontinue injection in any patient who complains of limb pain.

- Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures and respiratory depression; use caution (AAP 1997; Zar 2007).

**Other warnings/precautions:**

- Acute pain: Use with caution in patients with acute or chronic pain; paradoxical excitement could be induced or important symptoms could be masked.

- Withdrawal: Anticonvulsants should not be discontinued abruptly because of the possibility of increasing seizure frequency; therapy should be withdrawn gradually to minimize the potential of increased seizure frequency, unless safety concerns require a more rapid withdrawal.

**Warnings: Additional Pediatric Considerations** Rapid IV administration may cause respiratory depression, apnea, laryngospasm, or hypotension; use with caution in hemodynamically unstable patients (hypotension or shock). Phenobarbital may cause CNS depression and effects with other sedative drugs may be potentiated; when treating status epilepticus, additional respiratory support may be required particularly when maximizing loading dose or if concurrent sedative therapy (Hegenbarth 2008).

Cognitive deficits observed with phenobarbital were further described in a retrospective chart review of 280 pediatric patients who had received either phenobarbital, levetiracetam, or both for treatment of neonatal seizures. A subset of the study group (n=67) had a Bayley Scales of Infant Development (BSID) completed at 24 months corrected age. Based on the analysis of cumulative exposures, the investigators observed that increased phenobarbital exposure was associated with a significant decrease in BSID cognitive (8 points) and motor (9 points) scores and an increased probability for the development of cerebral palsy (2.3-fold) for every 100 mg/kg of phenobarbital exposure (Maitre 2013).

Pediatric patients may be at increased risk for vitamin D deficiency; with chronic therapy; phenobarbital may cause catabolism of vitamin D; the daily vitamin D requirement may be increased in these patients (≥400 units/day); vitamin D status should be periodically monitored with laboratory data (Misra 2008; Wagner 2008). A retrospective study demonstrated that enzyme-inducing antiepileptic drugs (AEDs) (carbamazepine, phenobarbital, and phenytoin) increased systemic clearance of antieukemic drugs (teniposide and methotrexate) and were associated with a worse event-free survival, CNS relapse, and hematologic relapse (ie, lower efficacy), in B-lineage ALL children receiving chemotherapy; the authors recommend using nonenzyme-inducing AEDs in patients receiving chemotherapy for ALL (Relling 2000).

Some dosage forms may contain propylene glycol; in neonates large amounts of propylene glycol delivered orally, intravenously (eg, >3,000 mg/day), or topically have been associated with potentially fatal toxicities which can include metabolic acidosis, seizures, renal failure, and CNS depression; toxicities have also been
reported in children and adults including hyperosmolality, lactic acidosis, seizures, and respiratory depression; use caution (AAP 1997; Shehab 2009).

**Metabolism/Transport Effects**  **Substrate** of CYP2C19 (major), CYP2C9 (minor), CYP2E1 (minor);

**Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential;

**Induces** CYP1A2 (strong), CYP2A6 (strong), CYP2B6 (weak), CYP2C8 (strong), CYP2C9 (strong), CYP3A4 (strong), UGT1A1

**Drug Interactions**

(For additional information: [Launch drug interactions program](#) Lexicomp®)

Abiraterone Acetate: CYP3A4 Inducers (Strong) may decrease the serum concentration of Abiraterone Acetate. Management: Avoid whenever possible. If such a combination cannot be avoided, increase abiraterone acetate dosing frequency from once daily to twice daily during concomitant use. **Risk X: Avoid combination**

Acetaminophen: Barbiturates may increase the metabolism of Acetaminophen. This may 1) diminish the effect of acetaminophen; and 2) increase the risk of liver damage. **Risk C: Monitor therapy**

Afatinib: PHENobarbital may decrease the serum concentration of Afatinib. Management: Per US labeling: if requiring chronic use of phenobarbital, increase afatinib dose by 10 mg as tolerated; reduce to original afatinib dose 2-3 days after stopping phenobarbital. Per Canadian labeling: avoid combination if possible. **Risk D: Consider therapy modification**

Albendazole: PHENobarbital may decrease serum concentrations of the active metabolite(s) of Albendazole. **Risk C: Monitor therapy**

Alcohol (Ethyl): CNS Depressants may enhance the CNS depressant effect of Alcohol (Ethyl). **Risk C: Monitor therapy**

Amphetamines: May decrease the serum concentration of PHENobarbital. **Risk C: Monitor therapy**

Analgesics (Opioid): CNS Depressants may enhance the CNS depressant effect of Analgesics (Opioid). Management: Avoid concomitant use of opioid analgesics and benzodiazepines or other CNS depressants when possible. These agents should only be combined if alternative treatment options are inadequate. If combined, limit the dosages and duration of each drug. **Risk D: Consider therapy modification**

Antihepaviral Combination Products: CYP3A4 Inducers (Strong) may decrease the serum concentration of Antihepaviral Combination Products. **Risk X: Avoid combination**

Apixaban: CYP3A4 Inducers (Strong) may decrease the serum concentration of Apixaban. **Risk X: Avoid combination**

Apremilast: CYP3A4 Inducers (Strong) may decrease the serum concentration of Apremilast. **Risk X: Avoid combination**

Aprepitant: CYP3A4 Inducers (Strong) may decrease the serum concentration of Aprepitant. **Risk X: Avoid combination**

ARIPiprazole: CYP3A4 Inducers (Strong) may decrease the serum concentration of ARIPiprazole. Management: Double the oral aripiprazole dose and closely monitor. Reduce oral aripiprazole dose to 10-15 mg/day (for adults) if the inducer is discontinued. Avoid use of strong CYP3A4 inducers for more than 14 days with extended-release injectable aripiprazole. **Risk D: Consider therapy modification**

https://www.uptodate.com/contents/phenobarbital-pediatric-drug-information?source=see_link
ARIPiprazole Lauroxil: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of ARIPiprazole Lauroxil. Management: Patients taking the 441 mg dose of aripiprazole lauroxil increase their dose to 662 mg if used with a strong CYP3A4 inducer for more than 14 days. No dose adjustment is necessary for patients using the 662 mg or 882 mg doses of aripiprazole lauroxil. **Risk D: Consider therapy modification**

Artemether: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Artemether. Specifically, dihydroartemisinin concentrations may be reduced. CYP3A4 Inducers (Strong) may decrease the serum concentration of Artemether. **Risk X: Avoid combination**

Asunaprevir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Asunaprevir. **Risk X: Avoid combination**

Axitinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Axitinib. **Risk X: Avoid combination**

Azelastine (Nasal): CNS Depressants may enhance the CNS depressant effect of Azelastine (Nasal). **Risk X: Avoid combination**

Bazedoxifene: PHENobarbital may decrease the serum concentration of Bazedoxifene. This may lead to loss of efficacy or, if bazedoxifene is combined with estrogen therapy, an increased risk of endometrial hyperplasia. **Risk C: Monitor therapy**

Bedaquiline: CYP3A4 Inducers (Strong) may decrease the serum concentration of Bedaquiline. **Risk X: Avoid combination**

