OPVEE
(nalmefene) NASAL SPRAY 2.7mg

DURING AN OPIOID OVERDOSE,

EVERY SECOND MATTERS[1,2]

OPVEE® is for emergency treatment of known or suspected overdose induced by natural or synthetic opioids in patients 12 years and older, as manifested by respiratory and/or central nervous system depression. OPVEE® is for immediate administration as emergency therapy in settings where opioids may be present and is not a substitute for emergency medical care.[3]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: Do not use in patients who are allergic to nalmefene or any of the other ingredients.

WARNINGS AND PRECAUTIONS

Risk of Recurrent Respiratory and Central Nervous System Depression: While the duration of action of nalmefene is as long as most opioids, a recurrence of slowed breathing (respiratory depression) is possible after treatment with OPVEE®. Watch patients and give repeat doses of OPVEE® using a new device, as necessary, while awaiting emergency medical assistance.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

As the opioid epidemic evolves, so must we

1970

OVERDOSE DEATHS RISE[4]

About 7100 drug overdose deaths are reported in the US.

1971

NALOXONE (IV/IM) IS APPROVED[5]

The US Food and Drug Administration (FDA) approves naloxone hydrochloride for intravenous (IV) and intramuscular (IM) administrations to treat opioid overdose.

1999

WAVE 1 BEGINS[6-9]

The opioid epidemic began in 1999 with increased prescribing of opioids. Between 1999 and 2010, rates of prescriptions and overdose deaths tripled.

Leading the wave was OxyContin®, marketed as "less addictive" than some of its predecessors when it hit the market in 1995.

⚠ **8050 deaths** are attributed to opioid overdose this year.

2001

THE FDA FOCUSES ON REDUCING OPIOID PRESCRIPTION ABUSE[10]

The FDA begins its educational and legal effort to curtail prescription opioid abuse.

2009

DEATHS CONTINUE TO RISE[9]

⚠ **20,422** opioid overdose deaths this year:

48%
Natural and semisynthetic opioids, including some prescription opioids like OxyContin®

23%
Methadone

16%
Heroin

14%
Synthetic opioids other than methadone

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists: Improvement in respiratory depression caused by medicines such as buprenorphine and pentazocine may not be complete. Repeat doses of OPVEE® may be required.

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2010

WAVE 2 BEGINS[6,7,11]

The second wave of the opioid epidemic begins with an increase in heroin-related overdoses.

More than **80%** of heroin users report misusing prescription opioids before using heroin.

2013

WAVE 3 BEGINS[7,12–14]

An increase in deaths related to synthetic opioids, like fentanyl, marks a new period in the opioid epidemic.

Synthetic opioids are detected circulating in the heroin drug supply. They are cost-effective for drug traffickers because they can be produced in illegal labs and made to look like a variety of medications and other drugs.

2014

THE DEA SEES AN INCREASE IN FENTANYL SEIZURES[15]

The US Drug Enforcement Administration (DEA) sees more than 4500 illicit fentanyl seizures– a drastic increase from 618 seizures in 2012.

Even a very small dose –2 mg– can result in a life-threatening overdose.[14]

Image: NH State Police Forensics Laboratory.[16]

2015

DEATHS CONTINUE TO RISE[9,12]

Overdose deaths from opioids reach over 30,000–more than quadruple the rate from 1999.

Of these,

⚠ **9580**

deaths were caused by synthetic opioids, representing almost 35% of all opioid overdose deaths.

According to drug seizure data from the DEA National Forensics Laboratory Information Service, fentanyl reports increased

⇧ **1400%**

between 2013 and 2015.

2015

NARCAN® (naloxone HCl) NASAL SPRAY IS APPROVED[17,18]

The FDA approves NARCAN® to treat opioid overdose.

2017

THE NIH CALLS FOR BETTER[19]

The National Institutes of Health (NIH) resolves to work with private partners to develop stronger, longer-acting formulations of antagonists, including naloxone, to counteract the very high-potency synthetic opioids that are now claiming thousands of lives each year.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may cause symptoms of opioid withdrawal like body aches, fever, sweating, runny nose, sneezing, goose bumps, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, and rapid heart rate. Some patients may become aggressive when an opioid overdose is treated.

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2017

A PUBLIC HEALTH EMERGENCY IS DECLARED[20–22]

The US government declares the opioid epidemic a public health emergency.

