

**FDA warns that abuse and misuse of the nasal decongestant propylhexedrine causes serious harm**

*This includes heart and mental health problems or death*

**3-25-2021 FDA Drug Safety Communication**

**What safety concern is FDA announcing?**

The U.S. Food and Drug Administration (FDA) is warning that the abuse and misuse of the over-the-counter (OTC) nasal decongestant propylhexedrine can lead to serious harm such as heart and mental health problems. Some of these complications, which include fast or abnormal heart rhythm, high blood pressure, and paranoia, can lead to hospitalization, disability, or death. Reports of individuals abusing and misusing propylhexedrine have increased in recent years. Propylhexedrine is safe and effective when used as directed.

**What is FDA doing?**

We are requesting that all manufacturers of OTC propylhexedrine nasal decongestant inhalers consider product design changes that support its safe use. For example, modifying the product to create a physical barrier that would make tampering with the device and abusing the propylhexedrine inside more difficult. In addition, decreasing the amount of medicine the device contains could also reduce the risk of serious side effects if abused or misused. We continue to evaluate this safety issue and will determine if additional FDA actions are needed.

**What is propylhexedrine and how can it help me?**

Propylhexedrine is a nasal decongestant that is available OTC in an inhaler. It is used short term to temporarily relieve nasal congestion due to colds, hay fever, or other upper respiratory allergies. It works by reducing swelling and inflammation of the mucous membrane lining of the nose. The recommended dose for adults and children older than 6 years is two inhalations in each nostril not more often than every 2 hours. Do not use it for more than 3 days at a time. Prolonged use may cause nasal congestion to recur or worsen. Currently, propylhexedrine is only marketed under the brand name Bensedrex.

**What should consumers do?**

Consumers should only use propylhexedrine according to the directions on the [Drug Facts label](#). Do not use it in ways other than by inhalation because doing so can cause serious harm, such as heart and mental health problems. Some of these problems can lead to death. Seek medical attention immediately by calling 911 or [poison control](#) at 1-800-222-1222 for anyone using propylhexedrine who experiences the following:

- Severe anxiety or agitation, confusion, hallucinations, or paranoia
- Rapid heartbeat or abnormal heart rhythm
- Chest pain or tightness

Ask a pharmacist or your health care professional if you have any questions about propylhexedrine, how to use it, or whether a medicine you are taking may interact with it. Always tell your health care professionals about all medicines you are taking, including OTC medicines.

### **What should health care professionals do?**

Health care professionals should be aware that some individuals are abusing or misusing propylhexedrine, particularly using it by routes other than nasal inhalation, which can result in serious cardiac and psychiatric adverse events or death. In the event of a suspected overdose, attempt to determine whether a patient used propylhexedrine alone or with other substances. There is no specific reversal agent in cases of acute intoxication, so symptomatic and supportive care should be provided. (See Additional Information for Health Care Professionals for more information).

### **What did FDA find?**

We reviewed cases from U.S. poison control center calls, case reports submitted to FDA, the medical literature, and emergency department visits.<sup>\*1-5</sup> In the 20 years between January 1, 2000, and December 31, 2019, U.S. poison control centers documented 460 cases of propylhexedrine abuse (415 cases) or misuse (45 cases). Annual cases increased from 11 cases in 2011 to 74 cases in 2019, with abuse cases making up the majority of this increase. Most of the cases involved abuse or misuse of propylhexedrine alone without other substances. The most commonly reported side effects included rapid heart rate, agitation, high blood pressure, chest pain, tremor, hallucinations, delusions, confusion, nausea, and vomiting. Among the 460 cases, 21 had severe outcomes (adverse effects that were life-threatening), with 13 resulting in intensive care admissions.

Fifty-three cases of propylhexedrine abuse and misuse were voluntarily reported to FDA in the several decades from January 1969 through January 31, 2020.<sup>†</sup> An additional seven cases of serious adverse events related to propylhexedrine abuse were found from emergency department visits<sup>\*</sup> in the 3 years between January 1, 2016, and December 31, 2018. There are likely additional cases that we have not identified. Some harms occurred several hours after abuse. Of these 60 cases, 23 experienced life-threatening adverse events or hospitalization, and nine died. Most of the deaths resulted from propylhexedrine abuse in combination with other substances.