Bendamustine: CYP1A2 Inducers (Strong) may decrease the serum concentration of Bendamustine. Concentrations of active metabolites may be increased. **Risk C: Monitor therapy**

Benperidol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Benperidol. **Risk C: Monitor therapy**

Beta-Blockers: Barbiturates may decrease the serum concentration of Beta-Blockers. **Exceptions:** Atenolol; Levobunolol; Metipranolol; Nadolol. **Risk C: Monitor therapy**

Blonanserin: CNS Depressants may enhance the CNS depressant effect of Blonanserin. **Risk D: Consider therapy modification**

Blood Pressure Lowering Agents: Barbiturates may enhance the hypotensive effect of Blood Pressure Lowering Agents. **Risk C: Monitor therapy**

Boceprevir: PHENobarbital may decrease the serum concentration of Boceprevir. **Risk X: Avoid combination**

Bortezomib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Bortezomib. **Risk X: Avoid combination**

Bosutinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Bosutinib. **Risk X: Avoid combination**

Brentuximab Vedotin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Brentuximab Vedotin. Specifically, concentrations of the active monomethyl auristatin E (MMAE) component may be decreased. **Risk C: Monitor therapy**

Brexpiprazole: CYP3A4 Inducers (Strong) may decrease the serum concentration of Brexpiprazole. Management: If brexpiprazole is used together with a strong CYP3A4 inducer, the brexpiprazole dose should gradually be doubled over the course of 1 to 2 weeks. **Risk D: Consider therapy modification**
Brimonidine (Topical): May enhance the CNS depressant effect of CNS Depressants. **Risk C: Monitor therapy**

Buprenorphine: CNS Depressants may enhance the CNS depressant effect of Buprenorphine. Management: Consider reduced doses of other CNS depressants, and avoiding such drugs in patients at high risk of buprenorphine overuse/self-injection. Initiate buprenorphine patches (Butrans brand) at 5 mcg/hr in adults when used with other CNS depressants. **Risk D: Consider therapy modification**

Cabozantinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Cabozantinib. Management: Avoid use of strong CYP3A4 inducers with cabozantinib if possible. If combined, cabozantinib dose adjustments are recommended and vary based on the cabozantinib product used and the indication for use. See monograph for details. **Risk D: Consider therapy modification**

Calcifediol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Calcifediol. **Risk C: Monitor therapy**

Calcium Channel Blockers: Barbiturates may increase the metabolism of Calcium Channel Blockers. Management: Monitor for decreased therapeutic effects of calcium channel blockers with concomitant barbiturate therapy. Calcium channel blocker dose adjustments may be necessary. Nimodipine Canadian labeling contraindicates concomitant use with phenobarbital. **Exceptions:** Clevidipine. **Risk C: Monitor therapy**

Canagliflozin: PHENobarbital may decrease the serum concentration of Canagliflozin. Management: Consider increasing canagliflozin dose to 300 mg/day in patients with estimated GFR >60 mL/min/1.73 m2 who tolerate canagliflozin 100 mg/day and require greater glycemic control. Consider alternatives in patients with estimated GFR 45-60 mL/min/1.73 m2. **Risk D: Consider therapy modification**

Cannabidiol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Cannabidiol. **Risk C: Monitor therapy**

Cannabis: CYP3A4 Inducers (Strong) may decrease the serum concentration of Cannabis. More specifically, tetrahydrocannabinol and cannabidiol serum concentrations may be decreased. **Risk C: Monitor therapy**

Cannabis: May enhance the CNS depressant effect of CNS Depressants. **Risk C: Monitor therapy**

Cariprazine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Cariprazine. **Risk X: Avoid combination**

Ceritinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ceritinib. **Risk X: Avoid combination**

Chloramphenicol: May decrease the metabolism of Barbiturates. Barbiturates may increase the metabolism of Chloramphenicol. **Risk D: Consider therapy modification**

Chlormethiazole: May enhance the CNS depressant effect of CNS Depressants. Management: Monitor closely for evidence of excessive CNS depression. The chlormethiazole labeling states that an appropriately reduced dose should be used if such a combination must be used. **Risk D: Consider therapy modification**

Chlorphenesin Carbamate: May enhance the adverse/toxic effect of CNS Depressants. **Risk C: Monitor therapy**

Cholestryamine Resin: May decrease the serum concentration of PHENobarbital. Management: Administer phenobarbital at least 1 hour before or 4-6 hours after administration of cholestryamine in order to minimize the risk for any significant interaction. **Risk D: Consider therapy modification**
Clarithromycin: CYP3A4 Inducers (Strong) may increase serum concentrations of the active metabolite(s) of Clarithromycin. Clarithromycin may increase the serum concentration of CYP3A4 Inducers (Strong). CYP3A4 Inducers (Strong) may decrease the serum concentration of Clarithromycin. Management: Consider alternative antimicrobial therapy for patients receiving a CYP3A inducer. Drugs that enhance the metabolism of clarithromycin into 14-hydroxyclarithromycin may alter the clinical activity of clarithromycin and may impair clarithromycin efficacy. Risk D: Consider therapy modification

Clindamycin (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of Clindamycin (Systemic). Refer to the specific clindamycin (systemic) - rifampin drug interaction monograph for information concerning that combination. Risk C: Monitor therapy

CloZAPine: CYP3A4 Inducers (Strong) may decrease the serum concentration of CloZAPine. Risk X: Avoid combination

CNS Depressants: May enhance the adverse/toxic effect of other CNS Depressants. Risk C: Monitor therapy

Cobicistat: PHENobarbital may decrease the serum concentration of Cobicistat. Risk X: Avoid combination

Cobimetinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Cobimetinib. Risk X: Avoid combination

Contraceptives (Estrogens): Barbiturates may diminish the therapeutic effect of Contraceptives (Estrogens). Contraceptive failure is possible. Management: Use of a non-hormonal contraceptive is recommended. Risk D: Consider therapy modification

Contraceptives (Progestins): Barbiturates may diminish the therapeutic effect of Contraceptives (Progestins). Contraceptive failure is possible. Management: Use of alternative, nonhormonal contraceptives is recommended. Risk D: Consider therapy modification

Corticosteroids (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of Corticosteroids (Systemic). Exceptions: Hydrocortisone (Systemic); PredniSONE. Risk C: Monitor therapy

Cosyntropin: May enhance the hepatotoxic effect of PHENobarbital. Risk C: Monitor therapy

Crizotinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Crizotinib. Risk X: Avoid combination

CycloSPORINE (Systemic): Barbiturates may increase the metabolism of CycloSPORINE (Systemic). Risk D: Consider therapy modification

CYP1A2 Substrates: CYP1A2 Inducers (Strong) may increase the metabolism of CYP1A2 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. Risk D: Consider therapy modification

CYP2A6 Substrates: CYP2A6 Inducers (Strong) may increase the metabolism of CYP2A6 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. Risk D: Consider therapy modification

