
PUBLIC SUMMARY OF RISK MANAGEMENT PLAN

AMORION COMP 500/125 MG, FILM-COATED TABLET

ORION OYJ

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VI.2 Elements for a public summary

VI.2.1 *Overview of disease epidemiology*

Bacteria are microscopic organisms that have only one cell. There are thousands of different kinds, and they live in every conceivable environment all over the world. Bacteria are very common in our bodies and in the world around us. Some bacteria live in the bodies of people and animals—on the skin and in the airways, mouth, and digestive, reproductive, and urinary tracts—often without causing any harm. Most bacteria are not harmful and many of them are helpful. Less than 1% of bacteria will actually make us sick. They are called pathogens. When they do make us sick, it is called a "bacterial infection." Pathogens reproduce quickly in your body. Many give off chemicals called toxins, which can damage tissue and make you sick.

Bacterial infections usually have to be treated with antibiotics. The specific type of antibiotic depends on the type of bacteria that is causing the infection. The active substances in Amorion Comp are amoxicillin and clavulanic acid. The combination of amoxicillin and clavulanic acid is used to treat certain infections caused by bacteria.

Amorion Comp is used in adults and children to treat the following infections:

- middle ear and sinus infections (middle ear is the space immediately behind the eardrum and sinuses are hollow cavities in the bones around the nose)
- respiratory tract infections (respiratory tract starts at the nose and mouth and continues through the airways and the lungs)
- urinary tract infections (urinary tract consists of kidneys, ureters, bladder and urethra)
- skin and soft tissue infections including dental infections (examples of soft tissues are muscles, fat, tendons, ligaments and blood vessels; examples of dental infections are infection of the mouth, tooth, face, jaw or throat)
- bone and joint infections (joints are the junction between two or more bones).

VI.2.2 Summary of treatment benefits

Amorion Comp is an antibiotic and works by killing bacteria that cause infections. It belongs to the group of medicines called penicillins. It contains two active ingredients called amoxicillin and clavulanic acid. Amoxicillin has the major antibacterial effect whereas clavulanic acid mainly protects amoxicillin from destructive effects of certain bacteria, thus making it effective against wider range of bacteria than amoxicillin alone.

VI.2.3 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Hypersensitivity (allergic) reactions	Serious hypersensitivity (allergic) reactions have been reported in patients on penicillin therapy. In some cases hypersensitivity reaction has led to death of the patient.	<ul style="list-style-type: none">• Before starting treatment with Amorion Comp, careful enquiry should be made, if the patient has earlier had hypersensitivity reactions in association with antibiotic therapy• Amorion Comp should not be used in patients with known hypersensitivity to amoxicillin/clavulanic, to any other penicillin or to any of the excipients of this product.• In addition Amorion Comp should not be used in patients who have earlier had severe immediate hypersensitivity reaction to certain other antibiotics called beta-lactam antibiotics.• If allergic/hypersensitivity reaction occurs, therapy with Amorion Comp must be stopped and appropriate treatment should be given if necessary
Liver problems	<ul style="list-style-type: none">• Liver problems in association with amoxicillin/clavulanic acid therapy have been reported, mostly in men and in elderly patients, very rarely in children.• Liver problems may be severe and extremely rarely lead to death of the patient. In those cases the patient	<ul style="list-style-type: none">• Monitoring of the liver function with laboratory tests in long-term therapy• Amorion Comp should not be used in patients who have earlier had yellowness of the skin/insufficient liver function in association with amoxicillin/clavulanic acid therapy.

