

## FENTANYL

(Trade Names: Actiq<sup>®</sup>, Fentora<sup>™</sup>, Abstral<sup>®</sup>, Subsys<sup>™</sup>, Lazanda<sup>®</sup>, Duragesic<sup>®</sup>)

### Introduction:

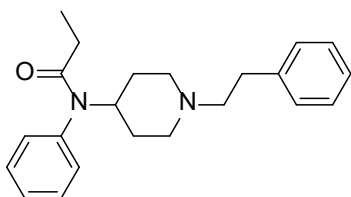
Fentanyl is a potent synthetic opioid. It was introduced into medical practice as an intravenous anesthetic under the trade name of Sublimaze<sup>®</sup> in the 1960s. Illicitly manufactured fentanyl has increasingly infiltrated the United States illicit opioid supply and has been implicated in an unprecedented number of fatal and nonfatal opioid overdoses.

### Licit Uses:

Prescription fentanyl is used to manage moderate to severe pain or as a component of anesthesia in surgeries. Fentanyl pharmaceutical products are available as oral transmucosal lozenges (“lollipops”), tablets (buccal and sublingual), sprays (sublingual and nasal), transdermal patches, and injectable formulations. According to IQVIA National Prescription Audit<sup>™</sup>, total prescriptions dispensed in the United States for fentanyl was approximately 6.0 million in 2016, 4.0 million in 2018, 2.7 million in 2020, 2.1 million in 2022, and 1.7 million in 2024.

### Chemistry:

Fentanyl [CAS: 437-38-7; *N*-phenyl-*N*-[1-(2-phenylethyl)-4-piperidinyl]propanamide] has a core scaffold of four main components: a piperidine ring, an aniline ring, an amide group, and an *N*-alkyl chain. Variations and substitutions at these four points create a vast array of fentanyl-related substances.



### Pharmacology:

Fentanyl is about 100 times more potent than morphine as an analgesic. It is a  $\mu$ -opioid receptor (MOR) agonist with a rapid onset and short duration of effects. Fentanyl rapidly crosses the blood-brain barrier. It is similar to other MOR agonists (like morphine or oxycodone) in its pharmacological effects and produces analgesia (pain relief), sedation, nausea, vomiting, itching, and respiratory depression. Fentanyl is misused for its intense euphoric effects. As with other opioids, fentanyl misuse can lead to addiction, overdose and death. Fentanyl overdose can be reversed by naloxone.

### Illicit Uses:

Licit fentanyl can be diverted and misused. However, most fentanyl on the illicit marketplace comes from clandestine manufacturing. Illicitly manufactured fentanyl is often found in powders or fake prescription pills that may be sold as fentanyl or as other opioids like heroin or oxycodone. Illicit fentanyl may be injected, smoked, or snorted. Fentanyl is often mixed with other drugs, such as heroin and cocaine. Users may take these drugs without the knowledge that they contain fentanyl, which greatly

increases the risk of poisoning. Fentanyl misuse initially appeared in mid-1970s and has increased in recent years. According to the Centers for Disease Control and Prevention (CDC) Wide-ranging ONline Data for Epidemiologic Research (WONDER) database, there were over 73,000 drug overdose deaths involving synthetic opioids (excluding methadone), which included fentanyl, in the United States in 2022. CDC's provisional estimates for drug overdose deaths indicate that the number of deaths involving synthetic opioids (excluding methadone) in the 12 month-ending December 2024 was over 75,000 in 2023 and 49,000 in 2024.

### Illicit Distribution:

According to the Drug Enforcement Administration's (DEA) 2025 National Drug Threat Assessment, Mexican Transnational Criminal Organizations have cemented their role in supplying fentanyl to the United States. In 2024, DEA seized 9,950 kilograms of fentanyl and 61.1 million fake pills, which was approximately 29% and 24% less than in 2023, respectively.

DEA's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by federal, state, and local forensic drug laboratories. NFLIS-Drug, however, does not distinguish between pharmaceutical and illicitly manufactured fentanyl. NFLIS-Drug has received over 1.2 million reports of fentanyl since 1998. The annual number of reports peaked in 2023 at over 182,000 reports before decreasing to over 152,000 reports in 2024.

### Clandestine Manufacture:

Following an outbreak of non-pharmaceutical fentanyl associated deaths in the mid-2000s, DEA immediately developed regulations to control precursor chemicals used by clandestine laboratories to illicitly manufacture fentanyl. In 2007, DEA designated *N*-phenethyl-4-piperidone (NPP) as a list I chemical, and 4-anilino-*N*-phenethylpiperidine (ANPP) as a schedule II immediate precursor in 2010. DEA subsequently completed additional regulations to add benzylfentanyl, 4-anilinopiperidine (4-AP), and 4-piperidone as list I chemicals and to control norfentanyl as a schedule II immediate precursor to fentanyl. DEA has since expanded the definition of 4-AP to include amides, carbamates, and halides.

### Control Status:

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

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email [DPE@dea.gov](mailto:DPE@dea.gov).