

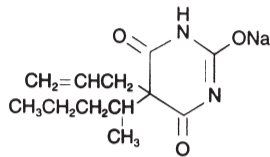
SECONAL SODIUM®
SECOBARBITAL SODIUM
CAPSULES, USP
Rx only



DESCRIPTION

The barbiturates are nonselective central nervous system (CNS) depressants that are primarily used as sedative hypnotics. In subhypnotic doses, they are also used as anticonvulsants. The barbiturates and their sodium salts are subject to control under the Federal Controlled Substances Act.

Seconal Sodium® (Secobarbital Sodium Capsules, USP) is a barbituric acid derivative and occurs as a white, odorless, bitter powder that is very soluble in water, soluble in alcohol, and practically insoluble in ether. Chemically, the drug is sodium 5-allyl-5-(1-methylbutyl) barbiturate, with the molecular formula $C_{12}H_{17}N_2NaO_3$. Its molecular weight is 260.27. The structural formula is as follows:



Each capsule contains 100 mg (0.38 mmol) of secobarbital sodium. It also contains dimethicone, FD&C Red No. 3, FD&C Yellow No. 10, gelatin, magnesium stearate, pregelatinized starch, and titanium dioxide.

CLINICAL PHARMACOLOGY

Barbiturates are capable of producing all levels of CNS mood alteration, from excitation to mild sedation, hypnosis, and deep coma. Overdosage can produce death. In high enough therapeutic doses, barbiturates induce anesthesia. Barbiturates depress the sensory cortex, decrease motor activity, alter cerebellar function, and produce drowsiness, sedation, and hypnosis.

Barbiturate-induced sleep differs from physiologic sleep. Sleep laboratory studies have demonstrated that barbiturates reduce the amount of time spent in the rapid eye movement (REM) phase, or dreaming stage of sleep. Also, Stages III and IV sleep are decreased. Following abrupt cessation of regularly used barbiturates, patients may experience markedly increased dreaming, nightmares, and/or insomnia. Therefore, withdrawal of a single therapeutic dose over 5 or 6 days has been recommended to lessen the REM rebound and disturbed sleep that contribute to drug withdrawal syndrome (for example, decreasing the dose from 3 to 2 doses a day for 1 week).

In studies, secobarbital sodium and pentobarbital sodium have been found to lose most of their effectiveness for both inducing and maintaining sleep by the end of 2 weeks of continued drug administration, even with the use of multiple doses. As with secobarbital sodium and pentobarbital sodium, other barbiturates (including amobarbital) might be expected to lose their effectiveness for inducing and maintaining sleep after about 2 weeks. The short-, intermediate-, and to a lesser degree, long-acting barbiturates have been widely prescribed for treating insomnia. Although the clinical literature abounds with claims that the short-acting barbiturates are superior for producing sleep whereas the intermediate-acting compounds are more effective in maintaining sleep, controlled studies have failed to demonstrate these differential effects. Therefore, as sleep medications, the barbiturates are of limited value beyond short-term use.

Barbiturates have little analgesic action at subanesthetic doses. Rather, in subanesthetic doses, these drugs may increase the reaction to painful stimuli. All barbiturates exhibit anticonvulsant activity in anesthetic doses. However, of the drugs in this class, only phenobarbital, mephobarbital, and metharbital are effective as oral anticonvulsants in subhypnotic doses. Barbiturates are respiratory depressants, and the degree of depression is dependent on the dose. With hypnotic doses, respiratory depression is similar to that which occurs during physiologic sleep accompanied by a slight decrease in blood pressure and heart rate.

Studies in laboratory animals have shown that barbiturates cause reduction in the tone and contractility of the uterus, ureters, and urinary bladder. However, concentrations of the drugs required to produce this effect in humans are not reached with sedative-hypnotic doses. Barbiturates do not impair normal hepatic function, but have been shown to induce liver microsomal enzymes, thus increasing and/or altering the metabolism of barbiturates and other drugs (see Drug Interactions *under* Precautions).

Pharmacokinetics—Barbiturates are absorbed in varying degrees following oral or parenteral administration. The salts are more rapidly absorbed than are the acids. The rate of absorption is increased if the sodium salt is ingested as a dilute solution or taken on an empty stomach.

Duration of action, which is related to the rate at which the barbiturates are redistributed throughout the body, varies among persons and in the same person from time to time.

