Morphine Orion

Date: 19-12-2016, Version 1.3

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

This medicine is indicated for relief of severe pain.

Acute pain is a major problem after surgery and trauma. Although acute pain management has improved, still more than 50% of patients have severe to intolerable pain after surgery and trauma.[1]

Chronic moderate to severe pain afflicts one in five adults. Surveys of households reveal that over a third have chronic pain sufferers in Europe (36%) and in the USA (42%). Non-cancer chronic pain burdens especially three kind of groups of conditions: osteo- and rheumatoid arthritis (40%), operations and injuries (25%), and spine problems (20%). 19% of the general adult population of Europe have had moderate or severe chronic pain for a median of 7 years. One in five of those with chronic pain had suffered for over 20 years.[1]

Pain is the first symptom of cancer in 20–50% of all cancer patients, and 75–90% of advanced or terminal cancer patients must cope with chronic pain syndromes related to chemotherapy, failed treatment, and/or tumour progression.[2]

Pain prevalence increases with age, and is higher in females and in those with physically strenuous work or less education. Racial or ethnic minority status predicts substandard access to appropriate pain assessment and treatment in the United States and Western Europe.[1]

VI.2.2 Summary of treatment benefits

Management of pain is an important element in any therapeutic intervention. Failure to adequately manage pain can have important negative consequences on physiological function, causing reduced mobility, muscle wasting, joint stiffening and decalcification, and can contribute to deleterious changes in the psychological state (depression, helplessness syndromes, anxiety).[3]

Morphine, like other opioids, acts directly on the central nervous system to relieve pain and is still considered the gold standard in the treatment of severe acute and chronic pain.[3]

VI.2.3 Unknowns relating to treatment benefits

There is insufficient evidence to recommend routine use of opioids (e.g. morphine) to reduce pain in newborn babies (full-term or preterm) with breathing difficulties on breathing machines.[4] Recent studies have shown insufficient effect of morphine in preterm newborn babies on breathing machines and possible negative long term effects of therapy in these patients.[5]

Disparities are known to exist in the prescription of opioid analgesics among racial and ethnic groups in the management of postoperative, cancer, and emergency department pain in patients across all ages, including children.[6]

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Abnormally slow and shallow breathing (Respiratory depression)	Respiratory depression is known side effect of morphine, which may affect up to 1 from 100 patients. Morphine may cause breathing impairment by acting on the breathing centre in brain. The respiratory depressive effect is dose dependent and rarely constitutes any clinical problem. The risk is higher when therapeutic dose is exceeded or patient already has breathing disorders.	Respiratory depression may be prevented by close dose monitoring and avoiding of use in high risk groups: Morphine Orion should not be used in conditions with much mucous in the airways or in reduced breathability.
Hepatic impairment (Liver disease)	In case of acute liver disease a rapid deterioration of liver function is observed when morphine is used. There are many factors leading to the development of this condition, like intoxications (drug overdose, food toxins, alcohol and chemicals), adverse drug reactions, viral infections etc. The early sign of acute liver disease is jaundice. Patients with acute liver disease may show signs of overdose including coma due to weak morphine elimination in liver.	Caution should be exercised and the dosage initially reduced in morphine treatment in patients with hepatic impairment. Morphine Orion must not be used in acute liver disease.
Drug interactions	If Morphine Orion is taken simultaneously with certain other medicines, the effect of treatment may be affected. The effect of morphine is enhanced by (causing e.g. impaired respiratory function) in concomitant use with tranquilizers and sleeping pills, medicines to treat depression (eg. MAO inhibitors) and alcohol. The effect of Morphine Orion decreases when co-administered with some other analgesics (eg. buprenorphine). During	Morphine Orion should not be used in combination with tranquilizers, sleeping pills and alcohol. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. During concomitant use with certain medicines dose adjustment and close monitoring for any signs of central nervous system or respiratory depression may be considered.

Risk	What is known	Preventability
	concomitant therapy with rifampicin, the dose of Morphine Orion may need to be increased.	
Drug dependency	Repeated use is associated with the development of habituation. It is characterized by an overwhelming need to keep taking the drug that is caused by the physical requirement for the drug in order to avoid withdrawal symptoms and behavioural features including drug craving, compulsive use, and strong tendency to relapse after withdrawal. Although this is less of a problem with legitimate therapeutic use, particularly for the treatment of severe cancer pain, dependence may develop rapidly when morphine is regularly abused.	Drug dispensing should be controlled, considering precautions when prescribing this medication, monitoring the size and frequency of the dose, and the duration of drug use.
Renal impairment	Impaired renal function can affect the elimination on morphine and cause accumulation of morphine in the body and thus overdose or adverse reactions.	Morphine dosage in patients with renal impairmet should be assessed and reduced individually.
Overdose	If Morphine Orion is used in certain patient groups like patients with reduced liver or kidney function, elderly, infants or young children, morphine may accumulate in the body thus increasing the risk of overdose.	Morphine should be used with caution and the dosage assessed individually in patients with hepatic or renal impairment, elderly, infants and young children.
Use in pregnancy and lactation	If Morphine Orion is used long-term or regularly during pregnancy the newborn baby may experience newly born abstinence symptoms such as seizures, irritability and vomiting. Increased mortality have also been observed. The use of morphine during labour may cause reduced respiratory function in the newborn baby. Morphine is excreted into breast milk.	Morphine Orion should not be used during pregnancy, especially not during the third trimester of pregnancy, unless the benefit for the mother outweighs the potential risk to the foetus. Morphine Orion should not be used when breast-feeding.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
-	

Missing information

Risk	What is known
Newborn babies	Recent studies have shown insufficient effect of morphine in preterm newborn babies on breathing machines and possible negative long term effects of therapy in these patients.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) 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 this medicinal product can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable.