VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Microbial pathogens, such as bacteria, have accompanied humanity for centuries and continue to represent significant causes of morbidity and mortality worldwide. Bacterial infections have significant personal and public health effects. Immunocompromised persons such as diabetic patients, persons with severe illnesses and patients receiving immunosuppressants are more prone to get severe bacterial infections and infection related complications.

VI.2.2 Summary of treatment benefits

Pathogenic bacterial infections may lead to complications, suffering and in serious cases even death. Therefore appropriate and effective treatment is important.

Active ingredient of this medicinal product, ciprofloxacin, is a broad spectrum antibacterial agent that belongs to the group of antibiotics called fluoroquinolones. It has a long history of known safety and efficacy in adults, children and adolescents. Ciprofloxacin is approved for the treatment of uncomplicated and complicated infections caused by bacteria susceptible to ciprofloxacin and thus a broad variety of infections in adults. Sometimes it is also necessary to combine other antibiotic to the treatment.

Ciprofloxacin can also be used in the treatment of certain infections in children and adolescents. The use of ciprofloxacin in children and adolescents should follow available official guidance. Ciprofloxacin treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.

VI.2.3 Unknowns relating to treatment benefits

Bacteria strains that are resistant to ciprofloxacin may occur. The prevalence of acquired resistance may vary geographically and with time for selected species. Therefore local information on bacteria's ciprofloxacin resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of ciprofloxacin in at least some types of infections is questionable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Abnormal heart rhythm (Prolongation of QTc interval)	Ciprofloxacin can cause potentially life-threatening changes on the ECG, that is a prolongation of the QT-interval i.e. delayed conduction of electrical signals in heart. Elderly patients and women may be more sensitive to QTc interval prolonging medications.	Patients who were born with or have had any condition with abnormal heart rhythm (seen on ECG, electrical recording of the heart), have salt imbalance in the blood (especially low level of potassium or magnesium in the blood), have a very slow heart rhythm (called 'bradycardia'), have a weak heart (heart

Risk	What is known	Preventability
	Therefore, caution should be taken when using fluoroquinolones, including ciprofloxacin, in these populations.	failure), have a history of abnormal heart rhythm, or patients who are taking other medicines that result in abnormal ECG changes should take caution when using Ciprofloxacin Orion. Patients who are currently taking any medicine that decrease their blood potassium levels must consult doctor before taking Ciprofloxacin Orion. If patient experiences palpitations or irregular heart beat during the period of treatment, patient should inform doctor immediately. Doctor may perform an ECG to measure patient's heart rhythm.
Hypersensitivity (allergic reactions)	Hypersensitivity/ allergic reactions may occur following a single dose of ciprofloxacin and may be life-threatening.	Patients who are allergic to the ciprofloxacin, to other quinolone antibiotics or to any of the excipients of the preparation, must not take this medicine. If symptoms of acute serious allergic reactions appear, treatment should be discontinued and doctor should be contacted immediately. Symptoms can be e.g. tightness in the chest, feeling dizzy, sick or faint, or experiencing dizziness when standing up.
Antibiotic associated diarrhoea including Pseudomembranous colitis (severe bowel inflammation)	Diarrhoea may develop while taking antibiotics, including ciprofloxacin, and even several weeks after antibiotic therapy has been stopped. In severe cases condition may be life-threatening.	If diarrhoea becomes severe or persistent or if stool contains blood or mucus, ciprofloxacin therapy should be stopped immediately, and doctor should be contacted. Medicines that stop or slow down bowel movements should not be taken.
Liver toxicity (Hepatotoxicity)	Cases of sudden liver inflammation with strong symptoms potentially leading to	Ciprofloxacin Orion must not be used in patients with impaired liver function and in patients