Seconal Sodium is classified as a short-acting barbiturate when taken orally. Its onset of action is 10 to 15 minutes and its duration of action ranges from 3 to 4 hours.

Barbiturates are weak acids that are absorbed and rapidly distributed to all tissues and fluids, with high concentrations in the brain, liver, and kidneys. Lipid solubility of the barbiturates is the dominant factor in their distribution within the body. The more lipid soluble the barbiturate, the more rapidly it penetrates all tissues of the body. Barbiturates are bound to plasma and tissue proteins to a varying degree, with the degree of binding increasing directly as a function of lipid solubility.

Phenobarbital has the lowest lipid solubility, lowest plasma binding, lowest brain protein binding, the longest delay in onset of activity, and the longest duration of action. At the opposite extreme is secobarbital, which has the highest lipid solubility, highest plasma protein binding, highest brain protein binding, the shortest delay in onset of activity, and the shortest duration of action. The plasma half-life for secobarbital sodium in adults ranges between 15 to 40 hours, with a mean of 28 hours. No data are available for pediatric patients and newborns.

Barbiturates are metabolized primarily by the hepatic microsomal enzyme system, and the metabolic products are excreted in the urine and, less commonly, in the feces. The excretion of unmetabolized barbiturate is 1 feature that distinguishes the long-acting category from those belonging to other categories, which are almost entirely metabolized. The inactive metabolites of the barbiturates are excreted as conjugates of glucuronic acid.

INDICATIONS AND USAGE

A. Hypnotic, for the short-term treatment of insomnia, since it appears to lose its effectiveness for sleep induction and sleep maintenance after 2 weeks (see Clinical Pharmacology).

B. Preanesthetic

CONTRAINDICATIONS

Seconal Sodium is contraindicated in patients who are hypersensitive to barbiturates. It is also contraindicated in patients with a history of manifest or latent porphyria, marked impairment of liver function, or respiratory disease in which dyspnea or obstruction is evident.

WARNINGS

Because sleep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after a careful eval-

uation of the patient. **The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated.** Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with sedative-hypnotic drugs. Because some of the important adverse effects of sedative-hypnotics appear to be dose related (see Precautions and Dosage and Administration), it is important to use the smallest possible effective dose, especially in the elderly.

Complex behaviors such as "sleep-driving" (i.e., driving while not fully awake after ingestion of a sedative-hypnotic, with amnesia for the event) have been reported. These events can occur in sedative-hypnotic-naïve as well as in sedative-hypnotic-experienced persons. Although behaviors such as sleep-driving may occur with sedative-hypnotics alone at therapeutic doses, the use of alcohol and other CNS depressants with sedative-hypnotics appears to increase the risk of such behaviors, as does the use of sedative-hypnotics at doses exceeding the maximum recommended dose. Due to the risk to the patient and the community, discontinuation of sedative-hypnotics should be strongly considered for patients who report a "sleep-driving" episode. Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with sleep-driving, patients usually do not remember these events.

1. **Habit-Forming**—Seconal Sodium may be habit-forming. Tolerance and psychological and physical dependence may occur with continued use (see Drug Abuse and Dependence and Pharmacokinetics under Clinical Pharmacology). Patients who have psychological dependence on barbiturates may increase the dosage or decrease the dosage interval without consulting a physician and subsequently may develop a physical dependence on barbiturates. To minimize the possibility of overdosage or development of dependence, the prescribing and dispensing of sedative-hypnotic barbiturates should be limited to the amount required for the interval until the next appointment. The abrupt cessation after prolonged use in a person who is dependent on the drug may result in withdrawal symptoms, including delirium, convulsions, and possibly death. Barbiturates should be withdrawn gradually from any patient known to be taking excessive doses over long periods of time (see Drug Abuse and Dependence).

2. **Acute or Chronic Pain**—Caution should be exercised when barbiturates are administered to patients with acute or chronic pain, because paradoxical excitement could be induced or important symptoms could be masked.

3. **Usage in Pregnancy**—Barbiturates can cause fetal harm when administered to a pregnant woman. Retrospective, case-controlled studies have suggested that there may be a connection between the maternal consumption of barbiturates and a higher than expected incidence of fetal abnormalities. Barbiturates readily cross the placental barrier and are distributed throughout fetal tissues; the highest concentrations are found in the placenta, fetal liver, and brain. Fetal blood levels approach maternal blood levels following parenteral administration.