We also reviewed 49 case reports and an observational study published in the medical literature.<sup>6-25</sup> These publications showed similar findings compared to the cases identified from poison control calls and emergency department visits and the cases reported to FDA.

<sup>\*</sup>[National Electronic Injury Surveillance System-Cooperative Adverse Event Surveillance Project \(NEISS-CADES\)](#).

<sup>†</sup>The cases were reported to the [FDA Adverse Event Reporting System \(FAERS\) database](#).

### **How do I report side effects from propylhexedrine?**

To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving propylhexedrine or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

### **How can I get new safety information on medicines I’m prescribing or taking?**

You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

## Facts about propylhexedrine

- Propylhexedrine is an over-the-counter (OTC) inhaled nasal decongestant that is used to temporarily relieve nasal congestion due to colds, hay fever, or other upper respiratory allergies.
- Propylhexedrine works by reducing swelling and inflammation of the mucous membrane lining of the nose.
- The recommended dosage of propylhexedrine for adults and children older than 6 years is two inhalations in each nostril not more than every 2 hours. For children younger than 6, consult a health care professional before using. Do not exceed the recommended dosage.
- Do not use propylhexedrine for more than 3 days. Prolonged use may cause nasal congestion to recur or worsen.
- Use propylhexedrine only as directed.
- Propylhexedrine is marketed under the brand name Benzedrex.
- Common side effects of propylhexedrine may include temporary discomfort such as burning, stinging, sneezing, or increasing nasal discharge.

## Additional Information for Consumers

- FDA is warning that abuse or misuse of propylhexedrine, an over-the-counter (OTC) nasal decongestant, can lead to serious heart and mental health problems. These include fast or abnormal heart rhythms, high blood pressure, heart attack, heart failure, agitation, delusions, paranoia, hallucinations, and death even after a few hours of abuse or misuse.
- Seek medical attention immediately by calling 911 or [poison control](#) at 1-800-222-1222 for anyone using propylhexedrine who experiences the following:
  - Severe anxiety or agitation, confusion, hallucinations, or paranoia
  - Rapid heartbeat or abnormal heart rhythm
  - Chest pain or tightness
- Only use propylhexedrine according to the directions listed on the [Drug Facts label](#).
- Do not exceed recommended dosage or use for more than 3 days. Prolonged use may cause nasal congestion to recur or worsen.
- Do not share inhalers, as use of the product by more than one person may spread infection.
- Ask a pharmacist or your health care professional if you have any questions about propylhexedrine, how to use it, or whether another medicine you are taking may interact with it.
- Always tell your health care professionals about all the medicines you are taking, including OTC medicines such as propylhexedrine, vitamins, and other supplements. It is helpful to keep a list of all your current medicines in your wallet or another location where it is easily retrieved. You can fill out and print a copy of [My Medicine Record](#).
- To help FDA track safety issues with medicines, report side effects from propylhexedrine or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

## **Additional Information for Health Care Professionals**

- FDA is warning that some individuals are abusing or misusing the over-the-counter (OTC) nasal decongestant propylhexedrine, including by ingesting or injecting it which can result in serious cardiac and psychiatric adverse events and possibly death.
- In the event of a suspected overdose, attempt to determine whether a patient used propylhexedrine alone or with other substances.
- There is no specific reversal agent in cases of acute propylhexedrine intoxication, so management is symptomatic and supportive.
- Major issues that may have to be managed in the context of intoxication include severe agitation, tachycardia, hypertension, myocardial infarction, hyperthermia, stroke, bowel obstruction, pulmonary hypertension, and seizures. Long-term use can also lead to lung damage, arrhythmias, and cardiac damage.
- Counsel consumers not to use more than the recommended dose of propylhexedrine listed on the [Drug Facts label](#) or to use it in ways other than intended, as doing so can result in serious adverse events.
- To help FDA track safety issues with medicines, report adverse events involving propylhexedrine or other medicines to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of this page.
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

## **Data Summary**

In response to increasing reports of abuse and misuse of propylhexedrine, we reviewed several sources of data. These included calls to U.S. poison control centers, case reports submitted to FDA and published in the medical literature, cases presenting to U.S. emergency departments participating in NEISS-CADES, and an observational study.