CYP2C19 Inducers (Strong): May increase the metabolism of CYP2C19 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. Risk D: Consider therapy modification
CYP2C19 Inhibitors (Moderate): May decrease the metabolism of CYP2C19 Substrates. *Risk C: Monitor therapy*

CYP2C19 Inhibitors (Strong): May decrease the metabolism of CYP2C19 Substrates. *Risk D: Consider therapy modification*

CYP2C8 Substrates: CYP2C8 Inducers (Strong) may increase the metabolism of CYP2C8 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

CYP2C9 Substrates: CYP2C9 Inducers (Strong) may increase the metabolism of CYP2C9 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Exceptions: Buprenorphine; Etizolam; HYDROcodone; Zolpidem. Risk D: Consider therapy modification*

Dabrafenib: CYP2C8 Inducers (Strong) may decrease the serum concentration of Dabrafenib. *Risk X: Avoid combination*

Dabrafenib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dabrafenib. *Risk X: Avoid combination*

Daclatasvir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Daclatasvir. *Risk X: Avoid combination*

Dapsone (Topical): May enhance the adverse/toxic effect of Methemoglobinemia Associated Agents. *Risk C: Monitor therapy*

Darunavir: May decrease the serum concentration of PHENobarbital. *Risk C: Monitor therapy*

Dasabuvir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dasabuvir. *Risk X: Avoid combination*

Dasabuvir: CYP2C8 Inducers (Strong) may decrease the serum concentration of Dasabuvir. *Risk X: Avoid combination*

Dasatinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dasatinib. Management: Avoid when possible. If such a combination cannot be avoided, consider increasing dasatinib dose and monitor clinical response and toxicity closely. *Risk D: Consider therapy modification*

Deferasirox: PHENobarbital may decrease the serum concentration of Deferasirox. Management: Avoid combination when possible; if the combination must be used, consider a 50% increase in initial deferasirox dose, with monitoring of serum ferritin concentrations and clinical responses to guide further dosing. *Risk D: Consider therapy modification*

Deflazacort: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Deflazacort. *Risk X: Avoid combination*

Delamanid: CYP3A4 Inducers (Strong) may decrease the serum concentration of Delamanid. *Risk X: Avoid combination*
Dexamethasone (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of Dexamethasone (Systemic). Management: Consider dexamethasone dose increases in patients receiving strong CYP3A4 inducers and monitor closely for reduced steroid efficacy. **Risk D: Consider therapy modification**

Dexmethylenidate: May increase the serum concentration of PHENobarbital. **Risk C: Monitor therapy**

Diclofenac (Systemic): CYP2C9 Inducers (Strong) may decrease the serum concentration of Diclofenac (Systemic). **Risk C: Monitor therapy**

Dienogest: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dienogest. Management: Avoid use of dienogest for contraception when using medications that induce CYP3A4 and for at least 28 days after discontinuation of a CYP3A4 inducer. An alternative form of contraception should be used during this time. **Risk X: Avoid combination**

Diethylstilbestrol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Diethylstilbestrol. **Risk C: Monitor therapy**

Dimethindene (Topical): May enhance the CNS depressant effect of CNS Depressants. **Risk C: Monitor therapy**

Disopyramide: PHENobarbital may decrease the serum concentration of Disopyramide. **Risk C: Monitor therapy**

Dolutegravir: PHENobarbital may decrease the serum concentration of Dolutegravir. **Risk X: Avoid combination**

Doxercalciferol: CYP3A4 Inducers (Strong) may increase serum concentrations of the active metabolite(s) of Doxercalciferol. **Risk C: Monitor therapy**

DOXOrubicin (Conventional): CYP3A4 Inducers (Strong) may decrease the serum concentration of DOXOrubicin (Conventional). Management: Seek alternatives to strong CYP3A4 inducers in patients treated with doxorubicin. One U.S. manufacturer (Pfizer Inc.) recommends that these combinations be avoided. **Risk D: Consider therapy modification**

Doxycycline: Barbiturates may decrease the serum concentration of Doxycycline. **Risk D: Consider therapy modification**

Doxylamine: May enhance the CNS depressant effect of CNS Depressants. Management: The manufacturer of Diclegis (doxylamine/pyridoxine), intended for use in pregnancy, specifically states that use with other CNS depressants is not recommended. **Risk C: Monitor therapy**

Dronabinol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dronabinol. **Risk C: Monitor therapy**

Dronabinol: May enhance the CNS depressant effect of CNS Depressants. **Risk C: Monitor therapy**

Dronedarone: CYP3A4 Inducers (Strong) may decrease the serum concentration of Dronedarone. **Risk X: Avoid combination**

Droperidol: May enhance the CNS depressant effect of CNS Depressants. Management: Consider dose reductions of droperidol or of other CNS agents (e.g., opioids, barbiturates) with concomitant use. **Risk D: Consider therapy modification**

Eliglustat: CYP3A4 Inducers (Strong) may decrease the serum concentration of Eliglustat. **Risk X: Avoid combination**
Elvitegravir: PHENobarbital may decrease the serum concentration of Elvitegravir. Risk X: Avoid combination

Enzalutamide: CYP2C8 Inducers (Strong) may decrease the serum concentration of Enzalutamide. Risk X: Avoid combination

Enzalutamide: CYP3A4 Inducers (Strong) may decrease the serum concentration of Enzalutamide. Management: Consider using an alternative agent that has no or minimal CYP3A4 induction potential when possible. If this combination cannot be avoided, increase the dose of enzalutamide from 160 mg daily to 240 mg daily. Risk X: Avoid combination

Erlotinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Erlotinib. Management: Avoid combination if possible. If combination must be used, increase erlotinib dose by 50 mg increments every 2 weeks as tolerated, to a maximum of 450 mg/day. Risk D: Consider therapy modification

Eslicarbazepine: PHENobarbital may decrease the serum concentration of Eslicarbazepine. Risk C: Monitor therapy

Estriol (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of Estriol (Systemic). Risk C: Monitor therapy

Estriol (Topical): CYP3A4 Inducers (Strong) may decrease the serum concentration of Estriol (Topical). Risk C: Monitor therapy

Etizolam: CYP3A4 Inducers (Strong) may decrease the serum concentration of Etizolam. Risk C: Monitor therapy

Etoposide: CYP3A4 Inducers (Strong) may decrease the serum concentration of Etoposide. Management: When possible, seek alternatives to strong CYP3A4-inducing medications in patients receiving etoposide. If these combinations cannot be avoided, monitor patients closely for diminished etoposide response. Risk D: Consider therapy modification

Etoposide Phosphate: CYP3A4 Inducers (Strong) may decrease the serum concentration of Etoposide Phosphate. Management: When possible, seek alternatives to strong CYP3A4-inducing medications in patients receiving etoposide phosphate. If these combinations cannot be avoided, monitor patients closely for diminished etoposide phosphate response. Risk D: Consider therapy modification

Etravirine: PHENobarbital may decrease the serum concentration of Etravirine. Risk X: Avoid combination