Withdrawal symptoms occur in infants born to women who receive barbiturates throughout the last trimester of pregnancy (see Drug Abuse and Dependence). If Seconal Sodium is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

4. **Synergistic Effects**—The concomitant use of alcohol or other CNS depressants may produce additive CNS-depressant effects.

PRECAUTIONS

General—Barbiturates may be habit-forming. Tolerance and psychological and physical dependence may occur with continuing use (see Drug Abuse and Dependence). Barbiturates should be administered with caution, if at all, to patients who are mentally depressed, have suicidal tendencies, or have a history of drug abuse.

Elderly or debilitated patients may react to barbiturates with marked excitement, depression, or confusion. In some persons, especially pediatric patients, barbiturates repeatedly produce excitement rather than depression.

In patients with hepatic damage, barbiturates should be administered with caution and initially in reduced doses. Barbiturates should not be administered to patients showing the premonitory signs of hepatic coma.

Information for Patients

"Sleep-Driving" and other complex behaviors:

There have been reports of people getting out of bed after taking a sedative-hypnotic and driving their cars while not fully awake, often with no memory of the event. If a patient experiences such an episode, it should be reported to his or her doctor immediately, since "sleep-driving" can be dangerous. This behavior is more likely to occur when sedative-hypnotics are taken with alcohol or other central nervous system depressants (see WARNINGS). Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with sleep-driving, patients usually do not remember these events.

The following information should be given to patients receiving Seconal Sodium:

1. The use of Seconal Sodium carries with it an associated risk of psychological and/or physical dependence. The patient should be warned against increasing the dose of the drug without consulting a physician.

2. Seconal Sodium may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery. The patient should be cautioned accordingly.

3. Alcohol should not be consumed while taking Seconal Sodium. The concurrent use of Seconal Sodium with other CNS depressants (eg, alcohol, narcotics, tranquilizers, and antihistamines) may result in additional CNS-depressant effects.

Laboratory Tests—Prolonged therapy with barbiturates should be accompanied by periodic laboratory evaluation of organic systems, including hematopoietic, renal, and hepatic systems (see General under Precautions and Adverse Reactions).

Drug Interactions—Most reports of clinically significant drug interactions occurring with the barbiturates have involved phenobarbital. However, the application of these data to other barbiturates appears valid and warrants serial blood level determinations of the relevant drugs when there are multiple therapies.

1. **Anticoagulants**—Phenobarbital lowers the plasma levels of dicumarol and causes a decrease in anticoagulant activity as measured by the prothrombin time. Barbiturates can induce hepatic microsomal enzymes, resulting in increased metabolism and decreased anticoagulant response of oral anticoagulants (eg, warfarin, acenocoumarol, dicumarol, and phenprocoumon). Patients stabilized on anticoagulant therapy may require dosage adjustments if barbiturates are added to or withdrawn from their dosage regimen.

2. **Corticosteroids**—Barbiturates appear to enhance the metabolism of exogenous corticosteroids, probably through the induction of hepatic microsomal enzymes. Patients stabilized on corticosteroid therapy may require dosage adjustments if barbiturates are added to or withdrawn from their dosage regimen.

3. **Griseofulvin**—Phenobarbital appears to interfere with the absorption of orally administered griseofulvin, thus decreasing its blood level. The effect of the resultant decreased blood levels of griseofulvin on therapeutic response has not been established. However, it would be preferable to avoid concomitant administration of these drugs.

4. **Doxycycline**—Phenobarbital has been shown to shorten the half-life of doxycycline for as

MEDICATION GUIDE
SEDATIVE-HYPNOTIC TABLETS/CAPSULES C-II

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Read this Medication Guide before you start taking a SEDATIVE-HYPNOTIC and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or treatment. You and your doctor should talk about the SEDATIVE-HYPNOTIC when you start taking it and at regular checkups.

What is the most important information I should know about SEDATIVE-HYPNOTICS?

After taking a SEDATIVE-HYPNOTIC, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. You have a higher chance for doing these activities if you drink alcohol or take other medicines that make you sleepy with a SEDATIVE-HYPNOTIC. Reported activities include:

- driving a car ("sleep-driving")
- making and eating food
- talking on the phone
- having sex
- sleep-walking

Important:

1. Take SEDATIVE-HYPNOTICS exactly as prescribed

- Do not take more SEDATIVE-HYPNOTICS than prescribed.
- Take the SEDATIVE-HYPNOTIC right before you get in bed, not sooner.

