VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

The active ingredient in Penomax, pivmecillinam, is an antibiotic which is used to treat uncomplicated lower urinary tract infections (UTIs), also known as acute cystitis or bladder infection, and urethra infection. When UTI occurs in a healthy person with a normal, unobstructed urinary tract, the term uncomplicated is used to describe the infection.

Urinary tract infections are common types of infections. Women are especially prone to UTIs for anatomical reasons. UTIs in men are not as common as in women but can be serious when they occur. People with spinal cord injuries or other nerve damage around the bladder are more prone to UTIs. They have difficulty emptying their bladder completely, thus allowing bacteria to grow in the urine. Other factors that increase the risk for UTIs are abnormality of the urinary tract that obstructs the flow of urine—a kidney stone or enlarged prostate, diabetes or problems with the body's natural defense system.

VI.2.2 Summary of treatment benefits

Pivmecillinam was introduced in the early 1980's as an option for the treatment of acute uncomplicated UTI. The efficacy of pivmecillinam for empiric treatment of acute uncomplicated urinary infection was reported in a series of clinical trials completed in the 1970s and 1980s . It has been used in the treatment of acute cystitis for many years.

Urinary tract infections are generally self-limiting, but antibiotic treatment shortens the duration of symptoms and prevents complications.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Hypersensitivity reactions	Like all antibiotics, Penomax may cause hypersensitivity reactions including anaphylactic reaction (severe allergic reactions characterized especially by breathing difficulty, faintness due to low blood pressure, itching and hives).	Patients who are allergic (hypersensitive) to pivmecillinam, penicillin, cephalosporin antibiotics or any of the ingredients of Penomax should not use this medicine. If symptoms of allergic (hypersensitivity) reactions appear, Penomax should be discontinued and patient should seek medical advice. In case of serious reactions, urgent medical treatment is needed.
Lack of carnitine (Carnitine is an amino-acid acquired mostly through the diet. It is used by cells to process fats and produce energy)	Body is using carnitine when processing pivmecillinam in the liver. After 7–10 days of treatment with the highest recommended dose of pivmecillinam the total carnitine reserve in body is reduced by approximately 10 %. Normally that does not cause any problems, but some patients are prone to carnitine deficiency due to inherited genetic factors, already existing carnitine deficiency, unstable diabetes mellitus, abnormally small muscle mass and certain other concomitant medications (e.g. antiepileptic valproate). Carnitine deficiency may cause symptoms such as muscle weakness and even serious/life-threating symptoms if deficiency is severe.	Patients with inherited genetic metabolic abnormalities (e.g. carnitine transporter deficiency) that may result in too low carnitine levels should not take Penomax. Penomax should be used with caution in patients with known carnitine deficiency, unstable diabetes mellitus, and abnormally small muscle mass. Concurrent treatment with valproate should be avoided. Long-term (over 3 weeks) or frequently repeated treatment should be avoided.

Risk	What is known	Preventability
Inflammation in food pipe (esophagus) and administration in patients with strictures in food pipe and/or obstructive changes in the digestive system	Tablets may irritate food pipe if they get stuck and cause inflammation in food pipe	Patients whose food pipe has become too narrow or who have blockages in digestive system should not take Penomax. Penomax tablets should be taken in sitting or standing position. Patients should drink at least half a glass of water or other beverage, when taking the tablet. Tablets should be taken preferably with meal in order to avoid stomach symptoms.
Administration in patients with porphyria	Porphyrias are rare disorders that affect mainly the skin or nervous system and may cause abdominal pain. These disorders are usually inherited. When a person has a porphyria, cells fail to change body chemicals called porphyrins and porphyrin precursors into heme, the substance that gives blood its red color. Certain medicines, such as pivmecillinam, may trigger symptoms of porphyria.	Penomax should not be used by patients suffering from porphyria, since pivmecillinam has been associated with acute attacks of porphyria.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Diarrhoea/pseudomembranous colitis (bowel inflammation) caused by certain bacteria type (*Clostridium difficile)*	As with other antibiotics, severe form of diarrhoea/pseudomembranous colitis caused by *Clostridium difficile* may occur during the Penomax therapy. Patients should contact doctor, if they experience diarrhoea during the treatment with Penomax.

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 Penomax can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

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

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment

Part VII: Annexes

Table of contents

Annex 2 - SmPC & Package Leaflet

Proposed SmPC and Package leaflet are located in section 1.3.1.

Annex 3 - Worldwide marketing authorisation by country (including EEA)

For each product in the RMP provide:

A3.1 Licensing status in the EEA

Country	Current licence status	Date of licence action [1]	Date first marketed in country	Brand name(s)	Comments

[1] Enter the date of the most recent change to the licence status: eg date of approval or date of suspension

A3.2 Licensing status in the rest of the world

Country	Current licence status	Date of licence action 1	Date first marketed in country	Brand name(s)	Comments