



FENTANYL (Trade Names: Actiq®, Fentora™, Duragesic®)

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DEA/OD/ODE

Introduction:

Fentanyl is a potent synthetic opioid. It was introduced into medical practice as an intravenous anesthetic under the trade name of Sublimaze in the 1960s.

Licit Uses:

In 2013 and 2014, there were 6.75 million and 6.64 million fentanyl prescriptions, respectively, dispensed in the U.S. (IMS Health™). Fentanyl pharmaceutical products are currently available in the dosage forms of oral transmucosal lozenges, commonly referred to as the fentanyl "lollipops" (Actiq®), effervescent buccal tablets (Fentora™), transdermal patches (Duragesic®), and injectable formulations. Oral transmucosal lozenges and effervescent buccal tablets are used for the management of breakthrough cancer pain in patients who are already receiving opioid medication for their underlying persistent pain. Transdermal patches are used in the management of chronic pain in patients who require continuous opioid analgesia. Fentanyl citrate injections are administered intravenously, intramuscularly, spinally or epidurally for potent analgesia and anesthesia. Fentanyl is frequently used in anesthetic practice for patients undergoing heart surgery or for patients with poor heart function. Because of a concern about deaths and overdoses resulting from fentanyl transdermal patches (Duragesic® and generic version), on July 15, 2005, the Food and Drug Administration issued safety warnings and reiterated the importance of strict adherence to the guidelines for the proper use of these products.

Chemistry and Pharmacology:

Fentanyl is about 100 times more potent than morphine as an analgesic. It is a μ -opioid receptor agonist with high lipid solubility and a rapid onset and short duration of effects. Fentanyl rapidly crosses the blood-brain barrier. It is similar to other μ -opioid receptor agonists (like morphine or oxycodone) in its pharmacological effects and produces analgesia, sedation, respiratory depression, nausea, and vomiting. Fentanyl appears to produce muscle rigidity with greater frequency than other opioids. Unlike some μ -opioid receptor agonists, fentanyl does not cause histamine release and has minimal depressant effects on the heart.

Illicit Uses:

Fentanyl is abused for its intense euphoric effects. Fentanyl can serve as a direct substitute for heroin in opioid dependent individuals. However, fentanyl is a very dangerous substitute for heroin because it is much more potent than heroin and results in frequent overdoses that can lead to respiratory depression and death.

Fentanyl patches are abused by removing the gel contents from the patches and then injecting or ingesting these contents. Patches have also been frozen, cut into pieces and placed under the tongue or in the cheek cavity for drug absorption through the oral mucosa. Used patches

are attractive to abusers as a large percentage of fentanyl remains in these patches even after a 3-day use. Fentanyl oral transmucosal lozenges and fentanyl injectables are also diverted and abused.

Abuse of fentanyl initially appeared in mid-1970s and has increased in recent years. There have been reports of deaths associated with abuse of fentanyl products.

According to the Drug Abuse Warning Network (DAWN), emergency department visits associated with nonmedical use of fentanyl increased from an estimated 15,947 in 2007 to an estimated 20,034 in 2011.

According to the Florida Department of Law Enforcement Medical Examiners 2013 Annual Report, fentanyl was identified in 251 deceased persons in Florida in 2012 and increased 16.3% to being identified in 292 deceased persons in 2013. Of the 292 decedents with fentanyl identified, fentanyl caused the death in 185 of those persons (63.4%), which is a 36% increase from 2012.

Illicit Distribution:

Fentanyl is diverted via pharmacy theft, fraudulent prescriptions, and illicit distribution by patients and registrants (physicians and pharmacists). Theft has also been identified at nursing homes and other long-term care facilities. According to the National Forensic Laboratory Information System (NFLIS), 668 items/exhibits were identified as fentanyl in 2012 and 942 in 2013 by federal, state and local forensic laboratories in the United States. In 2014, the number of fentanyl reports increased significantly to 3,344.

Clandestine Manufacture:

From April 2005 to March 2007, an outbreak of fentanyl overdoses and deaths occurred. The Centers for Disease Control and Prevention (CDC)/Drug Enforcement Administration (DEA) surveillance system reported 1,013 confirmed non-pharmaceutical fentanyl-related deaths. Most of these deaths occurred in Delaware, Illinois, Maryland, Michigan, Missouri, New Jersey, and Pennsylvania. Consequently, DEA immediately undertook the development of regulations to control the precursor chemicals used by the clandestine laboratories to illicitly manufacture fentanyl. In 2007, DEA published an Interim Final Rule to designate N-phenethyl-4-piperidone (NPP) – a precursor to fentanyl, as a List 1 chemical. After the control of NPP, the number of fentanyl-related deaths continually declined. DEA also completed a scheduling action of designating another chemical precursor, 4-anilino-N-phenethyl-4-piperidine (ANPP) as a schedule II immediate precursor in 2010.

Control Status:

Fentanyl is a schedule II substance under the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section, Fax 202-353-1263, telephone 202-307-7183, or Email ODE@usdoj.gov.