Everolimus: CYP3A4 Inducers (Strong) may decrease the serum concentration of Everolimus. Management: Avoid concurrent use of strong CYP3A4 inducers, but if strong CYP3A4 inducers cannot be avoided, consider gradually (in 5 mg increments) increasing the everolimus dose from 10 mg/day to 20 mg/day (adult doses). Risk X: Avoid combination

Exemestane: CYP3A4 Inducers (Strong) may decrease the serum concentration of Exemestane. Management: Exemestane U.S. product labeling recommends using an increased dose (50 mg/day) in patients receiving concurrent strong CYP3A4 inducers. The Canadian product labeling does not recommend a dose adjustment with concurrent use of strong CYP3A4 inducers. Risk D: Consider therapy modification

Felbamate: PHENobarbital may decrease the serum concentration of Felbamate. Felbamate may increase the serum concentration of PHENobarbital. Management: In patients receiving phenobarbital, initiate felbamate at 1200 mg/day in divided doses 3-4 times daily and reduce phenobarbital dose by 20%. Monitor for increased phenobarbital concentrations/effects and decreased felbamate concentrations/effects. Risk D: Consider therapy modification
Flibanserin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Flibanserin. Risk X: Avoid combination

Flunitrazepam: CNS Depressants may enhance the CNS depressant effect of Flunitrazepam. Risk D: Consider therapy modification

Folic Acid: May decrease the serum concentration of PHENobarbital. Risk C: Monitor therapy

Fosphenytoin: May enhance the CNS depressant effect of PHENobarbital. Fosphenytoin may increase the serum concentration of PHENobarbital. PHENobarbital may decrease the serum concentration of Fosphenytoin. Risk C: Monitor therapy

Gefitinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Gefitinib. Management: In the absence of severe adverse reactions, increase gefitinib dose to 500 mg daily in patients receiving strong CYP3A4 inducers; resume 250 mg dose 7 days after discontinuation of the strong inducer. Carefully monitor clinical response. Risk D: Consider therapy modification

Gestrinone: PHENobarbital may decrease the serum concentration of Gestrinone. Risk C: Monitor therapy

Grazoprevir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Grazoprevir. Risk X: Avoid combination

Griseofulvin: Barbiturates may decrease the serum concentration of Griseofulvin. Risk C: Monitor therapy

GuanFACINE: CYP3A4 Inducers (Strong) may decrease the serum concentration of GuanFACINE. Management: Increase the guanfacine dose by up to double when initiating concomitant therapy with strong CYP3A4 inducers. Increase guanfacine dose gradually over 1-2 weeks if strong CYP3A4 inducer therapy is just beginning. Risk D: Consider therapy modification

Hemin: Barbiturates may diminish the therapeutic effect of Hemin. Risk X: Avoid combination

HYDROcodeine: CNS Depressants may enhance the CNS depressant effect of HYDROcodeine. Management: Avoid concomitant use of hydrocodeone and benzodiazepines or other CNS depressants when possible. These agents should only be combined if alternative treatment options are inadequate. If combined, limit the dosages and duration of each drug. Risk D: Consider therapy modification

Hydrocortisone (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of Hydrocortisone (Systemic). Risk C: Monitor therapy

HydROXYzine: May enhance the CNS depressant effect of Barbiturates. Management: Consider a decrease in the barbiturate dose, as appropriate, when used together with hydroxyzine. With concurrent use, monitor patients closely for excessive response to the combination. Risk D: Consider therapy modification

Ibrutinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ibrutinib. Risk X: Avoid combination

Idelalisib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Idelalisib. Risk X: Avoid combination

Ifosfamide: CYP3A4 Inducers (Strong) may increase serum concentrations of the active metabolite(s) of Ifosfamide. CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Ifosfamide. Risk C: Monitor therapy

Imatinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Imatinib. Management: Avoid concurrent use of imatinib with strong CYP3A4 inducers when possible. If such a combination
must be used, increase imatinib dose by at least 50% and monitor the patient's clinical response closely. 

Risk D: Consider therapy modification

Irinotecan Products: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Irinotecan Products. Specifically, serum concentrations of SN-38 may be reduced. CYP3A4 Inducers (Strong) may decrease the serum concentration of Irinotecan Products. Risk X: Avoid combination

Isavuconazonium Sulfate: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Isavuconazonium Sulfate. Specifically, CYP3A4 Inducers (Strong) may decrease isavuconazole serum concentrations. Risk X: Avoid combination

Itraconazole: CYP3A4 Inducers (Strong) may decrease the serum concentration of Itraconazole. Risk X: Avoid combination

Ivabradine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ivabradine. Risk X: Avoid combination

Ivacaftor: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ivacaftor. Risk X: Avoid combination

Ixabepilone: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ixabepilone.

Management: Avoid this combination whenever possible. If this combination must be used, a gradual increase in ixabepilone dose from 40 mg/m² to 60 mg/m² (given as a 4-hour infusion), as tolerated, should be considered. Risk D: Consider therapy modification

Ixazomib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ixazomib. Risk X: Avoid combination

Kava Kava: May enhance the adverse/toxic effect of CNS Depressants. Risk C: Monitor therapy

Lacosamide: PHENobarbital may decrease the serum concentration of Lacosamide. Risk C: Monitor therapy

Lamotrigine: Barbiturates may decrease the serum concentration of Lamotrigine. Management: See lamotrigine prescribing information for specific age-dependent dosing guidelines regarding concurrent use with a barbiturate, as well as for adjusting lamotrigine dosing if concurrent barbiturate therapy is discontinued. Risk D: Consider therapy modification

Lapatinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Lapatinib. Management: If therapy overlap cannot be avoided, consider titrating lapatinib gradually from 1,250 mg/day up to 4,500 mg/day (HER2 positive metastatic breast cancer) or 1,500 mg/day up to 5,500 mg/day (hormone receptor/HER2 positive breast cancer) as tolerated. Risk X: Avoid combination

Ledipasvir: PHENobarbital may decrease the serum concentration of Ledipasvir. Risk X: Avoid combination

Leucovorin Calcium-Levoleucovorin: May decrease the serum concentration of PHENobarbital. Risk C: Monitor therapy

Levomefolate: May decrease the serum concentration of PHENobarbital. Risk C: Monitor therapy

Linagliptin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Linagliptin.