Using data from the American Association of Poison Control Centers-National Poison Data System (AAPCC-NPDS), we identified 460 cases involving propylhexedrine abuse or misuse between January 1, 2000, and December 31, 2019. Poison control centers define misuse as the intentional, improper use for a reason other than self-harm or for achieving a psychotropic effect. Annual case numbers increased after 2011, with a sharp rise starting in 2015. They involved individuals 12 to 68 years, and most were males. Most cases (n=345, 75 percent) involved abuse or misuse of propylhexedrine alone. Ingestion was the most common route of exposure, followed by inhalation and injection. When more than one substance was involved (n=115, 25 percent), frequent co-exposures included cold and cough medicines, alcohol, antidepressants, opioids, sedatives/hypnotics/antipsychotics, and a variety of stimulants and street drugs. The most frequent clinical effects were tachycardia, agitation, hypertension, mydriasis, nausea, chest pain, tremor, hallucinations/delusions, diaphoresis, confusion, and vomiting. Frequently recommended and/or performed therapies for single-substance propylhexedrine abuse or misuse included benzodiazepines, intravenous fluids, sedation, charcoal, and oxygen. Among the 460

calls, 21 had adverse effects that were life-threatening, 13 of which resulted in intensive care unit admissions.

A search of the [FDA Adverse Event Reporting System \(FAERS\) database](#) from January 1969 through January 31, 2020, and the [National Electronic Injury Surveillance System-Cooperative Adverse Event Surveillance Project \(NEISS-CADES\)](#)<sup>1-5</sup> from January 1, 2016, through December 31, 2018, identified 60 U.S. cases, of serious adverse events related to propylhexedrine abuse, misuse, dependence, or withdrawal, 53 from FAERS and 7 from NEISS-CADES. Among the 60 cases, there were 57 cases of abuse, 18 cases of dependence, three cases of withdrawal, and one case of misuse. The majority of these 60 cases involved males (n=55, 92 percent) and adults 18 to 65 years (n=40, 66 percent). Among the 53 FAERS cases, oral ingestion (n=19, 36 percent) and intravenous (IV) injection (n=13, 25 percent) were the most common routes of exposure, and other routes included intranasal inhalation (n=3, 6 percent) and smoking (n=1, 2 percent). The amount abused ranged from part of one inhaler to the content of 10 inhalers per day, and the duration of abuse ranged from 3 days to 18 years. Each inhaler contains 250 mg of propylhexedrine and each inhalation contains 0.4-0.5 mg. Twenty-three of the 60 patients experienced life-threatening adverse events or hospitalization, and nine patients died. Among the nine deaths, propylhexedrine abuse in combination with other substances contributed to the cause of death in six cases, and propylhexedrine abuse alone was the cause of one death. For one of the two remaining deaths, the cause of death was not reported. The other reported the cause of death was multiple injuries sustained in a motor vehicle accident; however, the individual had a postmortem propylhexedrine blood concentration in the toxic range. The routes of exposure were reported in only four of the death cases and were IV (n=3) and oral (n=1). The amount and duration of abuse was not reported for the majority of death cases. A blood propylhexedrine level was reported for seven of the nine death cases, with only one explicitly stating the level was within the lethal range.

We also reviewed 49 case reports and an observational study published in the medical literature.<sup>6-25</sup> Most of these described young men abusing propylhexedrine and there were 18 deaths. The most common adverse events experienced in older literature reports included ischemic limb injury, cranial nerve dysfunction, psychosis, cardiomyopathy, adrenergic overstimulation, and anxiety or agitation. This is consistent with the frequently reported parenteral route of use. More recent literature was primarily associated with psychosis, adrenergic stimulation, and agitation. This is consistent with the frequently reported oral route of use. Also, consistent with FDA's analysis of poison control center call data, a retrospective study<sup>9</sup> described single-substance propylhexedrine abuse cases documented by U.S. Poison Control Centers from 2007-2016. The study identified 283 calls, which increased annually from 2007 (n=16) to 2016 (n=58). Most (66 percent) of calls involved males. The majority of adverse effects were sympathomimetic and no deaths were noted, although deaths are expected to be under-ascertained in poison control center data.

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**Related Information**

[OTC Drug Facts Label](#)

[The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)

[Think It Through: Managing the Benefits and Risks of Medicines](#)