SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Naloxon actrevo 3.6 mg nasal spray, solution in single-dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each nasal spray container delivers naloxone hydrochloride dihydrate equivalent to 3.6 mg naloxone.

Excipients with known effect:
Benzalkonium chloride 0.12 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, solution in single-dose container (nasal spray).
Clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<Product name> is intended for immediate administration as emergency therapy for known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression in both non-medical and healthcare settings.

<Product name> is indicated in adults and adolescents aged 14 years and over.

<Product name> is not a substitute for emergency medical care.

4.2 Posology and method of administration

Posology

Adults and adolescents aged 14 years and over

The recommended dose is 3.6 mg administered into one nostril (one nasal spray).

In some cases, further doses may be necessary. The appropriate maximum dose of <Product name> is situation specific. If the patient does not respond, the second dose should be administered after 2-3 minutes. If the patient responds to the first administration but then relapses again into respiratory depression, the second dose should be administered immediately. Further doses (if available) should be administered in alternate nostrils and the patient should be monitored whilst awaiting arrival of the emergency services. Emergency services may administer further doses according to local guidelines.

Paediatric population

The safety and efficacy of <Product name> in children below 14 years has not been established. No data are available.

Elderly

No adjustment of dose is required.

Method of administration

Nasal use.

<Product name> should be administered as soon as possible to avoid damage to the central nervous system or death.

<Product name> contains only one dose and therefore it must not be primed or tested prior to administration. Do not reuse the device after administration.

Detailed instructions on how to use <Product name> are provided in the Package Leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Instructing patients / users on the proper use of <Product name>

<Product name> is intended to be administered as a part of a resuscitation intervention in suspected overdose casualties, where opioid drugs may be involved or suspected, likely in a non-medical setting. Therefore, the healthcare professionals should take appropriate steps to ensure that the patient and/or any other person who might be in a position to administer <Product name> thoroughly understands the indications, the proper use of <Product name> and the importance of seeking medical assistance.

The healthcare professionals should describe the symptoms which allow presumptive diagnosis of central nervous system (CNS) / respiratory depression, the indication and the instructions for use with the patient and / or person who might be in a position to administer this product to a patient experiencing a known or suspected opioid overdose event. This should be performed in accordance with the educational guidance for <Product name>.

<Product name> is not a substitute for emergency medical care.

<Product name> contains one single dose of naloxone. Patients and care takers should therefore receive proper instructions on how to use the device, and that it should not be primed or tested prior to administration and that it cannot be reused after administration of the dose (see section 4.2)

Monitoring of the patient for a response

Patients who respond satisfactorily to <Product name> must be closely monitored. The effect of some opioids can be longer than the effect of naloxone, which could lead to reoccurrence of respiratory depression and therefore further doses of naloxone may be required.

The importance of seeking medical assistance

Patients should be kept under observation until qualified healthcare personnel are on site. The duration of action of most opioids may exceed that of <Product name> resulting in a return of respiratory and/or central nervous system depression after an initial improvement in symptoms. Therefore, it is necessary to seek emergency medical assistance immediately and to keep the patient under continued surveillance.

Opioid withdrawal syndrome

Receiving <Product name> can lead to a rapid reversal of the opioid effect which can cause an acute withdrawal syndrome (see section 4.8). Patients who are receiving opioids for the relief of chronic pain may experience pain and opioid withdrawal symptoms when <Product name> is administered.

Effectiveness of naloxone

Naloxone is not effective against CNS- or respiratory depression caused by non-opioid drugs.

Reversal of respiratory depression caused by partial agonists or mixed agonist/antagonists, such as buprenorphine and pentazocine, may be incomplete and may require higher doses of naloxone or repeated administrations. If an incomplete response occurs, respiration should be mechanically assisted.

Intranasal absorption and efficacy of naloxone can be altered in patients with damaged nasal mucosa and septal defects.

Paediatric population

Opioid withdrawal may be life-threatening in neonates if not recognised and properly treated and may include the following signs and symptoms: convulsions, excessive crying and hyperactive reflexes.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

<Product name> contains benzalkonium chloride
This medicine contains 0.012 mg benzalkonium chloride in each single-dose container which is equivalent to 0.12 mg/ml.
Benzalkonium chloride may cause irritation or swelling inside the nose, especially if used for a long time.