Management: Strongly consider using an alternative to any strong CYP3A4 inducer in patients who are being treated with linagliptin. If this combination is used, monitor patients closely for evidence of reduced linagliptin effectiveness. Risk D: Consider therapy modification
Lofexidine: May enhance the CNS depressant effect of CNS Depressants. *Risk C: Monitor therapy*

Lopinavir: PHENobarbital may decrease the serum concentration of Lopinavir. Management: Increased doses of lopinavir may be necessary when using these agents in combination. Do not use a once daily lopinavir/ritonavir regimen together with phenobarbital. Increase monitoring of therapeutic response in all patients using this combination. *Risk D: Consider therapy modification*

Lumacaftor: May decrease the serum concentration of CYP2C19 Substrates. *Risk C: Monitor therapy*

Lumefantrine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Lumefantrine. *Risk X: Avoid combination*

Lurasidone: CYP3A4 Inducers (Strong) may decrease the serum concentration of Lurasidone. *Risk X: Avoid combination*

Macitentan: CYP3A4 Inducers (Strong) may decrease the serum concentration of Macitentan. *Risk X: Avoid combination*

Magnesium Sulfate: May enhance the CNS depressant effect of CNS Depressants. *Risk C: Monitor therapy*

Manidipine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Manidipine. Management: Consider avoiding concomitant use of manidipine and strong CYP3A4 inducers. If combined, monitor closely for decreased manidipine effects and loss of efficacy. Increased manidipine doses may be required. *Risk D: Consider therapy modification*

Maraviroc: CYP3A4 Inducers (Strong) may decrease the serum concentration of Maraviroc. Management: Increase maraviroc adult dose to 600 mg twice daily when used with strong CYP3A4 inducers. This does not apply to patients also receiving strong CYP3A4 inhibitors. Do not use maraviroc with strong CYP3A4 inducers in patients with CrCl less than 30 mL/min. *Risk D: Consider therapy modification*

Mefloquine: May diminish the therapeutic effect of Anticonvulsants. Mefloquine may decrease the serum concentration of Anticonvulsants. Management: Mefloquine is contraindicated for malaria prophylaxis in persons with a history of convulsions. Monitor anticonvulsant concentrations and treatment response closely with concurrent use. *Risk D: Consider therapy modification*

Methadone: PHENobarbital may decrease the serum concentration of Methadone. *Risk C: Monitor therapy*

Methotrimeprazine: CNS Depressants may enhance the CNS depressant effect of Methotrimeprazine. Methotrimeprazine may enhance the CNS depressant effect of CNS Depressants. Management: Reduce adult dose of CNS depressant agents by 50% with initiation of concomitant methotrimeprazine therapy. Further CNS depressant dosage adjustments should be initiated only after clinically effective methotrimeprazine dose is established. *Risk D: Consider therapy modification*

Methoxyflurane: Barbiturates may enhance the nephrotoxic effect of Methoxyflurane. Barbiturates may increase the metabolism of Methoxyflurane. *Risk X: Avoid combination*

Methylfolate: May decrease the serum concentration of PHENobarbital. *Risk C: Monitor therapy*

Methylphenidate: May increase the serum concentration of PHENobarbital. *Risk C: Monitor therapy*

MethylPREDNISolone: CYP3A4 Inducers (Strong) may decrease the serum concentration of MethylPREDNISolone. Management: Consider methylprednisolone dose increases in patients receiving strong CYP3A4 inducers and monitor closely for reduced steroid efficacy. *Risk D: Consider therapy modification*
MetroNIDAZOLE (Systemic): PHENobarbital may decrease the serum concentration of MetroNIDAZOLE (Systemic). Risk C: Monitor therapy

MetyroSINE: CNS Depressants may enhance the sedative effect of MetyroSINE. Risk C: Monitor therapy

Mianserin: May enhance the CNS depressant effect of Barbiturates. Mianserin may diminish the therapeutic effect of Barbiturates. Barbiturates may decrease the serum concentration of Mianserin. Risk X: Avoid combination

Midostaurin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Midostaurin. Risk X: Avoid combination

MiFEPRiStone: CYP3A4 Inducers (Strong) may decrease the serum concentration of MiFEPRiStone. Risk X: Avoid combination

Minocycline: May enhance the CNS depressant effect of CNS Depressants. Risk C: Monitor therapy

Mirodenafil: CYP3A4 Inducers (Strong) may decrease the serum concentration of Mirodenafil. Management: Consider avoiding the concomitant use of mirodenafil and strong CYP3A4 inducers. If combined, monitor for decreased mirodenafil effects. Mirodenafil dose increases may be required to achieve desired effects. Risk D: Consider therapy modification

Multivitamins/Minerals (with ADEK, Folate, Iron): May decrease the serum concentration of Barbiturates. Risk C: Monitor therapy

Nabilone: May enhance the CNS depressant effect of CNS Depressants. Risk C: Monitor therapy

Naldemedine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Naldemedine. Risk X: Avoid combination

Nalmefene: PHENobarbital may decrease the serum concentration of Nalmefene. Risk C: Monitor therapy

Naloxegol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Naloxegol. Risk X: Avoid combination

Netupitant: CYP3A4 Inducers (Strong) may decrease the serum concentration of Netupitant. Risk X: Avoid combination

NIFEdipine: CYP3A4 Inducers (Strong) may decrease the serum concentration of NIFEdipine. Risk X: Avoid combination

Nilotinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Nilotinib. Risk X: Avoid combination

NiMODipine: CYP3A4 Inducers (Strong) may decrease the serum concentration of NiMODipine. Risk X: Avoid combination

Nisoldipine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Nisoldipine. Risk X: Avoid combination

Nitric Oxide: May enhance the adverse/toxic effect of Methemoglobinemia Associated Agents. Combinations of these agents may increase the likelihood of significant methemoglobinemia. Management: Monitor patients for signs of methemoglobinemia (e.g., hypoxia, cyanosis) when nitric oxide is used in combination with other agents associated with development of methemoglobinemia. Avoid lidocaine/prilocaine. Risk C: Monitor therapy
Olaparib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Olaparib. Risk X: Avoid combination

Ombitasvir, Paritaprevir, Ritonavir, and Dasabuvir: CYP2C8 Inducers (Strong) may decrease the serum concentration of Ombitasvir, Paritaprevir, Ritonavir, and Dasabuvir. Specifically, the serum concentrations of dasabuvir may decrease significantly. Risk X: Avoid combination

Orlistat: May decrease the serum concentration of Anticonvulsants. Risk C: Monitor therapy

Orphenadrine: CNS Depressants may enhance the CNS depressant effect of Orphenadrine. Risk X: Avoid combination

Osimertinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Osimertinib. Risk D: Consider therapy modification

OXcarbazepine: PHENobarbital may decrease serum concentrations of the active metabolite(s) of OXcarbazepine. Specifically, concentrations of the major active 10-monohydroxy metabolite may be reduced. OXcarbazepine may increase the serum concentration of PHENobarbital. Management: Consider increasing the initial adult oxcarbazepine extended release tablet (Oxellar XR) dose to 900 mg/day. No specific recommendations are available for other oxcarbazepine formulations. Risk D: Consider therapy modification

Oxomemazine: May enhance the CNS depressant effect of CNS Depressants. Risk X: Avoid combination

OxyCODONE: CNS Depressants may enhance the CNS depressant effect of OxyCODONE. Management: Avoid concomitant use of oxycodone and benzodiazepines or other CNS depressants when possible. These agents should only be combined if alternative treatment options are inadequate. If combined, limit the dosages and duration of each drug. Risk D: Consider therapy modification

Palbociclib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Palbociclib. Risk X: Avoid combination

Panobinostat: CYP3A4 Inducers (Strong) may decrease the serum concentration of Panobinostat. Risk X: Avoid combination

