Part VI: Summary of the risk management plan

Summary of risk management plan for Ventizolve (naloxone)

This is a summary of the risk management plan (RMP) for Ventizolve. The RMP details important risks of Ventizolve, how these risks can be minimised, and how more information will be obtained about Ventizolve's risks and uncertainties (missing information).

Ventizolve's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ventizolve should be used.

I. The medicine and what it is used for

Ventizolve is authorised for emergency therapy for known or suspected opioid overdose (see SmPC for the full indication). It contains naloxone as the active substance and it is given by nasal spray.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Ventizolve, together with measures to minimise such risks and the proposed studies for learning more about Ventizolves's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Ventizolve, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Ventizolve is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Ventizolve are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Ventizolve. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Opioid withdrawal syndrome • Recurrence of respiratory depression
Important potential risks	• Lack of efficacy due to medication error
Missing information	• Use if nasal mucosa is affected

II.B Summary of important risks

Important identified risk: Opioid withdrawal syndrome	
Evidence for linking the risk to the medicine	Opioids are known to be addictive and tolerance and withdrawal symptoms can occur with long term use. Abrupt withdrawal of opioids from persons with a dependency may cause withdrawal syndrome. Withdrawal symptoms may also follow the use of an opioid antagonist such as naloxone in opioid-dependent persons.
Risk factors and risk groups	Opioid addicts and patients on opioid substitution therapy. Neonatal abstinence syndrome may occur in the offspring of opioid-dependent mothers and these infants can suffer withdrawal symptoms at birth.
Risk minimisation measures	Routine risk minimisation measures: • *SmPC section 4.4, 4.5 and 4.8* • *PIL section 2 and 4* Additional risk minimisation measures: • *Guidance Document for Healthcare Professionals* • *Patient Information Card* • *Quick Start Guide* • *Training Video*
Additional pharmacovigilance activities	Additional pharmacovigilance activities:

	• *A non-interventional PAES to investigate the efficacy and safety of Ventizolve in real-life settings*

Important identified risk: Recurrence of respiratory depression	
Evidence for linking the risk to the medicine	Opioids are known to cause respiratory depression. Treatment with naloxone can temporarily counteract the symptoms of respiratory depression. Further medical assistance from health care professionals is required in order to prevent recurrence of respiratory depression.
Risk factors and risk groups	Opioid addicts and patients on opioid substitution therapy. Respiratory depression might occur in neonates of mothers that were treated with methadone chronically during pregnancy.
Risk minimisation measures	Routine risk minimisation measures: • *SmPC section 4.2 and 4.4* • *PIL section 2* Additional risk minimisation measures: • *Guidance Document for Healthcare Professionals* • *Patient Information Card* • *Quick Start Guide* • *Training Video*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • *A non-interventional PAES to investigate the efficacy and safety of Ventizolve in real-life settings*

Important potential risk: Lack of efficacy due to medication error	
Evidence for linking the risk to the medicine	In order to be effective, the medicinal product must be correctly administered, while also seeking medical assistance from health care professionals. First aid should be given. Failure to do these actions simultaneously will hinder the patient's recovery from the opioid overdose.
Risk factors and risk groups	Non-healthcare professionals.
Risk minimisation measures	Routine risk minimisation measures: • *SmPC section 4.2 and 4.4*

	• *PIL section 2 and 3* Additional risk minimisation measures: • *Guidance Document for Healthcare Professionals* • *Patient Information Card* • *Quick Start Guide* • *Training Video*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • *A non-interventional PAES to investigate the efficacy and safety of Ventizolve in real-life settings*

Missing information: Use if nasal mucosa is affected	
Risk minimisation measures	Routine risk minimisation measures: • *SmPC section 4.4* • *PIL section 2 and 3* Additional risk minimisation measures: *None*

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorisation:

A non-interventional PAES to investigate the efficacy and safety of Ventizolve in real-life settings

Purpose of the study:

The primary objective is to determine the frequency of patients that regain consciousness from a known or suspected opioid overdose following administration of Ventizolve by lay persons in a non-medical setting.

The secondary objectives are to determine the frequency of:

- patients needing a second dose of Ventizolve
- patients experiencing withdrawal symptoms post administration
- medication errors
- whether the Patient Information Card steps were followed (was the emergency number called?)

- reported overdose deaths in the investigated population by the prescribing physician.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Ventizolve.