4.5 Interaction with other medicinal products and other forms of interaction

Naloxone elicits a pharmacological response due to the interaction with opioids and opioid agonists. When administered to opioid dependent subjects, naloxone can cause acute withdrawal symptoms in some individuals. Hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described, more typically when naloxone is used post-operatively (see sections 4.4 and 4.8).

Administration of <Product name> may decrease the analgesic effects of opioids used primarily to provide pain relief, due to its antagonist properties (see section 4.4).

When administering naloxone to patients who have received buprenorphine as an analgesic, complete analgesia may be restored. It is thought that this effect is a result of the arch-shaped dose-response curve of buprenorphine with decreasing analgesia in the event of high doses. However, reversal of respiratory depression caused by buprenorphine is limited.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of naloxone in pregnant women. Studies in animals have shown reproductive toxicity only at maternally toxic doses (see section 5.3). The potential risk for humans is unknown. <Product name> should not be used during pregnancy unless the clinical condition of the woman requires treatment with naloxone.

In pregnant women who have been treated with <Product name>, the fetus should be monitored for signs of distress.

In opioid dependent pregnant women, naloxone administration can cause withdrawal symptoms in newborn infants (see section 4.4).

Breast-feeding

It is unknown whether naloxone is excreted in human breast milk and it has not been established whether infants who are breast-fed are affected by naloxone. However, as naloxone is practically not orally bioavailable its potential to affect a breast-fed infant is negligible. Caution should be exercised when naloxone is administered to a breast-feeding mother but there is no need to discontinue breast-feeding. Breast-fed babies from mothers who have been treated with <Product name> should be monitored to check for sedation or irritability.

Fertility

No clinical data on effects of naloxone on fertility are available, however data from rat studies (see section 5.3) indicate no effects.

4.7 Effects on ability to drive and use machines

Patients who have received naloxone to reverse the effects of opioids should be warned not to drive, to operate machinery or to engage in other activities demanding physical or mental exertion for at least 24 hours, since the effect of the opioids may return.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reaction (AR) seen with naloxone administration is nausea (frequency very common). Typical opioid withdrawal syndrome is expected with naloxone which may be caused by the abrupt withdrawal of opioid in persons physically dependent on them.

Tabulated list of adverse reactions

The following adverse reactions have been reported with <Product name> and/or other naloxone-containing medicinal products during clinical studies and post marketing experience. ARs are listed below by system organ class and frequency.

Frequency categories are assigned to those adverse reactions considered to be at least possibly causally related to naloxone and are defined as very common (≥ 1/10); common (≥ 1/100 < 1/10); uncommon (≥ 1/1 000 < 1/100); rare (≥ 1/10 000 < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

Immune system disorders	Very rare	Hypersensitivity, Anaphylactic shock
Nervous system disorders	Common	Dizziness, Headache
	Uncommon	Tremor
Cardiac disorders	Common	Tachycardia
	Uncommon	Arrhythmia, Bradycardia
	Very rare	Cardiac fibrillation, Cardiac arrest
Vascular disorders	Common	Hypotension, Hypertension
	Uncommon	Hyperventilation

Respiratory, thoracic and mediastinal disorders	Very rare	Pulmonary oedema
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting
	Uncommon	Diarrhoea, Dry mouth
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis
	Very rare	Erythema multiforme
General disorders and administration site conditions	Uncommon	Drug withdrawal syndrome (in patients dependent on opioids)

Description of selected adverse reactions

Drug withdrawal syndrome

Signs and symptoms of drug withdrawal syndrome include restlessness, irritability, hyperaesthesia, nausea, vomiting, gastrointestinal pain, muscle spasms, dysphoria, insomnia, anxiety, hyperhidrosis, piloerection, tachycardia, increased blood pressure, yawning, pyrexia. Behavioural changes including violent behaviour, nervousness and excitement may also be observed.