Risk	What is known	Preventability
	<p>has almost always had serious underlying disease or other concomitant medication known to have potential effects on liver.</p> <ul style="list-style-type: none"> • Liver problems may be associated with long-term treatment. 	<ul style="list-style-type: none"> • Caution should be administered when treating patients whose liver function may be insufficient
Insufficient kidney function and crystals in the urine	<ul style="list-style-type: none"> • Crystals in the urine have been noted very rarely in patients with reduced amount of urine 	<ul style="list-style-type: none"> • Enough liquids should be administered especially when high doses of Amorion Comp are used • Dose should be reduced in patients with insufficient kidney function • Monitoring of kidney function with laboratory tests in long-term treatment • Careful monitoring of patients with urinary catheters
Colitis i.e. infection/inflammation of the large intestine (colon)	<ul style="list-style-type: none"> • Antibiotic associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening. 	<ul style="list-style-type: none"> • The patient should consult doctor if diarrhoea occurs during or after Amorion Comp therapy • If antibiotic-associated colitis occur, amoxicillin/clavulanic acid should be immediately stopped and appropriate therapy should be given. • Medicines for diarrhoea that slower bowel movements (e.g. loperamide) should not be used if the patient has antibiotic-associated colitis
Mononucleosis (Infectious mononucleosis, is an infection caused by the Epstein-Barr virus. The virus spreads through saliva, which is why it's sometimes called "kissing disease)	<ul style="list-style-type: none"> • Certain type of rash (morbilliform rash) may appear, if the patient has mononucleosis while taking amoxicillin 	<ul style="list-style-type: none"> • Amorion Comp should be avoided if infectious mononucleosis is suspected

Risk	What is known	Preventability
Acute generalized exanthematous pustulosis (AGEP)	<ul style="list-style-type: none"> If the patient develops fever and generalised redness of the skin with pustules in the early phase of Amorion Comp therapy, those may be signs of condition called acute generalised exanthematous pustulosis (AGEP) 	<ul style="list-style-type: none"> If AGEP occurs, treatment should be discontinued and amoxicillin should be avoided in the future as well

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Lack of efficacy due to bacteria resistance	<p>If bacteria are resistant to Amorion Comp it means that Amorion Comp does not have desired effect on bacteria and treatment may fail.</p> <p>Certain bacteria are naturally resistant to amoxicillin/clavulanic acid and other bacteria may develop resistance. The prevalence of resistance may geographically and with time for selected bacteria species, and local information of resistance is desirable, particularly when treating patient with severe infection. Expert should be consulted, if necessary, and consideration should be given to official guidance on the appropriate use of antibacterial agents.</p>
Dental surface disorders in children in association with amoxicillin	Amoxicillin use during early childhood could be a risk factor for developmental defects on enamel surfaces, but further research is needed.
Cases of oral cleft in a child in association with mother's amoxicillin therapy during pregnancy	<p>If mother is treated with amoxicillin during the second or third month of pregnancy, the child may have increased risk of cleft lip with or without cleft palate.</p> <p>Use of Amorion Comp should be avoided during pregnancy, unless considered essential by the physician.</p>
Potential interference with medication used to prevent blood clots that are taken by mouth	<p>Oral anticoagulants (medication used to prevent blood clots) and penicillin antibiotics have been widely used in practice without reports of interaction. However, prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin/clavulanic acid.</p> <ul style="list-style-type: none"> Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly with Amorion Comp. Adjustments in the dose of oral anticoagulants may be necessary.

Risk	What is known (Including reason why it is considered a potential risk)
Potential interactions with certain medicines such as methotrexate (used e.g. for rheumatic diseases), allopurinol (used e.g. for gout), and mycophenolate (used to prevent rejection of transplanted organ).	<ul style="list-style-type: none"> • Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. • Penicillins may reduce the excretion of methotrexate causing a potential increase in its toxicity. • Careful clinical monitoring of the patient should be performed during the combination with mycophenolate and shortly after amoxicillin-clavulanic acid antibiotic treatment.

VI.2.4 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 Amorion Comp can be found in the Fimea's web page <http://www.fimea.fi>.

This medicine has no additional risk minimisation measures.

VI.2.5 Planned post authorisation development plan

Not applicable.

VI.2.6 Summary of changes to the Risk Management Plan over time

Not applicable.