



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

December 2016
DEA/DC/DR/DRE

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 2015, there were 6.5 million fentanyl prescriptions dispensed in the U.S. Similarly, in the first nine months of 2016, 4.55 million fentanyl prescriptions were dispensed (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™), sublingual tablet (Abstral®), sublingual spray (Subsys™), nasal spray (Lazanda®), 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. Because of a concern about deaths and overdoses resulting from fentanyl transdermal patches (Duragesic® and generic versions), 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, nausea, vomiting, itching, and respiratory depression. 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 multi-state death reports compiled by DEA, fentanyl-related overdose deaths jumped from around 550 deaths in 2013 to over 2,000 deaths in 2014 and again in 2015.

According to the Florida Department of Law Enforcement Medical Examiners Annual Reports, fentanyl was identified in 251 deceased persons in Florida in 2012 and was significantly increased by nearly 263% to 911 in 2015. Of the identified 911 decedents in 2015, fentanyl was the cause of death in 705 of those persons (77.4%), a 418% increase from 2012.

Illicit Distribution:

Licit fentanyl is diverted via theft, fraudulent prescriptions, and illicit distribution by patients, physicians, and pharmacists. Illicitly manufactured fentanyl is chiefly responsible for the current domestic crisis. According to the National Forensic Laboratory Information System (NFLIS), which does not distinguish between pharmaceutical and illicitly manufactured fentanyl, there were nearly 5,400 reports of fentanyl for 2014 and over 14,600 in 2015 by federal, state and local forensic laboratories in the United States. In the first six months of 2016, over 13,500 fentanyl reports were identified by forensic laboratories.

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 nonpharmaceutical 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. 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. After the control of ANPP, the number of fentanyl-related deaths declined until 2013.

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.