VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

During anaesthesia the patient undergoing anesthesia may experience a reduction in normal blood pressure (typically ≥ 20% decrease from normal blood pressure), i.e. hypotension. It is estimated that one-third of patients undergoing spinal anesthesia experience hypotension. This hypotension during spinal anaesthesia is considered to be due to decrease in amount of blood returned to the heart and due to reduction in amount of blood pumped out of heart.
Hypotension may also occur after general anesthesia. Prolonged hypotension during anesthesia is associated with increased mortality and also unwanted side effects related to both heart and other bodily systems. Therefore during the surgery restoration of blood pressure is the immediate requirement. Increased or normalised BP is the appropriate endpoint for a drug such as phenylephrine which acts by tightening blood vessels.
Also hypotension is one of the most important causes of nausea and vomiting particularly in the initial period after initiation of spinal anesthesia.

VI.2.2 Summary of treatment benefits

Phenylephrine is a very selective chemical agent which specifically binds to certain protein to increase the blood pressure when it is lower than normal blood pressure. It has the advantage of not being an agent which alters force of muscle contractions or heart rate. It strictly elevates the blood pressure without increasing the heart rate or contractility. This is especially useful if the heart is already prone to other heart muscle diseases or increase in heart rate.
Phenylephrine injection has been used in different medical settings, notably in critical care, cardiology and anesthesia for over 75 years. Currently, phenylephrine is one of the most commonly used drug to elevate the blood pressure during the care of women during and after pregnancy.

VI.2.3 Unknowns relating to treatment benefits

There are no adequate and well-controlled studies in use of phenylephrine in pregnant women. Limited data do not indicate any increased risk of birth defect malformations. Animal studies are insufficient with respect to effects on pregnancy, fetal development, parturition or postnatal development. The potential risk for humans is unknown. Therefore, phenylephrine should not be used during pregnancy unless clearly necessary.
A safety profile for use of phenylephrine in children has not been established. Information is limited and caution is advised when treating children.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Arterial hypertension	In the literature arterial hypertension is reportedly associated with phenylephrine.	Hypertension due to phenylephrine can be prevented by careful selection of dose and by monitoring of blood pressure during treatment.
Arrhythmia	Phenylephrine is known to cause arrhythmia	Warning about this risk and increased risk in patients with bradycardia and cardiac diseases are included in the SmPC and PIL.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Extravasation	Patients treated with drugs that constricts muscles in the blood vessels may be at an increased risk of severe tissue damage if they extravasate. For safe use should Fenylefrin Unimedic only be given by a healthcare professional with appropriate training and experience.
Medication error	Phenylpehrine Unimedic is also available as a concentrate, which might be mistaking for a ready solution for injection. A medication error might occur when the concentrate is not diluted properly, and patients can be exposed to an overdose. Healthcare professionals should pay attention to which presentation of Phenylephrine Unimedic that will be given to the patient.

Missing information

Risk	What is known
Use during pregnancy	There is no adequate data from clinical trials for use of phenylephrine in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, fetal development, parturition or postnatal development. The potential risk for humans is unknown. Phenylephrine should not be used during pregnancy unless clearly necessary.

Risk	What is known
Use in paediatric population	There is no adequate data from clinical trials for use of phenylephrine in paediatric population. The potential risk for this population is unknown. Should be used with caution because the available data are limited.

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 phenylephrine can be found in the phenylephrine's EPAR page.

Phenylephrine Unimedic has two SPCs covering different strengths:

- **Phenylephrine Unimedic 0.05 mg/ml and 0.1 mg/ml, solution for injection**
- **Phenylephrine Unimedic 10 mg/ml, concentrate for solution for injection/infusion**

This medicine has no additional risk minimisation measures.

In addition, the label on the ampoules is clearly distinguishable from each another to avoid medication errors due to the risk of mix-up between the '*0.05 and 0.1 mg/ml Solution for injection'* and the '*10 mg/ml, Concentrate for solution for injection/infusion,*. The labels for the solutions are in pink colour and for the concentrate in white colour. The boxes for the Solutions for injection are in white color and the Concentrate for solution for injection/infusion is in white color with pink areas. Furthermore, the printed solution concentrate '0.05 mg/ml' on the box has a background in red and the concentrate '10 mg/ml' is printed in red color with a black background.

VI.2.6 Planned post authorisation development plan

NA

VI.2.7 Summary of changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comments
01	20 October 2014		New
02	05 December 2014		Alignment with MPAs comments
03	28 September 2015		Alignment with MPAs comments
04	8 October 2015		Alignment with MPAs comments
05	16 July 2016		Additional strength added 10mg/ml

Version	Date	Safety Concerns	Comments
06	30 December 2016		Medication error added as an important potential risk
07	15 March 2017		Alignment with MPAs comments