

# Hydrocodone

# (Trade Names: Vicodin<sup>®</sup>, Lortab<sup>®</sup>, Lorcet-HD<sup>®</sup>, Hycodan<sup>®</sup>, Vicoprofen<sup>®</sup>)

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#### **Introduction:**

Since 2009, hydrocodone has been the second most frequently encountered opioid pharmaceutical in drug evidence submitted to federal, state, and local forensic laboratories as reported by DEA's National Forensic Laboratory Information System (NFLIS) and System to Retrieve Information from Drug Evidence (STRIDE)/STARLiMS databases.

#### **Licit Uses:**

Hydrocodone is an antitussive (cough suppressant) and narcotic analgesic agent for the treatment of moderate to moderately severe pain. Studies indicate that hydrocodone is as effective, or more effective, than codeine for cough suppression and nearly equipotent to morphine for pain relief.

Hydrocodone is the most frequently prescribed opioid in the United States with more than 136.7 million prescriptions for hydrocodone-containing products dispensed in 2013 along with 93.7 million dispensed in 2016 and 83.6 million sold to patients in 2017 (IQVIA™ formerly known as IMS Health™). There are several hundred brand name and generic hydrocodone products marketed, most of which are combination products. The most frequently prescribed combination is hydrocodone and acetaminophen (Vicodin®, Lortab®).

In response to the opioid crisis and revised clinical guidelines for prescribing opioids for chronic pain, there has been an ongoing effort to reduce the prescribing of opioid medication, in general, along with implementing best practices. So, in 2018, the number prescriptions of hydrocodone-containing products sold to patients within the U.S. continued to decrease to 70.9 million.

## Chemistry and Pharmacology:

Hydrocodone [4,5α-epoxy-3-methoxy-17-methyl-morphinan-6-one tartrate (1:1) hydrate (2:5), dihydrocodeinone] Hydrocodone [4,5α-epoxy-3-methoxy-17-methyl-morphinan-6-one tartrate (1:1) hydrate (2:5), dihydrocodeinone] is a semi-synthetic opioid most closely related to codeine in structure and morphine in producing opiate-like effects. The first report, that hydrocodone produces euphoria and habituation symptoms, was published in 1923. The first report of hydrocodone dependence and addiction was published in 1961.

Hydrocodone exerts its principle pharmacological effects through agonistic binding to opioid receptors. Hydrocodone primarily binds and activates the mu-opioid receptor in the CNS and possesses analgesic and antitussive effects. Binding of hydrocodone to this receptor also results in analgesia, euphoria, respiratory depression, decreased gastrointestinal motility and physical dependence. Additionally, hydrocodone is converted to hydromorphone by the cytochrome P 450 enzyme CYP2D6.

#### Illicit Uses:

Hydrocodone is abused for its opioid effects. Widespread diversion via bogus call-in prescriptions, altered prescriptions, theft, and illicit purchases from Internet sources are made easier by the present controls placed on hydrocodone products. Hydrocodone pills are the most frequently encountered dosage form in illicit traffic. Hydrocodone is generally abused orally, often in combination with alcohol.

Of particular concern is the prevalence of illicit use of hydrocodone among school-aged children. The 2018 Monitoring the Future Survey continues to report a decreasing trend, since 2012, in which 0.6%, 1.10% and 1.70% of 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> graders, respectively, used Vicodin<sup>®</sup> for nonmedical purposes in the past year.

The 2017 American Association of Poison Control Centers

(AAPCC) reports that there were 1,810 total exposures, 740 single exposures, and 1 death associated with hydrocodone in the U.S which is slightly lower than exposures for 2016. The 2016 National Survey on Drug Use and Health (NSDUH) reported that 6.9 million people in the U.S., aged 12 and older, misused hydrocodone in the past year compared to 7.2 million in 2015. More recently, misuse has significantly decreased from 6.9 million U.S. persons to 5.5 million in 2017 and 2018, respectively.

As with most opiates, abuse of hydrocodone is associated with tolerance, dependence, and addiction. The co-formulation with acetaminophen carries an additional risk of liver toxicity when high, acute doses are consumed. Some individuals who abuse very high doses of acetaminophen-containing hydrocodone products may be spared this liver toxicity if they have been chronically taking these products and have escalated their dose slowly over a long period of time.

## **User Population:**

Every age group has been affected by the relative ease of hydrocodone availability and the perceived safety of these products by medical prescribers. Sometimes viewed as a "white collar" addiction, hydrocodone abuse has increased among all ethnic and economic groups.

## Illicit Distribution:

Hydrocodone has been encountered in tablets, capsules, and liquid form in the illicit market. However, hydrocodone tablets with the co-ingredient, acetaminophen, is the most frequently encountered form. Hydrocodone is not typically found to be clandestinely produced; diverted pharmaceuticals are the primary source of the drug for abuse purposes. Doctor shopping, altered or fraudulent prescriptions, bogus call-in prescriptions, diversion by some physicians and pharmacists, and drug theft are also major sources of the diverted drug.

The National Forensic Laboratory Information System (NFLIS) is a DEA database that collects scientifically verified data on drug items and cases submitted to and analyzed by federal, state, and local forensic laboratories. The System to Retrieve Information from Drug Evidence (STRIDE)/STARLiMS provides information on drug seizures reported to and analyzed by DEA laboratories. In 2018 and 2017, there were 16,440 and 21,953 hydrocodone reports, respectively, identified in the NFLIS, a decrease from 25,095 reports in 2016.

# Control Status:

Hydrocodone is controlled in schedule II of the Controlled Substances Act.

(Correction): Previously, it was reported that, within the 2016 NSDUH, 11.5 million people in the U.S. population, aged 12 and older, misused hydrocodone in the past year compared to 12.5 million in 2015, a significant difference decrease. Actually, this reporting was for 'any prescription pain reliever' that indicates 11.5 million people in the U.S., aged 12 and older, misused 'any prescription pain reliever' in the past year compared to 12.5 million in 2015, a significant difference decrease.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@usdoj.gov.