2020

THE COVID-19 PANDEMIC EXACERBATES THE SYNTHETIC OPIOID CRISIS[23–28]

When the nation entered lockdown in early 2020 for COVID-19, resources were diverted, many people could not reach treatment centers, access to medications for opioid use disorder disappeared, and access to illicit drugs increased over social media.

⚠ **71%**
of adolescent overdose deaths
involved illicit fentanyls and other synthetics.

2021

OVER 106,000 PEOPLE DIE FROM A DRUG OVERDOSE[26,29–31]

More than 80,400, or 75%, of overall deaths are caused by opioids. Of the opioid overdose deaths, 88% involved synthetic opioids.

Synthetic opioids are a leading cause of death in people aged
18 to 45.

Overdose deaths involving synthetic opioids increased by nearly
⇧ 637%
in 6 years, 2015-2021.

2022

PROVISIONAL DATA FROM 2022 ESTIMATES THAT SYNTHETIC OPIOIDS, LIKE FENTANYL, CAUSE ABOUT 90% OF ALL OPIOID OVERDOSE DEATHS[14,23,32,*]

Illicit fentanyl is primarily manufactured in illegal foreign labs and smuggled into the US, where it spreads through the illicit drug supply.

6 out of 10 pills
seized by the DEA contain a potentially deadly amount of fentanyl.

*2022 data based on predicted provisional drug overdose death counts from the Centers for Disease Control and Prevention (CDC), last updated May 7, 2023.

2023

OPVEE® (nalmefene) NASAL SPRAY IS APPROVED[3]

OPVEE® is the first and only nasal opioid overdose rescue medicine specifically indicated for synthetic opioids, like fentanyl, as well as nonsynthetic opioids.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Abrupt postoperative reversal of opioid depression may result in adverse cardiovascular (CV) effects. These events have primarily occurred in patients with preexisting CV disorders or who received other drugs with similar adverse CV effects. Monitor these patients closely in an appropriate healthcare setting.

In newborns, opioid withdrawal may be life-threatening if not recognized and properly treated and may also include convulsions, excessive crying, and hyperactive reflexes. Monitor for symptoms of opioid withdrawal.

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OPVEE
(nalmefene) NASAL SPRAY 2.7mg

The opioid epidemic has changed... and continues to evolve

Recent rises in overdose deaths have been fueled by fentanyl and other synthetic opioids[9,23]

BY 2015:

Nearly 30%

of all opioid overdose deaths were caused by synthetic opioids like fentanyl[9]

IN 2022:

About 90%

of all opioid overdose deaths are caused by synthetic opioids like fentanyl[23,*]

*Data based on 2022 predicted provisional drug overdose death counts from the CDC, last updated May 7, 2023.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Opioid Overdose from Attempts to Overcome the Blockade: Taking large or repeated doses of opioids, such as heroin or prescription pain pills to overcome blockade, may lead to opioid intoxication and death.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

Synthetic opioids pose a triple threat

They're fast[33]

They're long-lasting[2,34]

They're strong[26]

Synthetic opioids can

INDUCE OVERDOSE IN MINUTES[33]

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS: Most common adverse reactions (incidence at least 2%) are nasal discomfort, headache, nausea, dizziness, hot flush, vomiting, anxiety, fatigue, nasal congestion, throat irritation, pain in the nose, decreased appetite, changes in sense of taste, skin redness, and increased sweating.

To report a pregnancy or side effects associated with taking OPVEE® or any safety related information, product complaint, request for medical information, or product query, please contact PatientSafetyNA@indivior.com or 1-877-782-6966. You are encouraged to report negative side effects of drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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OPVEE
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Synthetic opioids pose a triple threat

They're fast[33]

They're long-lasting[2,34]

They're strong[26]

Fentanyl has a quick effect but

STAYS IN THE BODY A LONG TIME[2,34]

Reoverdose can occur when the rescue medicine loses effect while opioids are still in the system, requiring additional doses of rescue medicine.[34]

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WARNINGS AND PRECAUTIONS

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Synthetic opioids pose a triple threat

They're fast[33]

They're long-lasting[2,34]

They're strong[26]

Fentanyl is up to

50x STRONGER THAN HEROIN AND 100x STRONGER THAN MORPHINE[26]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists: Improvement in respiratory depression caused by medicines such as buprenorphine and pentazocine may not be complete. Repeat doses of OPVEE® may be required.

