Suspension of Methadone oral solutions containing high molecular weight povidone

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Information on methadone containing povidone products

- Methadone is a synthetic opiod used in rehabilitation programs to prevent or reduce withdrawal symptoms in patients dependent on opioids such as heroin. Methadone is also used in the treatment of severe pain. Oral methadone medicines are available as solutions or tablets.
- Some formulations of methadone contain the additive povidone. Povidone is used in oral solutions (taken by mouth) as a suspending and dispersing agent, or as a binding agent for tablets. There are numerous solutions authorised in Malta that do not contain povidone.
- Different types of povidone are available, which vary in their molecular weight (a measure of the size of the molecule). The povidone contained in oral methadone solutions has a high molecular weight (known as K90), while the povidone used in methadone tablets has a low molecular weight (e.g. K25 and K30).
- Oral methadone solutions are intended for oral use only, however some patients may misuse oral methadone formulations by taking it in a different way. A number of oral solutions containing methadone are authorised for use in Malta.

Product Name	Pharmaceutical Form	Authorisation Number	Contains Povidone
Methadone 1mg/ml Oral Solution B.P. - Sugar Free	ORAL SOLUTION	AA055/02301	no
Methadone Hydrochloride Oral Solution 1mg/1ml Sugar Free	ORAL SOLUTION	MA091/00101	no
Methadone Mixture DTF Sugar-Free	ORAL SOLUTION	MA050/01101	no
Methadone Martindale Pharma Oral Solution 2mg/ml oral solution	ORAL SOLUTION	MA105/00501	yes
Pinadone Methadone DTF 1mg/ml Oral Solution	ORAL SOLUTION	MA143/00301	no
Pinadone Methadone DTF 1mg/ml Oral Solution Sugar Free	ORAL SOLUTION	MA143/00302	no

Information from the EMA on the safety concern

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- Medicines Authority Circular **P11/2014** described the start of review of the safety of oral methadone medicines containing povidone by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), following reports of serious adverse events in former or current drug abusers in Norway, which led to the suspension of methadone oral solutions containing povidone K90 from the Norwegian market.
- The PRAC assessed the available safety data on the risks associated with the misuse by injection of methadone medicines containing povidone from post-marketing reports and the published literature, and a group of experts (which included pathologists and addiction experts) was consulted for advice.
- The PRAC concluded that risk minimisation measures would be insufficient to mitigate the risks with oral solutions containing high molecular weight povidone, and therefore recommended that these products should be suspended and should be appropriately reformulated before being reintroduced on the European market.
- For methadone tablets containing povidone of lower molecular weight (e.g. K25 and K30), the available data showed that this kind of povidone is excreted from the body and does not accumulate inside the cells as high molecular weight povidone does. Therefore, these products will remain on the market and changes will be made to the product information (SmPC and package leaflet) to reinforce the message that tablets are for oral administration only and must not be taken in any other way.

As the PRAC recommendation was endorsed by consensus by the CMDh, it will now be implemented in all EU Member States where these medicines are marketed including Malta, according to an agreed timetable.

For more information please visit **www.ema.europa.eu**

Information on the suspension and recall of Methadone Martindale

The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)[1] has endorsed the recommendation of the Pharmacovigilance Risk Assessment Committee (PRAC)[1] to suspend the marketing authorisation of methadone oral solutions containing high molecular weight povidone.

These products will remain suspended until they have been reformulated. Additionally, the CMDh agreed that methadone tablets that contain low molecular weight povidone should remain on the market with changes to the product information.

In Malta;

A number of oral solutions containing methadone are authorised for use in Malta.

[1] The CMDh and PRAC are medicines regulatory bodies representing the European Union (EU) Member States.

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Information to Healthcare Professionals

- The risk of harm is reduced with low molecular weight povidone since it is expected to be readily excreted and not to accumulate inside cells. Methadone tablets as well as solutions not containing povidone will remain on the market. For tablets that contain povidone, their product information will be amended to reinforce the recommendation that these medicines are for oral administration only and must not be used in any other way.

Information to Patients

- Patients are directed to continue taking their prescribed medicine in line with their doctor's recommendations.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on methadone products. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicine Authority website for product safety updates as these are issued on an ongoing basis.

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