

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Abuse of heroin or other opioids is often a serious problem for those who suffer from it, their relatives, and the society. The problem is typically a result of a combination of social, psychological, and biological reasons. There is a strong scientific support that drug assisted rehabilitation have had positive effects. The most common treatment is with methadone but also other substances may be used. Side-effects may occur and the treatment will usually be very long lasting. Few patients succeed complete abstinence in the sense that they also stop taking the medication. Used under less controlled circumstances, methadone is easy to overdose and it has a high abuse potential. A criterion for treatment with Metadon Nordic Drugs oral solution is that the patient is participating in a "methadone program" with medication-assisted rehabilitation of drug addicts in accordance with guidelines provided by the health authorities.

VI.2.2 Summary of treatment benefits

The benefits of methadone treatment in opioid addicts in terms of reduced intake of illicit drugs and thereby improved physical and mental health, reduced independence on illegal income, reduced risk of contracting transmittable diseases like HIV and hepatitis, reduced risk of death at young age, promotion of psychosocial adjustment, reduced family disruption and increased productivity by far override the risks of methadone treatment in heroin addicts.

VI.2.3 Unknowns relating to treatment benefits

Not applicable, as there are no unknowns relating to treatment benefits, as methadone has been used for opioid dependency for decades.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Cardiac disease	<p>QT prolongation is a condition that depends on an electrical disorder in the heart muscle cells. This, combined with other factors, can create conditions for rapid abnormal heart rhythms that can lead to dizziness, fainting, or rarely sudden death. Cases of QT prolongation and Torsade de Pointes (TdP) have been reported during treatment with methadone, especially in high doses.</p>	<p>Due to the risk of QT prolongation and TdP, methadone should be administered with care to patients potentially at risk of developing QT prolongation and ECG monitoring should be considered in patients with known risk of developing QT prolongation, especially in women.</p>
Respiratory depression	<p>Respiratory depression is a well-known risk deemed to be the most serious side-effect during treatment with methadone</p> <p>Individual differences in the ability to metabolize methadone, along with imperfect cross-tolerance, may heighten risks of respiratory depression during the methadone induction period.</p> <p>The dose must be individually adjusted to each patient and usually dosed once daily. If more frequent, there is a risk for accumulation and overdosing which may cause respiratory depression.</p> <p>Concomitant treatment with certain drugs as well as misuse of other drugs or alcohol during treatment with methadone may cause respiratory depression.</p>	<p>Due to individual differences in the ability to metabolize methadone, along with imperfect cross-tolerance, the dose must be individually adjusted to each patient and assessment for potential contraindications, (eg. COPD, asthma) and interactions must be done.</p>
Use in patients with hepatic impairment	<p>Chronic viral hepatitis is common in drug addicts as are other factors that may accelerate the progression of liver disease.</p> <p>In patients with liver cirrhosis the metabolism is delayed wherefore there is a risk for higher plasma levels of methadone.</p> <p>Caution is advised if methadone must be used in patients with hepatic</p>	<p>The dose must be individually adjusted to each patient and should be administered at a lower dose than recommended. The clinical response of the patients should be used to guide further dosage.</p>

Risk	What is known	Preventability
	impairment.	
Use in patients with renal impairment	There is a potential for decreased elimination of methadone in patients with renal impairment.	The dose must be individually adjusted to each patient and should be administered at a lower initial dose than recommended. The clinical response of the patients should be used to guide further dosage.
Outcome of Drug interactions	When concomitant treatment with other medicinal products there is a potential for interactions causing high or low plasma levels of methadone, as well as interactions that exhibits synergism that may increase the side-effects of methadone.	Drugs administered concomitantly with methadone should, as for all medications, be evaluated for any potential interaction. The dose must be individually adjusted to each patient and the patients must be carefully monitored.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use in pregnancy and lactation	Prenatal exposure to methadone associated with a neonatal abstinence syndrome (NAS) characterized by central nervous system hyperirritability and autonomic nervous system dysfunction, which often requires medication and extended hospitalization. If the mothers are in the methadone programme the neonates are in better condition than if the mothers are abusing heroin.

Missing information

Risk	What is known
None	Not applicable.

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 minimising them. The SmPC and the Package leaflet for Metadon Nordic Drugs oral solution can be found in Annex 2.

Safety concern in lay terms (medical term)

VI.2.6 *Planned post authorisation development plan*

Not applicable since no studies are in a post authorisation plan..

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. This is the first version of the RMP.