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OPVEE
(nalmefene) NASAL SPRAY 2.7mg

Opioid relative strength compared with morphine

ILLUSTRATIVE

Morphine milligram equivalents[26,34-36]

*Relative strength reflects 1 mg to 20 mg of methadone per day; note that relative strength is increased at higher doses.[36]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may cause symptoms of opioid withdrawal like body aches, fever, sweating, runny nose, sneezing, goose bumps, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, and rapid heart rate. Some patients may become aggressive when an opioid overdose is treated.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

Overdose reversal is a race against time

Time is critical when reversing an opioid overdose. Rapid restoration of normal breathing may help minimize long-term damage or death.[34,37,38]

Overdoses have an even broader impact when we look beyond overdose deaths

For each opioid-induced fatality, it was estimated that there are between

6.4 and **8.4**

nonfatal overdoses, which takes a toll on overdose victims and society[2]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Abrupt postoperative reversal of opioid depression may result in adverse cardiovascular (CV) effects. These events have primarily occurred in patients with preexisting CV disorders or who received other drugs with similar adverse CV effects. Monitor these patients closely in an appropriate healthcare setting.

In newborns, opioid withdrawal may be life-threatening if not recognized and properly treated and may also include convulsions, excessive crying, and hyperactive reflexes. Monitor for symptoms of opioid withdrawal.

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Synthetic opioids pose a more dangerous challenge[23]

We could benefit from additional overdose rescue medicine options[39–42]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Opioid Overdose from Attempts to Overcome the Blockade: Taking large or repeated doses of opioids, such as heroin or prescription pain pills to overcome blockade, may lead to opioid intoxication and death.

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OPVEE®
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OPVEE® (nalmefene) Nasal Spray pharmacodynamic* and pharmacokinetic† studies[3]

*Pharmacodynamic studies evaluate what actions a drug might have on the body.[43]

†Pharmacokinetic studies assess how the body interacts with a drug from its administration to the time it is excreted from the body. This includes absorption, distribution, metabolism, and excretion.[44]

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS: Most common adverse reactions (incidence at least 2%) are nasal discomfort, headache, nausea, dizziness, hot flush, vomiting, anxiety, fatigue, nasal congestion, throat irritation, pain in the nose, decreased appetite, changes in sense of taste, skin redness, and increased sweating.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

Pharmacodynamic study trial design overview

A 2-part, open-label, experimental model evaluating pharmacodynamic effects of OPVEE® (nalmefene) Nasal Spray compared with intranasal (IN) naloxone to reverse remifentanil-induced suppression of carbon dioxide (CO_2)–induced increases in minute ventilation (MV)[3,45,46]

Part 1[46]

Healthy volunteers (n=15)

Primary Objective:
To determine the relationship between remifentanil dose and suppression of CO_2-induced increases in MV

Part 2[45,46]

*Hypercapnic gas mixture was given to elevate MV and was continued for the duration of the study, excluding mask holidays.[45]

†Following 10 minutes of hypercapnic gas mixture, remifentanil (IV bolus [0.5 µg/kg] + infusion [0.175 µg/kg/min]) was administered for 15 minutes prior to test agents and continued for the duration of the study.[3,45]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: Do not use in patients who are allergic to nalmefene or any of the other ingredients.

WARNINGS AND PRECAUTIONS

Risk of Recurrent Respiratory and Central Nervous System Depression: While the duration of action of nalmefene is as long as most opioids, a recurrence of slowed breathing (respiratory depression) is possible after treatment with OPVEE®. Watch patients and give repeat doses of OPVEE® using a new device, as necessary, while awaiting emergency medical assistance.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

