

its use. Although propoxyphene is listed as a "non-narcotic analgesic", it is capable of producing both psychic and physical dependence. Most of the individuals dependent upon the drug have a history of abuse of other drugs. Drug dependent users used to remove the aspirin pellet from the capsule of Darvon compound (propoxyphene hydrochloride with aspirin), dissolved the propoxyphene and used it for intravenous injection to obtain a euphoric effect. Propoxyphene hydrochloride is soluble in water. This practice was obviated by using an insoluble form of the salt of propoxyphene; namely the napsylate.

The reported cases of dependence upon propoxyphene obviously does not present a true picture of the problem because it does not account for the total number of addicts; yet, relatively speaking, the risk of dependence in non-drug dependent persons of propoxyphene appears to be low compared in non-dependent individuals to morphine and meperidine. The Committee on Problems for Drug Abuse of the National Academy of Sciences, National Research Council, and other groups have suggested that the term non-narcotic be deleted from advertising by manufacturers since its significance is misinterpreted. The designation "non-narcotic" does not mean that a drug does not produce dependence. It is a term with a legal connotation that indicates neither special narcotic prescriptions are required nor other narcotic controls are imposed prescribing the drug. The fact that propoxyphene hydrochloride (Darvon) was not subjected to the Federal Narcotic Control, plus the fact that it was widely promoted and the impression created that it was innocuous, to a large extent, explains the voluminous sales of this analgesic. Americans spent over \$140,000,000 in 1977 for Lilly manufactured Darvon and Darvon combinations products. The napsylate (Darvon-N Lilly) which was recently introduced is more stable than the hydrochloride. Because of differences in molecular weight, a dose of 100 mg of napsylate is required to provide the amount of propoxyphene equivalent to 65 mg of the hydrochloride. The pharmacologic effects of both salts are similar.

Propoxyphene has been one of the most frequently prescribed drugs in the Louisiana State Medicaid and Welfare Programs. It is now no longer on the list of drugs the State furnishes without cost. At Charity Hospital (an 1800 bed general hospital), where the drug has been controlled since its admission to the Hospital Formulary List, only 7000 units were prescribed in 1978. Reservations about the efficacy of propoxyphene continue to be expressed. In a recently published double-blind study of single doses of propoxyphene, aspirin and other oral analgesics in patients with cancer, Moertel and associates (Moertel, C.G. et al: New England Jour. Med. 286, 813, April 13, 1972) were unable to demonstrate that even 65 mg of propoxyphene was significantly superior to a placebo. In this study, aspirin was the most effective analgesic tested.

Until recently, the attitude towards Darvon has been one of complacency and indifference even though there has been doubt about efficacy all along because the drug was considered safe. The feeling has been "it may not do much good but it does not do any harm". Now, the question of safety has come sharply into focus and there is considerable concern about its continued use.

Propoxyphene is not without adverse effects. In non-dependent individuals, approximately 0.5% of the reactions that occur are minor consisting of nausea, vomiting, drowsiness, rash and vertigo. Hallucinations and disorientation are rare but have been observed. The drug may also cause encephalopathy in patients with diminished liver function. The frequency of adverse effects varies with dosage. There is no evidence that truly analgesic doses of propoxyphene are less harmful than equal analgesic doses of other drugs.

An increasing number of cases of ingestion of lethal and nearly lethal doses of propoxyphene is being reported. In general, the symptoms of overdosage are similar to those resulting with other narcotic drugs. Various degrees of respiratory, central nervous system and circulatory depression are usually present. On the other hand, convulsions, seldom seen with narcotics, as well as coma, have been reported and deaths have resulted. Death usually results from hypoxia accompanied by pulmonary edema and cardiac failure. Propoxyphene toxicity can be treated with narcotic antagonists, such as Naloxone.

The dependence to propoxyphene in narcotic dependent persons is now well documented. It is substantially less intense than that seen with morphine or heroin but nonetheless it does occur. Physical dependence has been observed particularly with high doses. Some physicians and pharmacologists have suggested that dependence would be more frequent if the drug were administered in high enough doses to provide effective analgesia. Orally administered propoxyphene