2. Do not take SEDATIVE-HYPNOTICS if you:

- drink alcohol
- take other medicines that can make you sleepy. Talk to your doctor about all of your medicines. Your doctor will tell you if you can take SEDATIVE-HYPNOTICS with your other medicines
- cannot get a full night's sleep

3. Call your doctor right away if you find out that you have done any of the above activities after taking the SEDATIVE-HYPNOTIC.

What are SEDATIVE-HYPNOTICS?

SEDATIVE-HYPNOTICS are sleep medicines. SEDATIVE-HYPNOTICS are used in adults for the short-term treatment of the symptom of trouble falling asleep from insomnia. SEDATIVE-HYPNOTICS do not treat other symptoms of insomnia which include waking up too early in the morning and waking up often during the night.

SEDATIVE-HYPNOTICS are not for children.

SEDATIVE-HYPNOTICS are federally controlled substances (Secobarbital Sodium Capsule is a C-II) because they can be abused or lead to dependence. Keep SEDATIVE-HYPNOTICS in a safe place to prevent misuse and abuse. Selling or giving away SEDATIVE-HYPNOTICS may harm others, and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take SEDATIVE-HYPNOTICS?

Do not take SEDATIVE-HYPNOTICS if you are allergic to anything in it. See the end of this Medication Guide for a complete list of ingredients in Secobarbital Sodium Capsules.

SEDATIVE-HYPNOTICS may not be right for you. Before starting SEDATIVE-HYPNOTICS, tell your doctor about all of your health conditions, including if you:

- have a history of depression, mental illness, or suicidal thoughts
- have a history of drug or alcohol abuse or addiction
- have kidney or liver disease
- have a lung disease or breathing problems
- are pregnant, planning to become pregnant, or breastfeeding

Tell your doctor about all of the medicines you take including prescription and nonprescription medicines, vitamins and herbal supplements. Medicines can interact, sometimes causing side effects. **Do not take SEDATIVE-HYPNOTICS with other medicines that can make you sleepy.**

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

How should I take SEDATIVE-HYPNOTICS?

- **Take SEDATIVE-HYPNOTICS exactly as prescribed.** Do not take more SEDATIVE-HYPNOTIC than prescribed for you.
- **Take SEDATIVE-HYPNOTICS right before you get into bed.** Or you can take the

SEDATIVE-HYPNOTIC after you have been in bed and have trouble falling asleep.

- Do not take SEDATIVE-HYPNOTICS with or right after a meal.
- **Do not take SEDATIVE-HYPNOTICS unless you are able to get a full night's sleep before you must be active again.**
- **Call your healthcare provider if your insomnia worsens or is not better within 7 to 10 days.** This may mean that there is another condition causing your sleep problem.
- If you take too much SEDATIVE-HYPNOTIC or overdose, call your doctor or poison control center right away, or get emergency treatment.

What are the possible side effects of SEDATIVE-HYPNOTICS?

Serious side effects of SEDATIVE-HYPNOTICS include:

- **getting out of bed while not being fully awake and do an activity that you do not know you are doing.** (See "What is the most important information I should know about SEDATIVE-HYPNOTICS?")
- **abnormal thoughts and behavior.** Symptoms include more outgoing or aggressive behavior than normal, confusion, agitation, hallucinations, worsening of depression, and suicidal thoughts or actions.
- **memory loss**
- **anxiety**
- **severe allergic reactions.** Symptoms include swelling of the tongue or throat, trouble breathing, and nausea and vomiting. Get emergency medical help if you get these symptoms after taking SEDATIVE-HYPNOTICS.

Call your doctor right away if you have any of the above side effects or any other side effects that worry you while using the SEDATIVE-HYPNOTIC.

Common side effects of SEDATIVE-HYPNOTICS include:

- drowsiness
- headache
- fatigue
- dizziness
- dry mouth
- upset stomach
- You may still feel drowsy the next day after taking the SEDATIVE-HYPNOTIC. **Do not drive or do other dangerous activities after taking the SEDATIVE-HYPNOTIC until you feel fully awake.**
- You may have withdrawal symptoms for 1 to 2 days when you stop taking the SEDATIVE-HYPNOTIC. Withdrawal symptoms include trouble sleeping, unpleasant feelings, stomach and muscle cramps, vomiting, sweating, shakiness, and seizures.

These are not all the side effects of SEDATIVE-HYPNOTICS. Ask your doctor or pharmacist for more information.

