Darvon® (Propoxyphene Hydrochloride, USP) is an odorless, white crystalline powder with a bitter taste. It is freely soluble in water. Chemically, it is \((\text{C}_2\text{H}_3\text{N})(\text{C}_3\text{H}_7\text{O}_2)\cdot\text{HCl}\). Its molecular weight is 375.94.

Each Pulvule contains 65 mg (172.9 µmol) propoxyphene hydrochloride. It also contains D & C Red No. 33, F & C Yellow No. 6, gelatin, magnesium stearate, silicon dioxide, starch, titanium dioxide, and other inactive ingredients.

Propoxyphene is a centrally acting narcotic analgesic agent. Equimolar doses of propoxyphene hydrochloride or napsylate provide similar plasma concentrations. Following administration of 65, 130, or 195 mg of propoxyphene hydrochloride, the bioavailability of propoxyphene is equivalent to that of 100, 200, or 300 mg respectively of propoxyphene napsylate. Peak plasma concentrations of propoxyphene are reached in 2 to 2.5 hours. After a 65-mg oral dose of propoxyphene hydrochloride, peak plasma levels of 0.05 to 0.1 µg/ml are achieved.

Repeated doses of propoxyphene at 4-hour intervals lead to increasing plasma concentrations, with a plateau after the ninth dose at 48 hours. Propoxyphene is metabolized in the liver to yield norpropoxyphene. Propoxyphene has a half-life of 6 to 12 hours, whereas that of norpropoxyphene is 30 to 36 hours.

Norpropoxyphene has substantially less central-, nervous-system-depressant effect than propoxyphene but a greater local anesthetic effect, which is similar to that of amitriptyline and antiarrhythmic agents, such as lidocaine and quinidine.

In animal studies in which propoxyphene and norpropoxyphene were continuously infused in large amounts, intracardiac conduction time (PR and QRS intervals) was prolonged. Any intracardiac conduction delay attributable to high concentrations of norpropoxyphene may be of relatively long duration.

**CLINICAL PHARMACOLOGY**

- Propoxyphene is a mild narcotic analgesic structurally related to methadone. The potency of propoxyphene hydrochloride is from two thirds to equal that of codeine.
- The CNS-depressant effect of propoxyphene is additive with that of other CNS depressants (for example, sedatives, tranquilizers, barbiturates, and alcohol). Propoxyphene 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.

**WARNINGS**

- Do not prescribe propoxyphene for patients who are suicidal or addiction-prone.
- Prescribe propoxyphene with caution for patients taking tranquilizers or antidepressants and patients who use alcohol in excess.
- Tell your patients not to exceed the recommended dose and to limit their intake of alcohol.

**CONTRAINDICATION**

Hypersensitivity to propoxyphene.

**CONTRAINDICATION**

Hypersensitivity to propoxyphene.

**ACTIONS**

Propoxyphene is a mild narcotic analgesic structurally related to methadone. The potency of propoxyphene hydrochloride is from two thirds to equal that of codeine.

**INDICATION**

For the relief of mild to moderate pain.

**ADVERSE REACTIONS**

- Anticonvulsants, or warfarin-like drugs. Severe neurologic signs, including coma, have occurred with concurrent use of carbamazepine.
- Usage in Pregnancy—Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Instances of withdrawal symptoms in the neonate have been reported following usage during pregnancy. Therefore, propoxyphene should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.
- Usage in Nursing Mothers—Low levels of propoxyphene have been detected in human milk. In postpartum studies involving nursing mothers who were given propoxyphene, no adverse effects were noted in infants receiving mother’s milk.
- Usage in Pediatric Patients—Safety and effectiveness in pediatric patients have not been established.
- Usage in the Elderly—The rate of propoxyphene metabolism may be reduced in some patients. Increased dosing interval should be considered.
- Propoxyphene has been associated with abnormal liver function tests, and rarely, with instances of reversible jaundice (including cholestatic jaundice).
- Subacute painful myopathy has occurred following chronic propoxyphene overdosage.