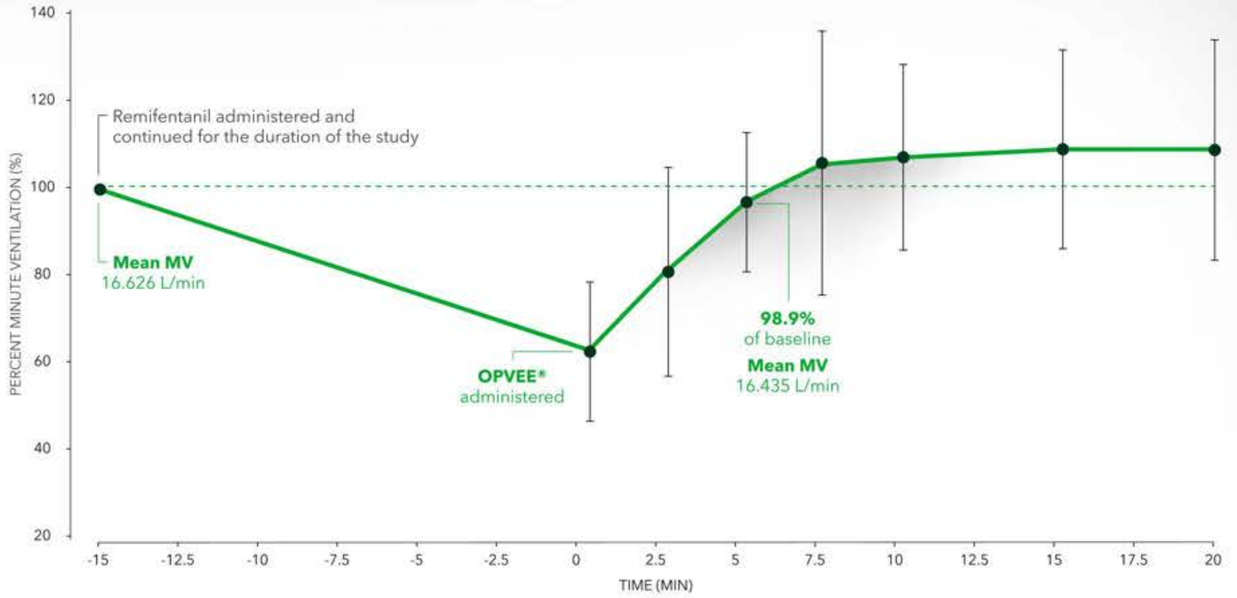
OPVEE® (nalmefene) Nasal Spray reversed remifentanil–induced respiratory depression by an average of 98.9% at 5 minutes[3,45]

The clinical relevance of these findings to a real-world overdose is unknown.

At 5 minutes, the mean increase in MV was 5.745 L/min (98.9% of pre-remifentanil levels).[3,45]

Full recovery of respiratory drive was noted as early as 5 minutes (between 5 and 15 minutes) after OPVEE® administration.[3]

PERCENTAGE RECOVERY OF RESPIRATORY DRIVE IN HEALTHY ADULT VOLUNTEERS TREATED WITH OPVEE®[3,45,46]



Values are represented as mean +/− standard deviation. The dashed line represents the baseline MV, artificially increased due to CO_2 administration, prior to remifentanil administration.[3]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists: Improvement in respiratory depression caused by medicines such as buprenorphine and pentazocine may not be complete. Repeat doses of OPVEE® may be required.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

Two PK studies were conducted to assess OPVEE® (nalmefene) Nasal Spray[3]

PK-001

In 68 healthy adult subjects, the relative bioavailability and other pharmacokinetic parameters of one 2.7-mg spray of OPVEE® in one nostril was compared with a single dose of nalmefene 1.0 mg administered as an intramuscular injection.

PK-002

In 24 healthy adult subjects, one 2.7-mg spray of OPVEE® in one nostril was compared with two 2.7-mg sprays of OPVEE® in one nostril and one 2.7-mg spray of OPVEE® in each nostril to compare the pharmacokinetics following 3 different dosing regimens.

The mean half-life* of OPVEE® in both studies was 11.4 hours.[3]

*The length of time needed for the concentration of a drug to decrease to half of its starting concentration in the body.[47]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may cause symptoms of opioid withdrawal like body aches, fever, sweating, runny nose, sneezing, goose bumps, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, and rapid heart rate. Some patients may become aggressive when an opioid overdose is treated.

