Drug Enforcement Administration
Office of Diversion Control
Drug & Chemical Evaluation Section

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:

The dispensing of fentanyl prescriptions has slightly decreased during the past few years. In 2008, there were 7.64 million prescriptions dispensed in the U.S., 7.00 million in 2009 and 6.86 million in 2010. In the first quarter of 2011, 1.73 million fentanyl prescriptions were dispensed in the U.S. (IMS Health™). Fentanyl pharmaceuticals 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 for pain. 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 100 times more potent than morphine as an analgesic. It is a *mu* 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 mu 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 mu 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 ED), emergency department visits associated with nonmedical use of fentanyl increased from an estimated 11,211 in 2005 to an estimated 20,945 in 2009.

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) and the System to Retrieve Information from Drug Evidence (STRIDE), 569 items/exhibits were identified in 2009 and 615 in 2010 as fentanyl by federal, state and local forensic laboratories in the United States. In the first quarter of 2011, 130 fentanyl items/exhibits were identified by forensic laboratories.

Clandestine Manufacture:

From April 2005 – March 2007, an outbreak of fentanyl overdoses and deaths occurred. The Centers for Disease Control and Prevention (CDC)/Drug Enforcement Administration 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. After the control of NPP, the number of fentanyl-related deaths continually declined. DEA also completed a scheduling action of designating ANPP as a schedule II immediate precursor in 2010.

Control Status:

Fentanyl is a schedule II substance under the Controlled Substances Act. Indiana enacted legislation to add certain fentanyl derivatives to schedule I of state law.

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.