Summary of the risk management plan for Zofran™ (ondansetron)

This is a summary of the risk management plan (RMP) for Zofran™. The RMP details important risks of Zofran, how these risks can be minimized and how more information will be obtained about Zofran's risks and uncertainties (missing information).

Zofran's Product information (PI) gives essential information to health care professionals and patients on how Zofran should be used.

Important new concerns or changes to the current ones will be included in updates of Zofran's RMP.

I. The medicine and what it is used for

Zofran is authorized for the management of chemotherapy-induced nausea and vomiting, radiotherapy-induced nausea and vomiting, and for the prevention of post-operative nausea and vomiting (see PI for the full indication). It contains ondansetron as the active substance, and it is given by oral, injectable, and rectal route.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Zofran together with measures to minimize such risks and the proposed studies for learning more about Zofran's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PI 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

II.A: List of important risks and missing information

Important risks of Zofran are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered/taken. 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 Zofran. 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).

Table 1 List of important risks and missing information

Important identified risk	None
Important potential risk	Adverse birth outcomes following use during pregnancy
Missing information	None

II.B: Summary of important risks

The safety information in the proposed PI is aligned to the reference medicinal product.

Table 2 Important identified risk

None

Table 3 Important potential risk: Adverse birth outcomes following use during pregnancy

Evidence for linking the risk to the medicine	Literature and post-marketing reports (Rynn et al 2008, National Institution of Health 2014). Major birth defects occur in 2-4% of the general population in the United States and Europe (Rynn et al 2008, Morris et al 2018).
Risk factors and risk groups	Use of Zofran for nausea and vomiting of pregnancy or hyperemesis gravidarum during pregnancy (off-label use). Use of Zofran for approved indications during pregnancy.
Risk minimization measures	**Routine risk minimization measures** This risk is appropriately communicated through current labeling. The use of Zofran in pregnancy is not recommended. It is recommended that mothers receiving Zofran should not breast-feed their babies. Pregnancy status should be verified for females of reproductive potential prior to starting the treatment with Zofran. Females of reproductive potential should be advised that it is possible that Zofran can cause harm to the developing fetus. Sexually active females of reproductive potential are recommended to use effective contraception (methods that result in less than 1 % pregnancy rates) when using Zofran during the treatment and for two days after stopping treatment with Zofran. Information present in section, 'Pregnancy and lactation'. Legal status: Prescription only medicine. **Additional risk minimization measures** None

Table 4 Missing information

None

II.C: Post-authorization development plan

II.C.1. Studies which are conditions of the marketing authorization

There are no studies which are conditions of the Marketing Authorization or specific obligation of Zofran.

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

There are no studies required for Zofran.