Propoxyphene is an abused drug and its abuse can and does lead to physical dependence. Propoxyphene is most often ingested. Intraveneous abuse of propoxyphene is usually a self-limiting process because of the resulting vascular and tissue damage. Patients who have histories of chronic pain, psychiatric disturbance, or multiple drug ingestion and who escalate the dosage of propoxyphene over rather long periods of time, abuse and/or become dependent on this drug. Patterns of abuse range from a single episode of ingestion to chronic daily use of high doses over long periods of time.

In 1976, when the Department of Health, Education and Welfare (HEW) concurred in the DEA proposal that propoxyphene be placed into Schedule IV of the Controlled Substances Act, the Secretary noted the following about the abuse potential and addiction liability of propoxyphene:

The abuse liability of propoxyphene is qualitatively similar to that of codeine although quantitatively less....Propoxyphene can produce a psychological and physical dependence which is qualitatively similar to that produced by 'classical' opiates (e.g., morphine or codeine) but which is quantitatively less.

Put another way, this means that propoxyphene affects most of the same systems of the body as morphine or codeine but the results are less intense.