Paraldehyde: CNS Depressants may enhance the CNS depressant effect of Paraldehyde. Risk X: Avoid combination

PAZOPanib: CYP3A4 Inducers (Strong) may decrease the serum concentration of PAZOPanib. Risk X: Avoid combination

Perampanel: CYP3A4 Inducers (Strong) may decrease the serum concentration of Perampanel. Management: Avoid use of perampanel with strong CYP3A inducers other than enzyme-inducing antiepileptic drugs (EIAEDs). Increase perampanel starting dose to 4 mg/day when used with EIAEDs such as phenytoin, carbamazepine, or oxcarbazepine. Risk X: Avoid combination

Phenytoin: May enhance the CNS depressant effect of PHENobarbital. PHENobarbital may decrease the serum concentration of Phenytoin. Phenytoin may increase the serum concentration of PHENobarbital. Risk C: Monitor therapy

Pimavanserin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Pimavanserin. Risk C: Monitor therapy

Pirfenidone: CYP1A2 Inducers (Strong) may decrease the serum concentration of Pirfenidone. Risk X: Avoid combination

Piribedil: CNS Depressants may enhance the CNS depressant effect of Piribedil. Risk C: Monitor therapy
PONATinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of PONATinib. Risk X: Avoid combination

Pramipexole: CNS Depressants may enhance the sedative effect of Pramipexole. Risk C: Monitor therapy

Praziquantel: CYP3A4 Inducers (Strong) may decrease the serum concentration of Praziquantel. Management: Avoid concomitant use of praziquantel with strong CYP3A4 inducers. Discontinue rifampin 4 weeks prior to initiation of praziquantel therapy. Rifampin may be resumed the day following praziquantel completion. Risk X: Avoid combination

PrednisolONE (Systemic): CYP3A4 Inducers (Strong) may decrease the serum concentration of PrednisolONE (Systemic). Risk C: Monitor therapy

PrednisONE: CYP3A4 Inducers (Strong) may decrease the serum concentration of PrednisONE. Risk C: Monitor therapy

Prilocaine: Methemoglobinemia Associated Agents may enhance the adverse/toxic effect of Prilocaine. Combinations of these agents may increase the likelihood of significant methemoglobinemia. Management: Monitor patients for signs of methemoglobinemia (e.g., hypoxia, cyanosis) when prilocaine is used in combination with other agents associated with development of methemoglobinemia. Avoid lidocaine/prilocaine in infants receiving such agents. Risk C: Monitor therapy

Primidone: May enhance the adverse/toxic effect of Barbiturates. Primidone is converted to phenobarbital, and thus becomes additive with existing barbiturate therapy. Risk C: Monitor therapy

Propacetamol: Barbiturates may increase the metabolism of Propacetamol. This may 1) diminish the desired effects of propacetamol; and 2) increase the risk of liver damage. Risk C: Monitor therapy

Propafenone: CYP3A4 Inducers (Strong) may decrease the serum concentration of Propafenone. Risk C: Monitor therapy

Pyridoxine: May increase the metabolism of Barbiturates. Apparent in high pyridoxine doses (eg, 200 mg/day) Risk C: Monitor therapy

QUEtiapine: CYP3A4 Inducers (Strong) may decrease the serum concentration of QUEtiapine. Management: Quetiapine dose increases to as much as 5 times the regular dose may be required to maintain therapeutic benefit. Reduce the quetiapine dose back to the previous/regular dose within 7-14 days of discontinuing the inducer. Risk D: Consider therapy modification

QuiNIDine: PHENobarbital may enhance the hepatotoxic effect of QuiNIDine. PHENobarbital may decrease the serum concentration of QuiNIDine. Risk C: Monitor therapy

QuiNINE: May increase the serum concentration of PHENobarbital. PHENobarbital may decrease the serum concentration of QuiNINE. Risk D: Consider therapy modification

Radotinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Radotinib. Management: Consider alternatives to this combination when possible as the risk of radotinib treatment failure may be increased. Risk D: Consider therapy modification

Ramelteon: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ramelteon. Risk C: Monitor therapy

Ranolazine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ranolazine. Risk X: Avoid combination
Reboxetine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Reboxetine. Risk C: Monitor therapy

Regorafenib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Regorafenib. Risk X: Avoid combination

Ribociclib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ribociclib. Risk X: Avoid combination

Rifamycin Derivatives: May increase the metabolism of Barbiturates. Risk C: Monitor therapy

Rilpivirine: PHENobarbital may decrease the serum concentration of Rilpivirine. Risk X: Avoid combination

Rivaroxaban: CYP3A4 Inducers (Strong) may decrease the serum concentration of Rivaroxaban. Risk X: Avoid combination

Roflumilast: CYP3A4 Inducers (Strong) may decrease the serum concentration of Roflumilast.
Management: Roflumilast U.S. prescribing information recommends against combining strong CYP3A4 inducers with roflumilast. The Canadian product monograph makes no such recommendation but notes that such agents may reduce roflumilast therapeutic effects. Risk X: Avoid combination

Rolapitant: CYP3A4 Inducers (Strong) may decrease the serum concentration of Rolapitant.
Management: Avoid rolapitant use in patients requiring chronic administration of strong CYP3A4 inducers. Monitor for reduced rolapitant response and the need for alternative or additional antiemetic therapy even with shorter-term use of such inducers. Risk D: Consider therapy modification

RomiDEPsin: CYP3A4 Inducers (Strong) may decrease the serum concentration of RomiDEPsin. Risk X: Avoid combination

Rotigotine: CNS Depressants may enhance the sedative effect of Rotigotine. Risk C: Monitor therapy

Rufinamide: May increase the serum concentration of PHENobarbital. PHENobarbital may decrease the serum concentration of Rufinamide. Risk C: Monitor therapy

SAXagliptin: CYP3A4 Inducers (Strong) may decrease the serum concentration of SAXagliptin. Risk C: Monitor therapy

Selective Serotonin Reuptake Inhibitors: CNS Depressants may enhance the adverse/toxic effect of Selective Serotonin Reuptake Inhibitors. Specifically, the risk of psychomotor impairment may be enhanced. Risk C: Monitor therapy

Sertraline: CYP3A4 Inducers (Strong) may decrease the serum concentration of Sertraline. Risk C: Monitor therapy

Simeprevir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Simeprevir. Risk X: Avoid combination

Sirolimus: CYP3A4 Inducers (Strong) may decrease the serum concentration of Sirolimus. Management: Avoid concomitant use of strong CYP3A4 inducers and sirolimus if possible. If combined, monitor for reduced serum sirolimus concentrations. Sirolimus dose increases will likely be necessary to prevent subtherapeutic sirolimus levels. Risk D: Consider therapy modification

Sodium Nitrite: Methemoglobinemia Associated Agents may enhance the adverse/toxic effect of Sodium Nitrite. Combinations of these agents may increase the likelihood of significant methemoglobinemia. Risk C: Monitor therapy
Sodium Oxybate: May enhance the CNS depressant effect of CNS Depressants. Management: Consider alternatives to combined use. When combined use is needed, consider minimizing doses of one or more drugs. Use of sodium oxybate with alcohol or sedative hypnotics is contraindicated. **Risk D: Consider therapy modification**

