VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Overactive bladder is a very common disorder of the urinary system and has a prevalence of 15.6% in men and 17.4% in women according to a study conducted in 6 European countries from 1997 – 1998. The most common symptom of overactive bladder was increased frequency (85%), followed by urgency (54%) and then involuntary urination (36%) in this study. An increase in prevalence of overactive bladder was observed with increased age, with 41.9% of men and 31.3% of women over the age of 75 suffering from it (1, 2).

VI.2.2 Summary of treatment benefits

Solifenacin belongs to a group of medicines called anticholinergics which are used to reduce the activity of an overactive bladder. Solifenacin is used to treat the symptoms of this condition including: having a strong, sudden urge to urinate without prior warning, having to urinate frequently or a patient wetting themselves because they could not get to the bathroom in time. With solifenacin treatment, patients can wait longer before having to go to the bathroom and have an increased volume of urine that can be held by their bladder.

In studies, treatment with solifenacin reduced the frequency of urination, number of episodes of urgency, involuntary urination and urinating at night compared to placebo. After 12 weeks of treatment, approximately 50% of patients suffering from involuntary urination before treatment

were free of such episodes, and in addition 35% of patients achieved a urination frequency of less than 8 urinations per day.

These studies were conducted for Vesicare by Astellas Pharma Ltd and not by Mylan.

VI.2.3 Unknowns relating to treatment benefits

No clinical data is available from women who became pregnant while taking solifenacin. The potential risk in pregnancy is unknown.

VI.2.4 Summary of safety concerns

Table 20 Part VI - Summary table of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Allergic reactions (Anaphylactic reactions)	Angioedema (skin allergy that results in the swelling that occurs in the tissue just below the surface of the skin) with airway obstruction (difficulty in breathing) can occur in some patients using solifenacin succinate. Allergic attack, or a severe skin reaction (e.g. blistering and peeling of the skin).	Do not use solifenacin use if you are allergic to the active substance or to any of the excipients. The drug should be stopped and appropriate therapy and/or measures should be taken if you develop allergic reactions.
Inability to empty the bladder completely (Urinary retention)	Build-up of urine in the bladder due to inability to empty the bladder completely	Do not use solifenacin if you have an inability to pass water or to empty your bladder

Risk	What is known	Preventability
	has been reported with use of solifenacin.	completely (urinary retention).
Disorder of the heart's electrical system (Cardiac rhythm disorders)	Changes in the electrical activity of the heart [(ECG) QT prolongation and Torsade de Pointes] have been observed in patients with risk factors, such as pre-existing heart's electrical system disorders and low potassium levels, with symptoms such as irregular and abnormally fast heart beat and feeling your heart beat.	Caution should be taken in patients with pre-existing heart's electrical system disorders or low potassium levels.
Increased pressure in eyes (Glaucoma)	Increased pressure in the eyes can occur with the use of solifenacin.	Do not take solifenacin if you suffer or are at risk of suffering from increased pressure in the eyes, with gradual loss of eye sight (glaucoma).
Partial or complete non-mechanical blockage of the small and/or large intestine (Ileus)	Complete blockage of the bowel can occur with the use of solifenacin.	Talk to your doctor or pharmacist if you have some obstruction of the digestive system (constipation) or are at risk of your digestive system slowing down (stomach and

Risk	What is known	Preventability
		bowel movements) before taking solifenacin.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use during lactation	No data on the excretion of solifenacin in human milk are available. However, in animal studies, solifenacin treatment of the mother during lactation caused dose-dependent lower post-delivery (immediately after the birth of a child till about six weeks) survival rate, decreased pup weight and slower physical development at clinically relevant levels. Use of solifenacin should be avoided during breast-feeding as it may get into your breast milk.

Missing information

Risk	What is known
Limited information on use in pregnancy	No clinical data are available from women who became pregnant while taking solifenacin. However, animal studies do not indicate direct harmful effects on fertility, embryonal / foetal development or child birth. The potential risk for humans is unknown. Ask your doctor or pharmacist for advice before taking this medicine.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) 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. The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No studies planned.

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

The RMP was updated from version 1 to version 2 (this version) in order to address the comments in the RMS Day 70 Preliminary Assessment Report NL/H/3223/001-002/DC for solifenacin dated 15-Jul-2014.

The RMP was updated from version 2 to 3 (this version) in order to address the comments from the Summary Assessment Report (PSUR WSP NL/H/PSUR/0012/002) for Vesicare (solifenacin succinate) PSUR (reporting period: 09-Jun-2011 to 08-Jun-2014). The Summary Assessment Report mentioned the following recommendations for RMP.

The MAH is requested to update the summary of safety concerns in the RMP:

- The safety concern ‘Use in pregnancy’ should be included as missing information.
- ‘Use during lactation’ should be included as an important potential risk, since pre-clinical data indicated a potential risk.
- The important identified risk ‘QTc prolongation and Torsade de Pointes’ should be amended into ‘Cardiac rhythm disorders’.

Since, RMP version 2.0 was in line with the recommendation except bullet point 3. Amendments as per point 3 has been made in this version. Additionally, few amendments have been done to include changes made in the product information during the procedure.