



Direct Healthcare Professional Communication

Sep 2023

Acefylline Piperazine +Phenobarbital /Acefylline Piperazine +Phenobarbitone

Risk of Drug interaction, Dependence and Many Side Effects in Long Term Use

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following risk of drug interaction, dependence and many side effects in long term use due to **Phenobarbital /phenobarbitone**:

Summary:

- **Barbiturate (Phenobarbital /phenobarbitone)** is known for being highly dependent and in prior years, found to be a common agent of choice for suicide attempts.
- **Barbiturate** is known to induce the liver's cytochrome p450 enzyme, so careful consideration is necessary when given concurrently with other medications
- The following undesirable effects have been reported following the use of combination **due to Phenobarbital /phenobarbitone**:
 - Complications associated with phenobarbital use are coma, decreased effort to breathe, and low blood pressure.
 - The more common adverse effects include incoordination, impaired balance, and drowsiness.
 - When used long-term, adverse events of irritability, loss of appetite, achiness in the bones, joints, or muscles, depression, and liver damage, although liver damage is a rare complication, are recorded. When taking barbiturates such as phenobarbital, patients may experience withdrawal symptoms if they stop taking the drug abruptly.
 - Tapering off the medication is necessary.
 - In post-marketing, surveillance of hospitalized patients using phenobarbital the following adverse reactions were reported.
 - **Nervous System:** Agitation, somnolence, confusion, CNS depression, hyperkinesia, ataxia, nervousness, nightmares, psychiatric disturbance, thinking abnormality, insomnia, anxiety, hallucinations, dizziness
 - **Respiratory System:** Apnea, hypoventilation





- **Cardiovascular System:** Hypotension, bradycardia, syncope
- **Digestive System:** Nausea, vomiting, constipation
- **Dermatologic Reactions:** Exfoliative dermatitis, toxic epidermic necrolysis, Stevens-Johnson syndrome (rare complication)
- **Other Reported Reactions:** Headache; hypersensitivity reactions, including but not limited to angioedema and skin rashes; injection site reactions; fever; liver damage and megaloblastic anemia in chronic users.

Further information:

Phenobarbital is one of the sedative-hypnotic agents which belongs to the barbiturates class of drugs. Phenobarbital can also be used to relieve insomnia and apprehensiveness, although addiction is a point of concern when using phenobarbital for insomnia.

Phenobarbital acts by increasing the amount of time chloride channels are open, consequently depressing the central nervous system. This action occurs by acting on GABA-A receptor subunits. When phenobarbital binds to these receptors, the chloride ion gates open and stay open, allowing a steady flow of these ions into neuronal cells. This action hyperpolarizes the cell membrane, increasing the action potential threshold

Phenobarbital is a cytochrome P450 inducer, so careful consideration is necessary when given concurrently with other medications.

Patients with underlying obstructive lung disease will have an increased risk of complications. The depression of the respiratory system associated with barbiturate toxicity compounded with an already compromised respiratory system can contribute to complications.

Research has also found that the drug interaction from combined oral medication and phenobarbital negatively impacted the combined Drug blood levels compared to plain drug.

References

NIH <https://www.ncbi.nlm.nih.gov/books/NBK532277/>

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: <https://primaryreporting.who-umc.org/EG>

QR Code:

Hotline: 15301