Sofosbuvir: PHENobarbital may decrease the serum concentration of Sofosbuvir. **Risk X: Avoid combination**

Somatostatin Acetate: May enhance the adverse/toxic effect of Barbiturates. Specifically, Somatostatin Acetate may enhance or prolong Barbiturate effects, including sedative effects. **Risk X: Avoid combination**

Sonidegib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Sonidegib. **Risk X: Avoid combination**

SORAfenib: CYP3A4 Inducers (Strong) may decrease the serum concentration of SORAfenib. **Risk X: Avoid combination**

Striptentol: PHENobarbital may decrease the serum concentration of Striptentol. **Risk X: Avoid combination**

Sulthiame: May enhance the adverse/toxic effect of PHENobarbital. **Risk C: Monitor therapy**

SUNItinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of SUNItinib. Management: Avoid when possible. If such a combination cannot be avoided, consider increasing sunitinib dose and monitor clinical response and toxicity closely. **Risk D: Consider therapy modification**

Suvorexant: CYP3A4 Inducers (Strong) may decrease the serum concentration of Suvorexant. **Risk X: Avoid combination**

Tadalafil: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tadalafil. Management: Erectile dysfunction: monitor for decreased effectiveness - no standard dose adjustments recommended. Avoid use of tadalafil for pulmonary arterial hypertension in patients receiving a strong CYP3A4 inducer. **Risk D: Consider therapy modification**

Tapentadol: May enhance the CNS depressant effect of CNS Depressants. Management: Avoid concomitant use of tapentadol and benzodiazepines or other CNS depressants when possible. These agents should only be combined if alternative treatment options are inadequate. If combined, limit the dosages and duration of each drug. **Risk D: Consider therapy modification**

Tasimelteon: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tasimelteon. **Risk X: Avoid combination**

Telaprevir: PHENobarbital may decrease the serum concentration of Telaprevir. **Risk X: Avoid combination**

Teniposide: Barbiturates may decrease the serum concentration of Teniposide. Management: Consider alternatives to combined treatment with barbiturates and teniposide due to the potential for decreased teniposide concentrations. If the combination cannot be avoided, monitor teniposide response closely. **Risk D: Consider therapy modification**

Tenofovir Alafenamide: PHENobarbital may decrease the serum concentration of Tenofovir Alafenamide. **Risk X: Avoid combination**

Tetracaine (Topical): May enhance the adverse/toxic effect of Methemoglobinemia Associated Agents. **Risk C: Monitor therapy**
Tetrahydrocannabinol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tetrahydrocannabinol. Risk C: Monitor therapy

Tetrahydrocannabinol: May enhance the CNS depressant effect of CNS Depressants. Risk C: Monitor therapy

Thalidomide: CNS Depressants may enhance the CNS depressant effect of Thalidomide. Risk X: Avoid combination

Thiazide and Thiazide-Like Diuretics: Barbiturates may enhance the orthostatic hypotensive effect of Thiazide and Thiazide-Like Diuretics. Risk C: Monitor therapy

TiaGABine: CYP3A4 Inducers (Strong) may decrease the serum concentration of TiaGABine.
Management: Approximately 2-fold higher tiagabine doses and a more rapid dose titration will likely be required in patients concomitantly taking a strong CYP3A4 inducer. Risk D: Consider therapy modification

Ticagrelor: CYP3A4 Inducers (Strong) may decrease serum concentrations of the active metabolite(s) of Ticagrelor. CYP3A4 Inducers (Strong) may decrease the serum concentration of Ticagrelor. Risk X: Avoid combination

Tipranavir: PHENobarbital may decrease the serum concentration of Tipranavir. Tipranavir may decrease the serum concentration of PHENobarbital. Risk D: Consider therapy modification

Tofacitinib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tofacitinib. Risk X: Avoid combination

Tolvaptan: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tolvaptan.
Management: If concurrent use is necessary, increased doses of tolvaptan (with close monitoring for toxicity and clinical response) may be needed. Risk X: Avoid combination

Toremifene: CYP3A4 Inducers (Strong) may decrease the serum concentration of Toremifene. Risk X: Avoid combination

Trabectedin: CYP3A4 Inducers (Strong) may decrease the serum concentration of Trabectedin. Risk X: Avoid combination

Treprostinil: CYP2C8 Inducers (Strong) may decrease the serum concentration of Treprostinil. Risk C: Monitor therapy

Tricyclic Antidepressants: Barbiturates may increase the metabolism of Tricyclic Antidepressants. Risk D: Consider therapy modification

Trimeprazine: May enhance the CNS depressant effect of CNS Depressants. Risk C: Monitor therapy

Tropisetron: CYP3A4 Inducers (Strong) may decrease the serum concentration of Tropisetron. Risk C: Monitor therapy

Udenafil: CYP3A4 Inducers (Strong) may decrease the serum concentration of Udenafil. Risk C: Monitor therapy

Ulipristal: CYP3A4 Inducers (Strong) may decrease the serum concentration of Ulipristal. Risk X: Avoid combination

Ulipristal: Barbiturates may decrease the serum concentration of Ulipristal. Risk X: Avoid combination

Valbenazine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Valbenazine. Risk X: Avoid combination
Valproate Products: May increase the serum concentration of Barbiturates. Barbiturates may decrease the serum concentration of Valproate Products. Risk C: Monitor therapy

Vandetanib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vandetanib. Risk X: Avoid combination

Velpatasvir: CYP2C8 Inducers (Strong) may decrease the serum concentration of Velpatasvir. Risk X: Avoid combination

Velpatasvir: CYP3A4 Inducers (Strong) may decrease the serum concentration of Velpatasvir. Risk X: Avoid combination

Vemurafenib: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vemurafenib. Risk X: Avoid combination

Venetoclax: CYP3A4 Inducers (Strong) may decrease the serum concentration of Venetoclax. Risk X: Avoid combination

Vilazodone: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vilazodone. Management: Consider increasing vilazodone dose by as much as 2-fold (do not exceed 80 mg/day), based on response, in patients receiving strong CYP3A4 inducers for > 14 days. Reduce to the original vilazodone dose over 1-2 weeks after inducer discontinuation. Risk D: Consider therapy modification

VinCRIStine (Liposomal): CYP3A4 Inducers (Strong) may decrease the serum concentration of VinCRIStine (Liposomal). Risk X: Avoid combination

Vinflunine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vinflunine. Risk X: Avoid combination

Vitamin K Antagonists (eg, warfarin): Barbiturates may increase the metabolism of Vitamin K Antagonists. Management: Monitor INR more closely. An anticoagulant dose increase may be needed after a barbiturate is initiated or given at an increased dose. Anticoagulant dose decreases may be needed following barbiturate discontinuation or dose reduction. Risk D: Consider therapy modification