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Two PK studies were conducted to assess OPVEE® (nalmefene) Nasal Spray[3]

	C_{max}*	T_{max}§	Half-life‖	Number of subjects
Data from study PK-001				
OPVEE® (intranasal)	10.4 ng/mL (62.6)†	15 mins (0.0833-2.0 hrs)	11.4 hours (20.8)	68
Nalmefene (1 mg intramuscular)	1.5 ng/mL (59.4)†	19.8 mins (0.117-18.0 hrs)	10.6 hours (18.5)	68
Data from study PK-002				
Single dose (2.7 mg)	9.75 ng/mL (49.4)‡	16 mins (0.167-2.03 hrs)	11.4 hours (22.0)	24
One dose in each nostril (5.4 mg)	18.9 ng/mL (88.0)‡	15 mins (0.117-3.0 hrs)	11.3 hours (16.6)	24
Two doses in same nostril (5.4 mg)	16.1 ng/mL (62.9)‡	15 mins (0.117-2.03 hrs)	11.3 hours (16.5)	24

*C_{max} is the highest concentration of the drug in the blood.[48]

†C_{max} presented as arithmetic mean (coefficient of variation percentage).

‡C_{max} presented as geometric mean (coefficient of variation percentage).

§T_{max} presented as median (range). T_{max} is the time to peak drug concentration (C_{max}).[49]

‖Half-life ($t_{½}$) presented as arithmetic mean (coefficient of variation percentage).

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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Most common adverse reactions in 3 separate studies in healthy adult volunteers[3]

Study type	Participants	Most common adverse reactions
Pharmacokinetic (PK-001)	66 healthy adult volunteers	Nasal discomfort and dizziness
Pharmacokinetic (PK-002)	24 healthy adult volunteers	Rhinalgia, nasal congestion, nasal discomfort, and nausea
Pharmacodynamic (OOD-001)	61 healthy adult volunteers	Headache, nausea, hot flush, and dizziness

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Opioid Overdose from Attempts to Overcome the Blockade: Taking large or repeated doses of opioids, such as heroin or prescription pain pills to overcome blockade, may lead to opioid intoxication and death.

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

Relative Frequencies of Treatment-Related Common Adverse Events That Occurred in Greater Than 2% of Healthy Adult Volunteers[3]

System Organ Class Preferred Term	OPVEE® 2.7 mg PD Study, n (%) N=61	OPVEE® 2.7 mg PK Studies, n (%) N=89
Respiratory, thoracic, and mediastinal disorders		
Nasal discomfort	5 (8.2%)	38 (42.7%)
Nasal congestion	2 (3.3%)	4 (4.5%)
Throat irritation	3 (4.9%)	3 (3.4%)
Rhinalgia	1 (1.6%)	3 (3.4%)
Dyspnea	2 (3.3%)	0
Oropharyngeal pain	2 (3.3%)	0
Nervous system disorders		
Headache	34 (55.7%)	6 (6.7%)
Dizziness	9 (14.8%)	5 (5.6%)
Dysgeusia	2 (3.3%)	1 (1.1%)
Paresthesia	2 (3.3%)	0
Gastrointestinal disorders		
Nausea	22 (36.1%)	3 (3.4%)
Vomiting	7 (11.5%)	2 (2.2%)

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS: Most common adverse reactions (incidence at least 2%) are nasal discomfort, headache, nausea, dizziness, hot flush, vomiting, anxiety, fatigue, nasal congestion, throat irritation, pain in the nose, decreased appetite, changes in sense of taste, skin redness, and increased sweating.

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Relative Frequencies of Treatment-Related Common Adverse Events That Occurred in Greater Than 2% of Healthy Adult Volunteers[3]

System Organ Class Preferred Term	OPVEE® 2.7 mg PD Study, n (%) N=61	OPVEE® 2.7 mg PK Studies, n (%) N=89
Vascular disorders		
Hot flush	12 (19.7%)	0
Psychiatric disorders		
Anxiety	7 (11.5%)	0
Agitation	2 (3.3%)	0
Claustrophobia	2 (3.3%)	0
General disorders and administration site conditions		
Fatigue	3 (4.9%)	3 (3.4%)
Chills	2 (3.3%)	0
Skin and subcutaneous tissue disorders		
Erythema	0	3 (3.4%)
Hyperhidrosis	3 (6.6%)	0
Metabolism and nutrition disorders		
Decreased appetite	2 (3.3%)	1 (1.1%)

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OPVEE (nalmefene) NASAL SPRAY 2.7mg

OPVEE® (nalmefene) Nasal Spray is the first and only nasal opioid rescue medicine specifically indicated for synthetic opioids, like fentanyl[3]

OPVEE® is...

***FAST*[3]** | ***LONG-LASTING*[3]**

In an experimental model in healthy adult subjects, OPVEE® reversed remifentanil-induced respiratory depression by an average of

98.9% at 5 minutes.[3]

Full recovery of respiratory drive was noted as early as 5 minutes (between 5 and 15 minutes).[3]

The clinical relevance of these findings to a real-world overdose is unknown.