How should I store SEDATIVE-HYPNOTICS?

- Store SEDATIVE-HYPNOTICS at room temperature between 68 - 77° F (20 - 25° C).
- **Keep SEDATIVE-HYPNOTICS and all medicines out of the reach of children.**

General Information about SEDATIVE-HYPNOTICS

- Medicines are sometimes prescribed for purposes not mentioned in a Medication Guide.
- Do not use the SEDATIVE-HYPNOTIC for a condition for which it was not prescribed.
- Do not give the SEDATIVE-HYPNOTIC to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about SEDATIVE-HYPNOTICS. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about the SEDATIVE-HYPNOTIC that was written for healthcare professionals.

If you would like more information, contact Marathon Pharmaceuticals, LLC, 1-866-562-4620.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What are the ingredients in the SEDATIVE-HYPNOTIC?

Active Ingredient: Secobarbital Sodium

Inactive Ingredients: dimethicone, FD&C Red No. 3, FD&C Yellow No. 10, gelatin, magnesium stearate, pregelatinized starch and titanium dioxide.

Manufactured for:
Marathon Pharmaceuticals, LLC
Deerfield, IL 60015 USA
by: Ohm Laboratories Inc.
North Brunswick, NJ 08902 USA

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long as 2 weeks after barbiturate therapy is discontinued.

This mechanism is probably through the induction of hepatic microsomal enzymes that metabolize the antibiotic. If barbiturates and doxycycline are administered concurrently, the clinical response to doxycycline should be monitored closely.

5. *Phenytoin, Sodium Valproate, Valproic Acid*—The effect of barbiturates on the metabolism of phenytoin appears to be variable. Some investigators report an accelerating effect, whereas others report no effect. Because the effect of barbiturates on the metabolism of phenytoin is not predictable, phenytoin and barbiturate blood levels should be monitored more frequently if these drugs are given concurrently. Sodium valproate and valproic acid increase the secobarbital sodium serum levels; therefore, secobarbital sodium blood levels should be monitored closely and appropriate dosage adjustments made as clinically indicated.

6. *CNS Depressants*—The concomitant use of other CNS depressants, including other sedatives or hypnotics, antihistamines, tranquilizers, or alcohol, may produce additive depressant effects.

7. *Monoamine Oxidase Inhibitors (MAOIs)*—MAOIs prolong the effects of barbiturates, probably because metabolism of the barbiturate is inhibited.

8. *Estradiol, Estrone, Progesterone, and Other Steroidal Hormones*—Pretreatment with or concurrent administration of phenobarbital may decrease the effect of estradiol by increasing its metabolism. There have been reports of patients treated with antiepileptic drugs (eg, phenobarbital) who become pregnant while taking oral contraceptives. An alternate contraceptive method might be suggested to women taking barbiturates.

Carcinogenesis—1. *Animal Data.* Phenobarbital sodium is carcinogenic in mice and rats after lifetime administration. In mice, it produced benign and malignant liver cell tumors. In rats, benign liver cell tumors were observed very late in life.

2. *Human Data*—In a 29-year epidemiologic study of 9,136 patients who were treated on an anticonvulsant protocol that included phenobarbital, results indicated a higher than normal incidence of hepatic carcinoma. Previously, some of these patients had been treated with thiorast, a drug that is known to produce hepatic carcinomas. Thus, this study did not provide sufficient evidence that phenobarbital sodium is carcinogenic in humans.

A retrospective study of 84 pediatric patients with brain tumors matched to 73 normal controls and 78 cancer controls (malignant disease other than brain tumors) suggested an association between exposure to barbiturates prenatally and an increased incidence of brain tumors.

Usage in Pregnancy—1. *Teratogenic Effects. Pregnancy Category D.* See Usage in Pregnancy under Warnings.

2. *Nonteratogenic Effects.* Reports of infants suffering from long-term barbiturate exposure *in utero* included the acute withdrawal syndrome of seizures and hyperirritability from birth to a delayed onset of up to 14 days (see Drug Abuse and Dependence).

Labor and Delivery—Hypnotic doses of barbiturates do not appear to impair uterine activity significantly during labor. Full anesthetic doses of barbiturates decrease the force and frequency of uterine contractions. Administration of sedative-hypnotic barbiturates to the mother during labor may result in respiratory depression in the newborn. Premature infants are particularly susceptible to the depressant effects of barbiturates. If barbiturates are used during labor and delivery, resuscitation equipment should be available.

