Summary of risk management plan for vinflunine

This is a summary of the risk management plan (RMP) for Javlor® concentrate for solution for infusion (sterile concentrate).

One mL of concentrate contains 25 mg of vinflunine (as ditartrate).

One 2 mL vial contains 50 mg of vinflunine (as ditartrate).

One 4 mL vial contains 100 mg of vinflunine (as ditartrate).

One 10 mL vial contains 250 mg of vinflunine (as ditartrate).

The RMP details important risks of Javlor® concentrate for solution for infusion (sterile concentrate), how these risks can be minimized, and how more information will be obtained on vinflunine risks and uncertainties (missing information).

The summary of product characteristics (SmPC) for Vinflunine and its package leaflet give essential information to healthcare professionals and patients on how Vinflunine should be used.

This summary of the RMP for Javlor® should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Repart (EPAR).

Important new concerns or changes to current concerns will be included in updates of the RMP for Javlor®.

I. The medicine and what it is used for

Javlor® is indicated in monotherapy for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen.

It contains vinflunine (as detartrate) as the active substance and is given by the intravenous infusion route of administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Javlor® concentrate for solution for infusion (sterile concentrate) are identified. Measures to minimize such 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 package leaflet and SmPC addressed to patients and healthcare professionals.
- Important advice on the medicine's packaging.
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with medical prescription by a physician qualified in the use of anticancer chemotherapy) 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 Javlor® concentrate for solution for infusion (sterile concentrate), are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered.
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 Navelbine soft capsules. 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 Part VI.1: Safety concerns

Important identified risks	- None
Important potential risks	- Torsade de pointe/QT prolongation
Missing information	- None

II.B Summary of important risks

Important identified risks for Vinflunine: None

Important potential risk for Vinflunine:

Table Part VI.2: Summary of important potential risk

Important potential risk: Torsade de pointe / QT prolongation	
Description of the risk title	Torsade de pointe ; QT prolongation
Evidence for linking the risk to the medicine	Vinca-alkaloids are not known to be associated with QTc interval prolongation and its associated pro-arrhythmic events. In VFL phase I studies, QTc prolongation was not observed except in 1 subject whose change in QTc from baseline was found to be 67 msec at distance (~ 167h) from the infusion of VFL, when plasma concentration of VFL had decreased to a low level of 3.7ng/mL (higher plasma concentration concentrations were not associated with QTc prolongation in this subject). Nevertheless, QT prolongation and Torsade de pointe were considered as a safety matter to be taken into account and an important potential risk in the RMP.
Risk factors and risk groups	• Vinflunine should be used with caution in patients with increase of the proarrhythmic risk (e.g., congestive heart failure, known history of QT interval prolongation, hypokalaemia) (see section 4.4 of the SmPC). • The concomitant use of two or more QT/QTc interval prolonging substances is not recommended (see section 4.5 of the SmPC).

Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4, 4.5, 4.8 and relevant PIL section. Special attention is recommended when vinflunine is administered to patients with prior history of myocardial infarction/ischaemia or angina pectoris with history of prolongation of cardiac conduction intervals, particularly QTc. In addition, co-administration with QT-prolonging drugs and co-administration with potent CYP3A4 inhibitors (regardless of their QT prolonging effects) are also risk factors for cardiac events with vinflunine.

Missing Information for vinflunine: None

II.C Post -authorisation development plan

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

None.

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

None.