If the patient does not respond or responds and then relapses into respiratory depression, readminister OPVEE® using a new nasal spray, in the nose, every 2 to 5 minutes.[3]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists: Improvement in respiratory depression caused by medicines such as buprenorphine and pentazocine may not be complete. Repeat doses of OPVEE® may be required.

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OPVEE® (nalmefene) Nasal Spray is the first and only nasal opioid rescue medicine specifically indicated for synthetic opioids, like fentanyl[3]

OPVEE® is...

FAST[3] | ***LONG-LASTING***[3]

In the pharmacokinetic studies, the mean half-life of OPVEE® was **11.4 hours**.[3]

The half-life of fentanyl varies greatly due to many factors, including the route of administration, dose, and formulation. The half-life of illicit fentanyl has not been studied; however, the half-life of fentanyl (when used as anesthesia) has been shown to be about 7.5 hours.[2,50,51]

The clinical relevance of these findings to a real-world overdose is unknown.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may cause symptoms of opioid withdrawal like body aches, fever, sweating, runny nose, sneezing, goose bumps, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, and rapid heart rate. Some patients may become aggressive when an opioid overdose is treated.

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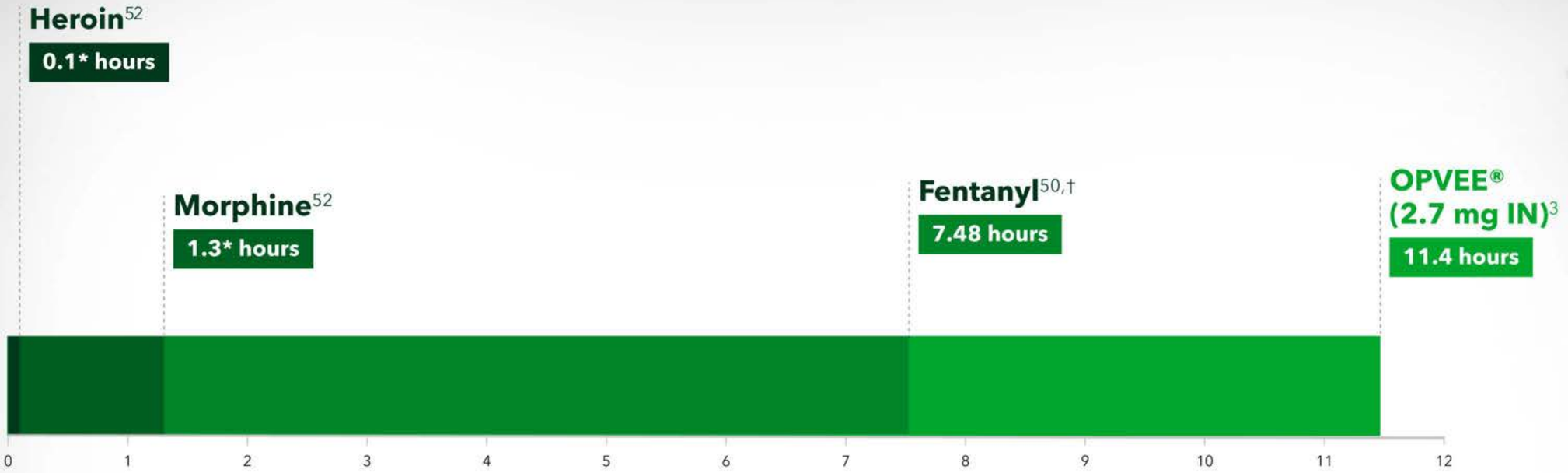
The mean half-life of OPVEE® (nalmefene) Nasal Spray in healthy adult subjects was 11.4 hours[3]



*Lower range is shown for heroin (0.1-.025) and morphine (1.3-6.7).[52]

†The half-life of fentanyl varies greatly due to many factors, including the route of administration, dose, and formulation. The half-life of illicit fentanyl has not been studied; however, the half-life of fentanyl when used as anesthesia has been shown to be about 7.5 hours.[2,50,51]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Abrupt postoperative reversal of opioid depression may result in adverse cardiovascular (CV) effects. These events have primarily occurred in patients with preexisting CV disorders or who received other drugs with similar adverse CV effects. Monitor these patients closely in an appropriate healthcare setting.