Data are not available to evaluate the effect of barbiturates when forceps delivery or other intervention is necessary or to determine the effect of barbiturates on the later growth, development, and functional maturity of the pediatric patient.

Nursing Mothers—Caution should be exercised when Seconal Sodium is administered to a nursing woman, because small amounts of barbiturates are excreted in the milk.

ADVERSE REACTIONS

The following adverse reactions and their incidences were compiled from surveillance of thousands of hospitalized patients who received barbiturates. Because such patients may be less aware of some of the milder adverse effects of barbiturates, the incidence of these reactions may be somewhat higher in fully ambulatory patients.

More than 1 in 100 Patients

The most common adverse reaction estimated to occur at a rate of 1 to 3 patients per 100 is the following:

Nervous System: Somnolence

Less than 1 in 100 Patients

Adverse reactions estimated to occur at a rate of less than 1 in 100 patients are listed below, grouped by organ system and by decreasing order of occurrence:

Nervous System: Agitation, confusion, hyperkinesia, ataxia, CNS depression, nightmares, nervousness, psychiatric disturbance, hallucinations, insomnia, anxiety, dizziness, abnormality in thinking

Respiratory System: Hypoventilation, apnea

Cardiovascular System: Bradycardia, hypotension, syncope

Digestive System: Nausea, vomiting, constipation

Other Reported Reactions: Headache, injection site reactions, hypersensitivity reactions (angioedema, skin rashes, exfoliative dermatitis), fever, liver damage, megaloblastic anemia following chronic phenobarbital use

DRUG ABUSE AND DEPENDENCE

Abuse and addiction are separate and distinct from physical dependence and tolerance. Abuse is characterized by misuse of the drug for non-medical purposes, often in combination with other psychoactive substances. Physical dependence is a state of adaptation that is manifested by a specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist. Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. Tolerance may occur to both the desired and undesired effects of drugs and may develop at different rates for different effects.

Addiction is primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Drug addiction is a treatable disease, utilizing a multidisciplinary approach, but relapse is common.

Controlled substance—Seconal Sodium Capsules are a Schedule II drug.

Dependence—Barbiturates may be habit-forming; tolerance, psychological dependence, and physical dependence may occur, especially following prolonged use of high doses of barbiturates. Daily administration in excess of 400 mg of secobarbital for approximately 90 days is likely to produce some degree of physical dependence. A dosage of 600 to 800 mg for at least 35 days is sufficient to produce withdrawal seizures. The average daily dose for the barbiturate addict is usually about 1.5 g. As tolerance to barbiturates develops, the amount needed to maintain the same level of intoxication increases; tolerance to a fatal dosage, however, does not increase more than twofold. As this occurs, the margin between intoxicating dosage and fatal dosage becomes smaller.

Symptoms of acute intoxication with barbiturates include unsteady gait, slurred speech, and sustained nystagmus. Mental signs of chronic intoxication include confusion, poor judgment, irritability, insomnia, and somatic complaints.

Symptoms of barbiturate dependence are similar to those of chronic alcoholism. If an individual appears to be intoxicated with alcohol to a degree that is radically disproportionate to the

amount of alcohol in his or her blood, the use of barbiturates should be suspected. The lethal dose of a barbiturate is far less if alcohol is also ingested.

The symptoms of barbiturate withdrawal can be severe and may cause death. Minor withdrawal symptoms may appear 8 to 12 hours after the last dose of a barbiturate. These symptoms usually appear in the following order: anxiety, muscle twitching, tremor of hands and fingers, progressive weakness, dizziness, distortion in visual perception, nausea, vomiting, insomnia, and orthostatic hypotension. Major withdrawal symptoms (convulsions and delirium) may occur within 16 hours and last up to 5 days after abrupt cessation of barbiturates. Intensity of withdrawal symptoms gradually declines over a period of approximately 15 days. Individuals susceptible to barbiturate abuse and dependence include alcoholics and opiate abusers, as well as other sedative-hypnotic and amphetamine abusers.