Vorapaxar: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vorapaxar. Risk X: Avoid combination

Voriconazole: Barbiturates may decrease the serum concentration of Voriconazole. Risk X: Avoid combination

Vortioxetine: CYP3A4 Inducers (Strong) may decrease the serum concentration of Vortioxetine. Management: Consider increasing the vortioxetine dose to no more than 3 times the original dose when used with a strong drug metabolism inducer for more than 14 days. The vortioxetine dose should be returned to normal within 14 days of stopping the strong inducer. Risk D: Consider therapy modification

Zaleplon: CYP3A4 Inducers (Strong) may decrease the serum concentration of Zaleplon. Management: Consider the use of an alternative hypnotic that is not metabolized by CYP3A4 in patients receiving strong CYP3A4 inducers. If zaleplon is combined with a strong CYP3A4 inducer, monitor for decreased effectiveness of zaleplon. Risk D: Consider therapy modification

Zolpidem: CNS Depressants may enhance the CNS depressant effect of Zolpidem. Management: Reduce the intermezzo brand sublingual zolpidem adult dose to 1.75 mg for men who are also receiving other CNS depressants. No such dose change is recommended for women. Avoid use with other CNS depressants at bedtime; avoid use with alcohol. Risk D: Consider therapy modification

Zonisamide: PHENOBARBITAL may decrease the serum concentration of Zonisamide. Risk C: Monitor therapy
Zuclopenthixol: CYP3A4 Inducers (Strong) may decrease the serum concentration of Zuclopenthixol.

Risk C: Monitor therapy

Food Interactions  Phenobarbital increases the hepatic metabolism of vitamin D to inactive compounds and reduces calcium absorption (Gough 1986). Management: Increase intake of foods rich in vitamin D. Supplementation of vitamin D and/or calcium may be necessary.

Pregnancy Risk Factor  D (show table)

Pregnancy Implications  Phenobarbital crosses the placenta (Harden 2009b). Barbiturates can be detected in the placenta, fetal liver, and fetal brain. Fetal and maternal blood concentrations may be similar following parenteral administration. An increased incidence of fetal abnormalities may occur following maternal use. When used during the third trimester of pregnancy, withdrawal symptoms may occur in the neonate, including seizures and hyperirritability; symptoms of withdrawal may be delayed in the neonate up to 14 days after birth. Use during labor does not impair uterine activity; however, respiratory depression may occur in the newborn; resuscitation equipment should be available, especially for premature infants. Use for the treatment of epilepsy should be avoided during pregnancy (Harden 2009a).

A registry is available for women exposed to phenobarbital during pregnancy: Pregnant women may enroll themselves into the North American Antiepileptic Drug (AED) Pregnancy Registry (888-233-2334 or http://www.aedpregnancyregistry.org).

Monitoring Parameters  CNS status, seizure activity, liver enzymes, CBC with differential, renal function, serum concentrations; signs and symptoms of suicidality (eg, anxiety, depression, behavior changes). With IV use: Respiratory rate, heart rate, blood pressure, IV site (stop injection if patient complains of pain in the limb). For treatment of hyperbilirubinemia: Monitor bilirubin (total and direct)

Reference Range

Therapeutic:

- Infants, Children, and Adolescents: 15-40 mcg/mL (SI: 65-172 micromole/L)
- Adults: 20-40 mcg/mL (SI: 86-172 micromole/L)
- Toxic: >40 mcg/mL (SI: >172 micromole/L)
- Toxic concentration: Slowness, ataxia, nystagmus: 35-80 mcg/mL (SI: 150-344 micromole/L)
- Coma with reflexes: 65-117 mcg/mL (SI: 279-502 micromole/L)
- Coma without reflexes: >100 mcg/mL (SI: >430 micromole/L)

Mechanism of Action  Long-acting barbiturate with sedative, hypnotic, and anticonvulsant properties. Barbiturates depress the sensory cortex, decrease motor activity, alter cerebellar function, and produce drowsiness, sedation, and hypnosis. In high doses, barbiturates exhibit anticonvulsant activity; barbiturates produce dose-dependent respiratory depression.

Pharmacodynamics/Kinetics (Adult data unless noted)

- Onset of action: Oral: ≥60 minutes; IV: 5 minutes
- Peak effect: IV: CNS depression: ≥15 minutes
- Duration: Oral: 10 to 12 hours; IV: >6 hours
Absorption: Oral: Rapid

Distribution:

- Neonates and Young Infants: $V_d$: 0.71 to 1.71 L/kg (Patsalos 2008)
- Older Infants and Children: $V_d$: 0.57 to 0.7 L/kg (Patsalos 2008)
- Adults: $V_d$: 0.54 to 0.73 L/kg (Patsalos 2008)

Protein binding:

- Neonates: 36% to 43% (Patsalos 2008)
- Adults: 50% to 60% (Patsalos 2008)

Metabolism: Hepatic by oxidation via CYP2C9 and to a lesser extent via CYP2C19 and CYP2E1, and by N-glucosidation (Patsalos 2008)

Bioavailability: Oral: Adults: 95% to 100% (Patsalos 2008)

Half-life elimination: Neonates (<48 hours old), Infants, and Children: ~110 hours (60 to 180 hours);
- Adults: ~79 hours (range: 53 to 118 hours)

Time to peak, serum: Oral: 1.4 hours (0.5 to 4 hours) (Pasalos 2008)

Excretion: Urine (25% to 50% as unchanged drug); feces (minimal)

Extemporaneous Preparations  An alcohol-free 10 mg/mL phenobarbital oral suspension may be made from tablets and one of two different vehicles (a 1:1 mixture of Ora-Plus and Ora-Sweet or a 1:1 mixture of Ora-Plus and Ora-Sweet SF). Crush ten phenobarbital 60 mg tablets in a glass mortar and reduce to a fine powder. Mix 30 mL of Ora-Plus and 30 mL of either Ora-Sweet or Ora-Sweet SF; stir vigorously. Add 15 mL of the vehicle to the powder and mix to a uniform paste. Transfer the mixture to a 2 ounce amber plastic prescription bottle. Rinse mortar and pestle with 15 mL of the vehicle; transfer to bottle. Repeat, then add quantity of vehicle sufficient to make 60 mL. Label "shake well." May mix dose with chocolate syrup (1:1 volume) immediately before administration to mask the bitter aftertaste. Stable for 115 days when stored in amber plastic prescription bottles at room temperature.  


Pricing: US

**Elixir (PHENobarbital Oral)**

- 20 mg/5 mL (473 mL): $91.80

**Solution (PHENobarbital Sodium Injection)**

- 65 mg/mL (1 mL): $24.96
- 130 mg/mL (1 mL): $64.78

**Tablets (PHENobarbital Oral)**

- 15 mg (100): $33.60
- 16.2 mg (100): $53.07
- 30 mg (100): $42.24
32.4 mg (100): $67.03  
60 mg (100): $52.80  
64.8 mg (100): $84.38  
97.2 mg (100): $119.03  
100 mg (100): $74.40

**Disclaimer:** The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

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