In newborns, opioid withdrawal may be life-threatening if not recognized and properly treated and may also include convulsions, excessive crying, and hyperactive reflexes. Monitor for symptoms of opioid withdrawal.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

OPVEE
(nalmefene) NASAL SPRAY 2.7mg

With the cause of an opioid overdose often unknown, it's important to be prepared[2,34,37]

OPVEE® (nalmefene) Nasal Spray is fast[3]

OPVEE® is long-lasting[3]

Not actual size.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Opioid Overdose from Attempts to Overcome the Blockade: Taking large or repeated doses of opioids, such as heroin or prescription pain pills to overcome blockade, may lead to opioid intoxication and death.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

OPVEE® (nalmefene) NASAL SPRAY 2.7mg

OPVEE® (nalmefene) Nasal Spray has a 28-month shelf life[53,*]

STORE OPVEE®	SHORT-TERM EXCURSIONS PERMITTED
BETWEEN	BETWEEN
59 °F and **77 °F**[3]	**39 °F** and **104 °F**[3]
(15 °C and 25 °C)	(4 °C and 40 °C)

Do not freeze. Protect from light.[3]

Store OPVEE® in the blister and cartons provided.

Do not open individual blister packs or test nasal spray devices before use.

Each unit-dose nasal spray device sprays one (1) time and cannot be re-used.

*From date of manufacture.

Not actual size.

2 devices per box[3]

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS: Most common adverse reactions (incidence at least 2%) are nasal discomfort, headache, nausea, dizziness, hot flush, vomiting, anxiety, fatigue, nasal congestion, throat irritation, pain in the nose, decreased appetite, changes in sense of taste, skin redness, and increased sweating.

To report a pregnancy or side effects associated with taking OPVEE® or any safety related information, product complaint, request for medical information, or product query, please contact PatientSafetyNA@indivior.com or 1-877-782-6966. You are encouraged to report negative side effects of drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

OPVEE (nalmefene) NASAL SPRAY 2.7mg

Choose OPVEE® (nalmefene) Nasal Spray today

Take action now–OPVEE® is available to order. Visit OPVEEdirect.com.

Qualifying direct purchasers, such as departments of health, emergency medical services, law enforcement, schools/universities, and community organizations, may be eligible to purchase OPVEE® at the public interest price, which is $37.50/dose or $75/2-pack.*

For other orders, the Wholesale Acquisition Cost (WAC)† of OPVEE® is $49/dose or $98/2-pack.*

Not actual size.

OPVEEdirect.com

*As of October 2, 2023.

†The WAC price represents the manufacturer's published catalog or list price for a drug product to wholesalers as reported to third-party drug price publishers. WAC does not represent actual transaction prices and does not include discounts, rebates, or reductions in price. Pricing information listed above does not imply safety or efficacy of the product, and no comparisons should be made.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: Do not use in patients who are allergic to nalmefene or any of the other ingredients.

WARNINGS AND PRECAUTIONS

Risk of Recurrent Respiratory and Central Nervous System Depression: While the duration of action of nalmefene is as long as most opioids, a recurrence of slowed breathing (respiratory depression) is possible after treatment with OPVEE®. Watch patients and give repeat doses of OPVEE® using a new device, as necessary, while awaiting emergency medical assistance.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

OPVEE (nalmefene) NASAL SPRAY 2.7mg

OPVEE® (nalmefene) Nasal Spray—a rescue medicine option for today's opioid epidemic

OPVEE® is FDA approved[3]

OPVEE® is the first and only nasal opioid overdose rescue medicine specifically indicated for synthetic opioids, like fentanyl, as well as nonsynthetic opioids.

OPVEE® is fast* and has a long half-life.

*In an experimental model of remifentanil-induced respiratory depression in healthy adult subjects.

The safety of OPVEE® is supported by safety and pharmacokinetic studies in healthy adult subjects[3]

OPVEE.com

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists: Improvement in respiratory depression caused by medicines such as buprenorphine and pentazocine may not be complete. Repeat doses of OPVEE® may be required.

Please see additional Important Safety Information throughout.
See full Prescribing Information and more information about OPVEE® at www.OPVEE.com.

OPVEE (nalmefene) NASAL SPRAY 2.7mg

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