Barbiturates are respiratory depressants. The degree of respiratory depression is dependent upon dose. With hypnotic doses, respiratory depression predominates. Barbiturates is similar to the one which occurs during physiologic sleep with slight decrease in blood pressure and heart rate.

Barbiturates do not impair normal hepatic function, but they have been shown to induce liver microsomal enzymes, thus increasing and/or altering the metabolism of barbiturates and other drugs (see Pharmacokinetic Interactions).

Pharmacokinetics: BUTISOL® (barbitural sodium tablets, USP and barbitural sodium oral solution, USP) is a non-selective central nervous system depressant which is used as a sedative or hypnotic. It is available for oral administration as Tablets containing 30 mg or 50 mg barbitural sodium; and as Oral Solution containing 30 mg/ml, with alcohol (by volume) 7%. Other ingredients in the Tablets are: calcium stearate, dibasic calcium phosphate, FD&C Blue No. 1 (30 mg only), FD&C Yellow No. 5 and 50 mg (30 and 50 mg — see Precautions). Barbitural Tablets, USP (50 mg only). Other ingredients in the Oral Solution are: D&C Green No. 5, dextrose, FD&C Yellow No. 6 (see Precautions). Sodium sulfate, sodium bicarbonate, butylated hydroxyanisole, purified water, saccharin sodium, sodium benzoate. Barbitural Tablets, USP (30 mg only) contains a white, bitter powder which is freely soluble in water and alcohol, but practically insoluble in benzene and ether. The structural formula for barbituric acid is:

\[
\text{H}_3\text{C} - \text{C} = \text{O} - \text{N} - \text{C}_6\text{H}_4 - \text{C}_2\text{H}_5
\]

Sodium 5-ethyl-5-ethylbarbiturate

Clinical Pharmacology

BUTISOL® (barbitural sodium tablets, USP and barbitural sodium oral solution, USP), like other barbiturates, is capable of reducing the amount of time spent in the rapid eye movement (REM) phase of sleep or dreaming stage. Also, Stages III and IV sleep are decreased. Following abrupt cessation of barbiturate usage, 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 which contribute to drug withdrawal syndrome (for example, decrease the dose from 3 to 2 doses a day for 1 week).

In studies, secobarbital and pentobarbital sodium have been found to lose most of their effects within 2 weeks of withdrawal of continuous drug administration, even with the use of multiple doses. As with secobarbital and pentobarbital sodium, other barbiturates 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 of the short-acting barbiturates being superior for producing sleep while 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 limited of value beyond short-term use.

BUTISOL® (barbitural sodium tablets, USP and barbitural sodium oral solution, USP)

IN-0110-13 Rev. 5/2015

IN-0110-12 R01-09 7/13/
Central nervous system/psychiatric: Agitation, confusion, hyperreflexia, ataxia, CNS depression, nightmares, nervousness, psychiatric disturbance, hallucinations, paranoia, delirium, anxiety, diziness, thinking abnormality. 

Respiratory: Hypoventilation, apnea. 

Cardiovascular: Bradycardia, hypotension. 

Gastrointestinal: Nausea, vomiting, constipation. 

Other reported reactions: Headache, hypersensitiveness (angiodynia, skin rashes, exfoliative dermatitis). 

Drug Abuse and Dependence 

Controlled substance: Schedule III. 

Abuse and dependence: Abuse and addiction are not distinguishable from those of other depressant drugs of this class. There is no evidence of increased abuse potential between Butisol Sodium and other barbiturates. 

Drug dependence and withdrawal: The average daily dose for patients with withdrawal seizures is 100 mg for every 10 years of age. Once withdrawal is terminated, the average daily dose may be decreased by 10% per day until the daily dose is less than the patient’s maintenance dose. In the elderly, it is recommended that the maintenance dose be increased by 10% per day. 

Overdosage 

Signs and symptoms: The toxic dose of barbiturates varies considerably. In general, an oral dose of 1 gram of most barbiturates produces serious poisoning in an adult. Death commonly occurs after 2 to 3 grams of ingested barbiturates. 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. 

Barbiturate intoxication may be confused with alcoholism, bromide intoxication, and with various neurological disorders. 

Acute overdose with barbiturates is marked by CNS and respiratory depression, and death may occur. In extreme overdose, all electrical activity in the brain may cease, in which case the patient is in “brain death.” This is generally in amounts exceeding the therapeutic dose. 

Complications: 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: Treatment of overdose is mainly supportive and consists of the following: 

1. Maintenance of an adequate airway, with assisted respiration and oxygen administration as necessary. 

2. Monitoring of vital signs and fluid balance. 

3. If the patient is conscious and has not lost the gag reflex, emesis may be induced with ipecac. 

4. If emesis is contraindicated, gastric lavage may be performed with a cuffed endotracheal tube in place with the patient in the face down position. Activated charcoal may be left in the emptied stomach and a saline cathartic administered. 

5. Fluid therapy and other standard treatment for shock, if needed. 

6. If renal function is normal, forced diuresis may aid in the elimination of the barbiturate. 

7. Although not recommended as a routine procedure, hemodialysis may be used in severe barbiturate intoxications or if the patient is anuric or in shock. 

8. Appropriate nursing care, including rolling patients from side-to-side every 30 minutes, to prevent hypostatic pneumonia, decubitus, aspiration, and other complications. 

Butisol Sodium® (Butabarbital Sodium Tablets, USP and Butabarbital Sodium Oral Solution, USP) 

IN-0110-15 

5. Phenyltoin, sodium valproate, valproic acid. The effect of barbiturates on the metabolism of phenytoin appears to be variable. Some investigators report an accelerating effect, while others report no effect. The effect of the drugs is particularly noted on the metabolism of phenytoin, which is predictable, phenytoin and barbiturate blood levels should be monitored more frequently because these drugs are given concurrently. Sodium valproate and valproic acid appear to decrease barbiturate metabolism; therefore, barbiturate blood levels and appropriate dosage adjustments made as indicated. 

6. Central nervous system. The concomitant use of other central nervous system depressants, including other sedatives or hypnotics, antihista- timines, tranquilizers, or alcohol, may produce additive depressant effects. 

7. Monoamine oxidase inhibitors (MAOIs). MAOIs prolong the effects of barbiturates probably because metabolism of these drugs is altered. 

8. Estradiol, estrone, progesterone, and other steroid hormones. Pretreatment with or concurrent administration of hormones may decrease the effect of estradiol by increasing its metabolism. There have been reports of patients treated with antiestrogenic drugs (e.g., phenobarbital) who become pregnant while taking oral contraceptives. 

9. An alternate contraceptive method might be suggested to the patient taking phenothiazines. 

10. Carcinogenesis, mutagenesis, impairment of fertility: No long-term studies in animals have been performed with Butisol Sodium to determine carcinogenic and mutagenic potential, or effects on fertility. 

Pregnancy: Teratogenic effects - Pregnancy category D (see Warnings - Use in pregnancy above). 

14. Nonteratogenic effects - Infants suffering from long-term barbiturate exposure may exhibit an 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 significantly impair uterine activity during labor. 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. 

Nursing mothers: Caution should be exercised when a barbiturate is administered to a nursing woman since small amounts of some barbiturates are excreted in the milk. 

Geriatric use: Clinical studies of Butisol Sodium Tablets/Oral Solution did not indicate any different in responses in these patients from the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.