Drug dependence on barbiturates arises from repeated administration on a continuous basis, generally in amounts exceeding therapeutic dose levels. The characteristics of drug dependence on barbiturates include the following: (a) a strong desire or need to continue taking the drug; (b) a tendency to increase the dose; (c) a psychic dependence on the effects of the drug related to subjective and individual appreciation of those effects; and (d) a physical dependence on the effects of the drug, requiring its presence for maintenance of homeostasis and resulting in a definite, characteristic, and self-limited abstinence syndrome when the drug is withdrawn. Treatment of barbiturate dependence consists of cautious and gradual withdrawal of the drug. Barbiturate-dependent patients can be withdrawn by using a number of withdrawal regimens. In all cases, withdrawal takes an extended period. One method involves substituting a 30 mg dose of phenobarbital for each 100 to 200 mg dose of barbiturate that the patient has been taking. The total daily amount of phenobarbital is then administered in 3 or 4 divided doses, not to exceed 600 mg daily. Should signs of withdrawal occur on the first day of treatment, a loading dose of 100 to 200 mg of phenobarbital may be administered IM in addition to the oral dose. After stabilization on phenobarbital, the total daily dose is decreased by 30 mg a day as long as withdrawal is proceeding smoothly. A modification of this regimen involves initiating treatment at the patient's regular dosage level and decreasing the daily dosage by 10% as tolerated by the patient.

Infants that are physically dependent on barbiturates may be given phenobarbital, 3 to 10 mg/kg/day. After withdrawal symptoms (hyperactivity, disturbed sleep, tremors, and hyperreflexia) are relieved, the dosage of phenobarbital should be gradually decreased and completely withdrawn over a 2-week period.

OVERDOSAGE

The toxic dose of barbiturates varies considerably. In general, an oral dose of 1 g of most barbiturates produces serious poisoning in an adult. Death commonly occurs after 2 to 10 g of ingested barbiturate. The sedated, therapeutic blood levels of secobarbital range between 0.5 to 5 mcg/mL; the usual lethal blood level ranges from 15 to 40 mcg/mL. Barbiturate intoxication may be confused with alcoholism, bromide intoxication, and various neurologic disorders. Potential tolerance must be considered when evaluating significance of dose and plasma concentration.

Signs and Symptoms—Symptoms of oral overdose may occur within 15 minutes and begin with central nervous system depression, underventilation, hypotension, and hypothermia, which may progress to pulmonary edema and death. Hemorrhagic blisters may develop, especially at pressure points.

In extreme overdose, all electrical activity in the brain may cease, in which case a "flat" EEG normally equated with clinical death cannot be accepted as indicative of brain death. This effect is fully reversible unless hypoxic damage occurs. Consideration should be given to the possibility of barbiturate intoxication even in situations that appear to involve trauma.

Complications such as pneumonia, pulmonary edema, cardiac arrhythmias, congestive heart failure, and renal failure may occur. Uremia may increase CNS sensitivity to barbiturates if renal function is impaired. Differential diagnosis should include hypoglycemia, head trauma, cerebrovascular accidents, convulsive states, and diabetic coma.

Treatment—To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*. In managing overdose, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Diuresis and peritoneal dialysis are of little value; hemodialysis and hemoperfusion enhance drug clearance and should be considered in serious poisoning. If the patient has chronically abused sedatives, withdrawal reactions may be manifest following acute overdose.

DOSE AND ADMINISTRATION

Dosages of barbiturates must be individualized with full knowledge of their particular characteristics. Factors of consideration are the patient's age, weight, and condition.

Adults—As a hypnotic, 100 mg at bedtime. Preoperatively, 200 to 300 mg 1 to 2 hours before surgery.

Pediatric Patients—Preoperatively, 2 to 6 mg/kg, with a maximum dosage of 100 mg.

Special patient population—Dosage should be reduced in the elderly or debilitated because these patients may be more sensitive to barbiturates. Dosage should be reduced for patients with impaired renal function or hepatic disease.

HOW SUPPLIED

Seconal Sodium capsules are orange and imprinted with RX679 on both the cap and the body:
NDC 42998-679-01 100 mg Bottles of 100
Store at 20 - 25° C (68 - 77° F). (See USP Controlled Room Temperature). Dispense in a tight container.

Manufactured for:
Marathon Pharmaceuticals, LLC
Deerfield, IL 60015 USA

by: Ohm Laboratories, Inc.
North Brunswick, NJ 08902 USA

September 2008



Literture Size : 10.75" x x 12.375" (273 x 314 mm)

Colour : Black

Font Size : 6.5 Pt.

Track : A13/08/08, R27/08/08, A28/08/08, A29/08/08

A01/09/08, PM 09/23/08