Risk	What is known	Preventability
	liver failure (including cases resulting to death) have been reported with ciprofloxacin.	with significantly increased liver enzyme levels. Patients should contact their doctor prior to continuing treatment if signs and symptoms of sudden liver disease with strong symptoms develop such as rapidly developing weakness associated with jaundice (yellowness of skin and whites of the eyes), dark urine, bleeding tendency or hepatic encephalopathy(a condition that causes temporary worsening of brain function in people with advanced liver disease). Liver function tests/investigations should be performed in cases where indications of liver dysfunction occur.
Exacerbation of *myasthenia gravis* (neurological condition that causes muscle weakness).	Symptoms of *myasthenia gravis* can be exacerbated during ciprofloxacin therapy.	Ciprofloxacin should be used with caution in patients with myasthenia gravis.
Tendon inflammation (tendinitis) and rupture	Tendon inflammation and rupture (especially Achilles tendon), sometimes in both sides, may occur with quinolone therapy including ciprofloxacin, even within 48 hours of starting treatment and have been reported up to several months after discontinuation of therapy. The risk of tendinitis and tendon rupture is increased in elderly patients and in those treated concurrently with corticosteroids.	Patients with a history of tendon disease/disorder related to quinolone treatment should generally not take Ciprofloxacin Orion. At the first sign of pain or inflammation, patients should discontinue treatment with ciprofloxacin, rest the affected limb(s) and consult their doctor immediately in order to initiate appropriate treatment (e.g. immobilisation) for the affected tendon.
Convulsions (Seizures)	Quinolone antibiotics such as levofloxacin are known to trigger seizures.	Patients who suffer from epilepsy or a condition which makes patient likely to have convulsions should talk to doctor before taking Ciprofloxacin Orion.

Risk	What is known	Preventability
		If convulsions appear, patient should stop taking this medicine and contact doctor immediately.
Mental disorders (Psychiatric reactions)	Psychiatric reactions may occur even after first administration of ciprofloxacin. In rare cases, depression or psychosis can progress to suicidal ideations/thoughts culminating in attempted suicide or completed suicide. In the occurrence of such cases, ciprofloxacin should be discontinued.	If severe changes in mental status appear, patient should stop taking this medicine and contact doctor immediately.
Nerve disorder (Peripheral neuropathy)	Cases of polyneuropathy (nerve disorder affecting several nerves) with neurological symptoms such as pain, burning, sensory disturbances or muscle weakness, alone or in combination have been reported in patients receiving ciprofloxacin.	Ciprofloxacin should be discontinued in patients experiencing symptoms of neuropathy, including pain, burning, tingling, numbness, and/or weakness in order to prevent the development of an irreversible condition.
Sensitivity to UV-light e.g. sun, solarium (Photosensitivity)	Ciprofloxacin has been shown to cause photosensitivity reactions.	Patients taking ciprofloxacin should avoid direct exposure to either extensive sunlight or UV irradiation, or solarium during treatment.
Blood disorders (Hemolytic disorders)	Anemia due to lysis of red blood cells (haemolytic anemia) has been reported in association with ciprofloxacin therapy.	Blood tests can be taken in order to detect possible adverse effects early.
Joint disorder (arthropathy) in children and growing adolescents	Ciprofloxacin has been shown to cause joint disease in weight-bearing joints of immature animals. Safety data from a randomised double-blind study on ciprofloxacin use in children revealed an incidence of suspected drug-related arthropathy.	The use of ciprofloxacin in children and adolescents should follow available official guidance. Ciprofloxacin treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents. Treatment should be initiated only after a careful benefit/risk evaluation, due to possible adverse events related to joints and/or surrounding tissue.

Risk	What is known	Preventability
Selection of bacteria that can resist ciprofloxacin (Selection of drug resistant isolates)	During or following a course of treatment with ciprofloxacin bacteria that demonstrate resistance to ciprofloxacin may be isolated, with or without a clinically apparent superinfection. There may be a particular risk of selecting for ciprofloxacin-resistant bacteria during extended durations of treatment and when treating certain types of infection.	Appropriate use of antibiotics such as ciprofloxacin is important to prevent development of bacteria strains that are resistant to ciprofloxacin.
Resistance development of Neisseria gonorrhoea (bacteria strain that can cause genital infections)	Neisseria gonorrhoea is bacteria that can cause genital infections. If bacteria are resistant to ciprofloxacin the treatment is not effective. In that case infection continues and may get worse.	When it is known or suspected that genital infections are caused by Neisseria gonorrhea, it is especially important to find information about local ciprofloxacin resistance and sensitivity should be confirmed with laboratory test. It can be necessary to combine treatment with another antibiotic and effect of the treatment is closely followed.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Adverse drug reaction that affects the skin and various internal organs [Drug rash with eosinophilia and systemic symptoms (DRESS)]	DRESS has been reported in association with ciprofloxacin therapy. DRESS characteristically has a long latency period (>2-3weeks) between starting treatment with drug and onset of symptoms, The classic clinical presentation of DRESS includes the triad of fever, rash, and internal organ involvement. Fever and rash are the most common clinical manifestations

Missing information

Not applicable.

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 this medicinal product 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 (if applicable)

Not applicable.

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

Not applicable.