**MANAGEMENT OF OVERDOSE**

- In all cases of suspected overdose, call your regional Poison Control Center to obtain the most up-to-date information about the treatment of overdose. This recommendation is made because, in general, information regarding the treatment of overdose may change more rapidly than do package inserts.
- Initial consideration should be given to the management of the CNS effects of propoxyphene overdose. Resuscitative measures should be initiated promptly.

**SYMPTOMS OF PROPOXYPHENE OVERDOSE**

- The manifestations of acute overdose with propoxyphene are those of narcotic overdosage. The patient is usually somnolent but may be stuporous or comatose and convulsing. Respiratory depression is characteristic. The ventilatory rate and/or tidal volume is decreased, which results in respiratory acidosis and an increase in the serum bicarbonate level. Cyanosis, Cheyne-Stokes respiration, and apnea may occur. Blood pressure and heart rate are usually normal initially, but blood pressure falls and cardiac performance deteriorates, which ultimately results in pulmonary edema and circulatory collapse, unless the respiratory depression is corrected and adequate ventilation is restored promptly. Cardiac arrhythmias and conduction delay may be present. A combined respiratory-metabolic acidosis occurs owing to retained CO₂ (hypercapnia) and to lactic acidosis due to anaerobic glycolysis. Acidosis may be severe if large amounts of salicylates have also been ingested. Death may occur.

**TREATMENT OF PROPOXYPHENE OVERDOSE**

- Treatment should be directed first to establishing a patent airway and to restoring ventilation. Mechanically assisted ventilation, with or without oxygen, may be required, and positive pressure respiration may be desirable if pulmonary edema is present. The narcotic antagonist naloxone will markedly reduce the degree of respiratory depression within 4 minutes. If naloxone is ineffective or partially effective, it should be repeated at 2- to 3-minute intervals for a total dose of 0.4 to 2 mg. Naloxone may be given intravenously if the patient is hypertensive. Cardiac arrhythmias may be managed with intravenous or oral lidocaine or other antiarrhythmic agents. Acidosis may be treated by intravenous sodium bicarbonate or sodium lactate, with or without oxygen. Electrocardiographic monitoring is essential. Prompt correction of hypoxia, acidosis, and electrolyte disturbance (when present) will help prevent those cardiac complications and will increase the effectiveness of agents administered to restore normal cardiac function.

**Precautions**

- General—Propoxyphene should be administered with caution to patients with hepatic or renal impairment since higher serum concentrations or delayed elimination may occur.
- Drug Interactions—The CNS-depressant effect of propoxyphene is additive with that of other CNS depressants, including alcohol.
- As is the case with many medicinal agents, propoxyphene may slow the metabolism of a concurrently administered drug. Should this occur, the higher serum concentrations of the drug may result in increased pharmacologic or adverse effects of that drug. Such occurrences have been reported when propoxyphene was administered to patients on antidepressants,
Propoxyphene may cause drowsiness or impair your mental and/or physical abilities; therefore, use caution when driving a vehicle or operating dangerous machinery. DO NOT perform any hazardous task until you have seen your response to this drug.

Propoxyphene may increase the concentration in the body of medications, such as anticoagulants (“blood thinners”), antidepressants, or drugs used for epilepsy. The result may be excessive or adverse effects of these medications. Make sure your doctor knows if you are taking any of these medications.

Dependence

You can become dependent on propoxyphene if you take it in higher than recommended doses over a long period of time. Dependence is a feeling of need for the drug and a feeling that you cannot perform normally without it.

Overdose

An overdose of Darvon, alone or in combination with other drugs, including alcohol, may cause weakness, difficulty in breathing, confusion, anxiety, and more severe drowsiness and dizziness. Extreme overdosage may lead to unconsciousness and death.

If the propoxyphene product contains acetaminophen, the overdose symptoms include nausea, vomiting, lack of appetite, and abdominal pain. Liver damage may occur.

