VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Opioids are potent respiratory depressants, and overdose is a leading cause of death among people who use them. Worldwide, an estimated 69000 people die from opioid overdose each year. The number of opioid overdoses has risen in recent years, in part due to the increased use of opioids in the management of chronic pain. In 2010, an estimated 16651 people died from an overdose of prescription opioids in the USA. Opioid overdose is treatable with naloxone, an opioid antagonist which rapidly reverses the effects of opioids (WHO, Nov 2014).

People dependent on opioids are the group most likely to experience an overdose. The incidence of fatal opioid overdose among opioid-dependent individuals is estimated at 0.65 per 100 person years. Non-fatal opioid overdoses are several times more common than fatal ones.
Death in opioid-overdose can be averted by emergency basic life support resuscitation and/or the timely administration of an opioid antagonist such as naloxone (WHO, Nov 2014).

VI.2.2 Summary of treatment benefits

The effect of continuous naloxone infusion on morphine-induced respiratory depression during morphine anaesthesia was evaluated in 46 postoperative patients using IV bolus followed by a six hour infusion and the results showed that it provided appropriate reversal of morphine anaesthesia (Maxwell LG et al, 2005).

Naloxone is effective in diagnosing physical dependence in opiate addicts. IV naloxone administration can be used for the diagnosis of opioid tolerance or acute opioid overdosage (naloxone challenge test). If signs or symptoms of withdrawal appear, the test is positive and no additional naloxone should be administered.

The use of naloxone to reverse opioid-induced respiratory depression in neonates was studied following the use of meperidine during labor. Respiratory rate was significantly increased in neonates receiving naloxone as compared to a control group (Evans JM, 1976).

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Precipitation of acute opioid withdrawal effects	In patients with opioid dependence; naloxone administration can cause withdrawal syndrome.	Medical supervision is necessary.
Cardiovascular adverse effects	This medicine should be used with precaution if the patient suffers from serious cardiovascular diseases.	Medical supervision is necessary.
Delayed respiratory depression due to short half-life of naloxone	Naloxone has a relatively short duration of action.	Medical supervision is necessary.
Hypersensitivity reactions/anaphylactic shock	All medicines can cause side effects, including allergic reactions to the active substance.	Evaluation of each patient's medical history before beginning of treatment is highly advisable and medical supervision is necessary to be able to stop in time.
Lack of effect in mixed overdose (concomitant overdose of non-opioid drugs)	Naloxone hydrochloride is not effective in central depression caused by agents other than opioids.	Medical supervision is necessary.

Important potential risks

Not applicable.

Missing information

Not applicable.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the

form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for X can be found in Annex 2 of this RMP.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable

List of studies in post authorisation development plan

Not applicable

Studies which are a condition of the marketing authorisation

Not applicable

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable