Part VI: Summary of the risk management plan

Summary of risk management plan for Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride)

This is a summary of the risk management plan (RMP) for Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride). The RMP details important risks of Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride), how these risks can be minimised, and how more information will be obtained about Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride)'s risks and uncertainties (missing information).

Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride)'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride) should be used.

Important new concerns or changes to the current ones will be included in updates Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride)'s RMP.

I. The medicine and what it is used for

Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride) is authorised

for the emergency treatment of opioid overdose in adults (see SmPC for the full indication). It contains naloxone hydrochloride as the active substance, and it is given as intranasal spray.

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

Important risks of Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride), together with measures to minimise such risks and the proposed studies for learning more about Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride)'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 Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride), 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.

II.A List of important risks and missing information

Important risks of Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride) 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 Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride).
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	Reoccurrence of respiratory depression Opioid withdrawal syndrome
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 risks

Reoccurrence of respiratory depression	
Evidence for linking the risk to the medicine	The medicine is intended for use in emergency situations, where an overdose with opioids is suspected. The recognition of signs and symptoms of such overdose can be challenging and even after a correct administration of naloxone, respiratory depression can re-occur and the patient starts to show signs and symptoms of an overdose again. In an emergency situation, there is often no time for the patient/caregiver to read the patient leaflet in the box and action is required to be immediate. Therefore, it is important for the patients/caregivers and emergency medical personnel to be well trained on the signs and symptoms of opioid overdose, the action of naloxone, potential complications and the correct use of the device.

Risk factors and risk groups	Patients that use opioids (use of illicit drugs, eg. heroin, or abuse of prescription pills, eg. oxycodone).
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4: need for patient monitoring PIL sections 2 and 3: instructions for use Pack size: One device per pack Additional risk minimisation measures: Quick Start Guide and Training Video Healthcare Professional Guide
Opioid withdrawal syndrome	
Evidence for linking the risk to the medicine	Naloxone displaces the opioid from opioid receptors and reverses the opioid's action, which, in case of an overdose, results in respiratory depression and loss of consciousness. In patients that are addicted to opioids, this displacement can cause the appearance of withdrawal symptoms, similarly as if they did not take the drug. Most commonly these symptoms include agitation, aggression, nausea, vomiting, tremor and sweating. The patient can become aggressive towards the rescuer, and this is something the rescuers need to be aware of.
Risk factors and risk groups	Patients that use opioids (use of illicit drugs, eg. heroin, or abuse of prescription pills, eg. oxycodone).
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 warning on appearance of withdrawal symptoms PIL sections 2 and 3: instructions for use Pack size: One device per pack Additional risk minimisation measures: Quick Start Guide and Training Video Healthcare Professional Guide
Lack of efficacy due to medication error	

Evidence for linking the risk to the medicine	The medicine is intended for use in emergency situations, where an overdose with opioids is suspected. The recognition of signs and symptoms of such overdose can be challenging since the patient is usually unconscious and unable to tell what happened. This is why it is very important for rescuers to recognize the signs and symptoms of an opioid overdose to: (1) avoid unnecessarily administer naloxone to a person that is unconscious for other reasons, (2) immediately administer naloxone to a patient where it is plausibly suspected that has overdosed on opioids, (3) avoid any delays in the administration of naloxone, if indicated, and (4) correctly administer the product with the delivery device.
Risk factors and risk groups	Patients that use opioids (use of illicit drugs, eg. heroin, or abuse of prescription pills, eg. oxycodone).
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.1 and 4.2 indications and posology PIL sections 2 and 3: instructions for use Pack size: One device per pack Additional risk minimisation measures: Quick Start Guide and Training Video Healthcare Professional Guide
Use if nasal mucosa is affected	
Evidence for linking the risk to the medicine	Naloxone in its intranasal form, is absorbed via the mucosa in the nose. If the mucosa is damaged due to concomitant use of illicit drugs, such as cocaine, metamphetamine or other opioids (eg. heroin), the absorption of naloxone can be unpredictable. Therefore, administration of intranasal naloxone to such patients can result in too little or too much naloxone effect.
Risk factors and risk groups	Patients that use intranasal (snorted) drugs such as cocaine, metamphetamine and/or other opiates (e.g. heroine).
Risk minimisation measures	Routine risk minimisation measures:

	SmPC sections 4. Warnings and precautioning on use on pregnancy and during breastfeeding PIL sections 2 and 3: instructions for use Pack size: One device per pack Additional risk minimisation measures: None proposed

II.C Post-authorisation development plan

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

There are no studies which are conditions of the marketing authorisation or specific obligation of Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride).

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

There are no other studies planned for Naloxone 3.6 mg nasal spray, solution in single-dose container (naloxone hydrochloride).