When the propoxyphene product contains aspirin, symptoms of taking too much of the drug are headache, dizziness, ringing in the ears, difficulty in hearing, dizziness, confusion, drowsiness, sweating, thirst, rapid breathing, nausea, vomiting, and, occasionally, diarrhea.

In any suspected overdosage situation, contact your doctor or nearest hospital emergency room. GET EMERGENCY HELP IMMEDIATELY.

KEEP THIS DRUG AND ALL DRUGS OUT OF THE REACH OF THE PEDIATRIC POPULATION.

Possible Side Effects

When propoxyphene is taken as directed, side effects are infrequent. Among those reported are drowsiness, dizziness, nausea, and vomiting. If these effects occur, it may help if you lie down and rest.

Less frequently reported side effects are constipation, abdominal pain, skin rashes, lightheadedness, headache, weakness, hallucinations, minor visual disturbances, and feelings of elation or disorientation.

If side effects occur and concern you, contact your doctor.

General Cautions

Heavy use of alcohol with propoxyphene is hazardous and may lead to overdosage symptoms (see “Overdose” below). THEREFORE, LIMIT YOUR INTAKEN OF ALCOHOL WHILE TAKING PROPOXYPHENE.

Combination of excessive doses of propoxyphene, alcohol, and tranquilizers are dangerous. Make sure your doctor knows if you are taking tranquilizers, sleep aids, antidepressant drugs, antihistamines, or any other drugs that make you sleepy. The use of these drugs with propoxyphene increases their sedative effects and may lead to overdosage symptoms, including death (see “Overdose” below).

Propoxyphene may cause drowsiness or impair your mental and/or physical abilities; therefore, use caution when driving a vehicle or operating dangerous machinery. DO NOT perform any hazardous task until you have seen your response to this drug.

Propoxyphene may increase the concentration in the body of medications, such as anticoagulants (“blood thinners”), antidepressants, or drugs used for epilepsy. The result may be excessive or adverse effects of these medications. Make sure your doctor knows if you are taking any of these medications.

Products containing propoxyphene and aspirin or acetaminophen are prescribed for the relief of pain or pain associated with fever.

Before Taking Darvon

Make sure your doctor knows if you have ever had an allergic reaction to propoxyphene, aspirin, or acetaminophen. Some forms of propoxyphene products contain aspirin to help relieve the pain. Your doctor should be advised if you have a history of ulcers or if you are taking an anticoagulant (“blood thinner”). The aspirin may irritate the stomach lining and may cause bleeding, particularly if an ulcer is present. Also, bleeding may occur if you are taking an anticoagulant. In a small group of people, aspirin may cause an asthma attack. If you are one of these people, be sure your drug does not contain aspirin.

The effect of propoxyphene in pediatric patients under 12 has not been studied. Therefore, use of the drug in this age group is not recommended.

Also, due to the possible association between aspirin and Reye Syndrome, those propoxyphene products containing aspirin should not be given to children, including teenagers, with chicken pox or flu unless prescribed by a physician. The following propoxyphene product contains aspirin:

Darvon® Compund-65 (Propoxyphene Hydrochloride, Aspirin, and Caffeine, USP)

How to Take Darvon

Follow your doctor’s directions exactly. Do not increase the amount you take without your doctor's approval. If you miss a dose of the drug, do not take twice as much the next time.

Pregnancy

Do not take propoxyphene during pregnancy unless your doctor knows you are pregnant and specifically recommends its use. Cases of temporary dependence in the newborn have occurred when the mother has taken propoxyphene consistently in the weeks before delivery. As a general principle, no drug should be taken during pregnancy unless it is clearly necessary.

Limit Your Intake of Alcohol While Taking This Drug

The safe and effective use of propoxyphene depends on your taking it exactly as directed. This drug has been prescribed specifically for you and your present condition. Do not give this drug to others who may have similar symptoms. Do not use it for any other reason.

If you would like more information about propoxyphene, ask your doctor or pharmacist. They have a more technical leaflet (professional labeling) you may read.

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