VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Clarithromycin 500 mg, powder for solution for infusion is indicated when parenteral therapy is required for treatment of severe infections, caused by clarithromycin-susceptible organisms in the following conditions:

- Acute exacerbation of chronic bronchitis
- Community acquired pneumonia
- Acute bacterial sinusitis
- Bacterial pharyngitis
- Skin and soft tissue infections, e.g. folliculitis, cellulitis and erysiphelas

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

VI.2.2 Summary of treatment benefits

Clarithromycin is an antibiotic that belongs to a group of medicines called macrolides. Antibiotics stop the growth of bacteria which cause infections. Clarithromycin prevents bacteria from growing by interfering with their protein synthesis. It binds to the subunit 50S of the bacterial ribosome and thus inhibits the translation of peptides. It is effective against infections caused by bacteria such as: Chest infections like acute bronchitis and pneumonia, throat and sinus infections, skin and tissue infections.

VI.2.3 Unknowns relating to treatment benefits

None.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Known hypersensitivity to macrolide antibiotic drugs or to any of its excipients.	Immediate hypersensitivity reactions may occur after administration as demonstrated by rare cases of urticaria, angioedema, rash,	Clarithromycin should not be used in patients with known hypersensitivity. Your doctor should suggest alternative

Risk	What is known	Preventability
	bronchospasm, oropharyngeal oedema and anaphylaxis.	treatment for your condition.
History of QT prolongation or ventricular cardiac arrhythmia, including torsades de pointes.	There is a risk of prolonged QT-interval in patients with a history of coronary heart disease when using clarithromycin.	Clarithromycin should not be used or used with caution.
Severe hepatic failure in combination with renal impairment.	Clarithromycin is excretes through the liver and impaired liver function in combination with impaired renal function posed as risk for overdose.	Clarithromycin should not be used or used with caution.
Hypokalaemia (risk of prolongation of QT-time).	Hyperkalaemia increased the risk of QT-prolongation as an adverse reaction to clarithromycin treatment.	Clarithromycin should not be used or used with caution.
Interactions: Concomitant use of: Astemizole, cisapride, pimozide, terfenadine as this may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and Torsade de Pointes. Concomitant use of: Clarithromycin and ergotamine or dihydro-ergotamine as this may result in ergot toxicity. Concomitant use of HMG-CoA reductase inhibitors (statins): Lovastatin or simvastatin, due to the risk of rhabdomyolysis. Treatment with these agents should be discontinued during clarithromycin treatment.	Clarithromycin treatment can be influenced by several different concomitant medications. The interaction may be due to other medicines influence on the enzyme that is involved in the metabolism of clarithromycin or the influence of clarithromycin on the enzyme metabolizing other medicines.	Clarithromycin should not be used or used with caution concomitant with other medicines and special monitoring should be instigated for some combinations.

Risk	What is known	Preventability
Concomitant use of colchicin in combination with renal- or hepatic impairment.		
Resistance to antibiotics	Clarithromycin can – as other antibiotics – cause resistance in certain bacteria.	The physician should be aware which national recommendations applies concerning the use of clarithromycin
Pregnancy (1.trimester)	Clarithromycin use during pregnancy should not be used unless you doctor find in unavoidable especially during 1. Trimester.	Other options for treatment should be used if possible.
Pseudomembranous colitis	Severe diarrhoea could indicate that you are suffering from a condition called "Pseudomembranous colitis"	You should contact your doctor for advice as to what to do.
Deterioration of Myasthenia Gravis	Clarithtomycin may cause aggrevation of Myasthenia Gravis.	If you suffer from Myasthenia Gravis you should be aware that treatment with clarithormycin can cause aggrevation and contact you doctor if this happends

Important potential risks
None.

Missing information
None.

VI.2.5 Summary of additional risk minimisation measures by safety concern

Routine Pharmacovigilance activities are applied for all Safety Concerns except for the below mentioned where additional risk minimisation measures are applied.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures

Resistance to antibiotics	The text in the proposed SmPC (and reflected in the PIL) is as follows: **4.1 Therapeutic indications** Local official guidelines regarding the use of antibacterial agents should be followed (see section 5.1).	Reporting of non-serious and serious cases concerning "lack-of-efficacy/reduced efficacy/altered efficacy" to the Competent Authorities

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 following additional risk minimisation measure applies to this product:

Risk minimisation measure(s): Resistance to antibiotics
Objective and rationale
• Summary description of main additional risk minimisation measures – key points
Resistance to antibiotics Reporting of non-serious and serious cases concerning "lack-of-efficacy/reduced efficacy/altered efficacy" to the Competent Authorities

VI.2.6 Planned post authorisation development plan (if applicable)

Not Applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not Applicable.

Table 1. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
<number>	<At time of authorisation dd/mm/yyyy>	<Identified Risks Potential Risks Missing information>	

Version	Date	Safety Concerns	Comment
<E.g. 7.0>	<E.g. 17/08/2012>	<E.g. Allergic conditions added as an identified risk Hypersensitivity removed as an identified risk Severe infection added as an identified risk Convulsions added as a potential risk>	<E.g. The previous term hypersensitivity was updated to allergic conditions to include angioedema and urticarial>
etc.			