Vascular disorders

In reports on intravenous/intramuscular naloxone: hypotension, hypertension, cardiac arrhythmia (including ventricular tachycardia and fibrillation) and pulmonary oedema have occurred with the postoperative use of naloxone. Adverse cardiovascular effects have occurred more frequently in postoperative patients with a pre-existing cardiovascular disease or in those receiving other medicinal products that produce similar adverse cardiovascular effects.

Paediatric population

<Product name> is intended for use in adolescents 14 years and over. Frequency, type and severity of adverse reactions in adolescents are expected to be the same as in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In view of the indication and the broad therapeutic margin, overdose is not to be expected.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidotes, ATC code: V03AB15

Mechanism of action and pharmacodynamic effects

Naloxone, a semisynthetic morphine derivative (N-allyl-nor-oxymorphone), is a specific opioid antagonist that acts competitively at opioid receptors. It reveals very high affinity for the opioid

receptor sites and therefore displaces both opioid agonists and partial antagonists. Naloxone does not possess the "agonistic" or morphine-like properties characteristic of other opioid antagonists. In the absence of opioids or agonistic effects of other opioid antagonists, it exhibits essentially no pharmacologic activity. Naloxone has not been shown to produce tolerance or cause physical or mental dependence.

As the duration of action of some opioid agonists may be longer than that of naloxone, the effects of the opioid agonist may return as the effects of naloxone disappear. This may necessitate repeat doses of naloxone – though the need for repeat naloxone doses is dependent on the quantity, type and route of administration of the opioid agonist that is being treated.

Paediatric population

No data are available.

5.2 Pharmacokinetic properties

Absorption

The absorption after intranasal administration of naloxone was rapid, with peak plasma concentration reached after approximately 0.3 hours (18 minutes). The bioavailability of the substance was approximately 50%.

Distribution

The volume of distribution of naloxone is 200L. Plasma protein binding is approximately 50%, mainly to albumin.The transfer of naloxone across the blood–brain barrier involves both diffusion and a saturable transporter. Naloxone crosses the placental barrier and rapidly appears in fetal blood. Following IV naloxone there was rapid transfer to the fetus and therapeutic plasma concentrations could be expected in 1 or 2 min.

Biotransformation

Naloxone is rapidly metabolized in the liver and metabolites excreted in the urine. It undergoes extensive hepatic metabolism mainly by glucuronide conjugation. The principal metabolites are naloxone-3-glucuronide, 6-beta-naloxol and its glucuronide.

Elimination

Approximately 25% to 40% of naloxone is eliminated as metabolites in urine within 6 hours post-administration, with up to 70% excreted within 72 hours. Following intranasal administration, the plasma half-life of naloxone hydrochloride ranges from 1.85 to 2.08 hours in healthy adults, exceeding that of intramuscular injection (1.24 hours).

Paediatric population

No robust data are available.

5.3 Preclinical safety data

Genotoxicity and carcinogenicity

Naloxone was weakly positive in Ames mutagenicity tests but was negative in the in vitro Chinese hamster V79 cell HGPRT mutagenicity assay and the in vivo rat bone marrow chromosome aberration study. Overall, the weight of evidence indicates that naloxone poses minimal, if any, risk for human genotoxicity and carcinogenicity.

Reproductive and developmental toxicity

Naloxone had no effect on fertility and reproduction in animal models and humans. In peri-post natal rat studies, naloxone produced increased pup deaths in the immediate post-partum period at the high doses that also caused significant maternal toxicity in rats (e.g. bodyweight loss, convulsions). Naloxone showed potential of altering neurobehavioral development in rats. The clinical relevance of this finding is unclear, as the effect was only observed at doses over 1 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride solution 50%
Disodium edetate
Sodium chloride
Hydrochloric acid (for pH-adjustment)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

Do not freeze. If accidentally frozen, the nasal spray will not function. Allow the nasal spray to thaw at least one hour; do not use if the contents are still frozen or not completely thawed. Freezing does not affect the shelf life of the product.

6.5 Nature and contents of container

The immediate container consists of a type I glass vial with siliconised chlorobutyl stopper containing 0.1 ml solution. The secondary packaging (actuator) is comprised of polypropylene and stainless steel. Each pack contains two single-dose nasal sprays.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

4 Mar 2026 <{MM/YYYY}>