VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Although the vast majority of bacteria are harmless or beneficial, some bacteria are pathogenic and can make people ill. They reproduce quickly in the human body and produce chemicals called toxins, which can cause tissue damage and make people sick. Amoxicillin belongs to a group of medicines called 'penicillins' that work by stopping the growth of bacteria. It is used to treat certain infections caused by bacteria which are sensitive for amoxicillin, including infections of the ear, throat, nose and sinuses, infections of the lower respiratory tract such as bronchitis and pneumonia, infections of the bladder, when there are bacteria in the urine during pregnancy (without symptoms), inflammation of the kidney and the renal pelvis, typhoid and paratyphoid fever, dental abscess, prosthetic joint infections, Lyme disease (from a tick bite), stomach ulcers caused by the bacterium *Helicobacter pylori* and prevention of heart infections during mouth or throat surgery.
Sometimes an infection caused by bacteria does not respond to a course of an antibiotic, for example because bacteria causing the infection are resistant to the antibiotic that is being taken. Therefore amoxicillin should only be used for infections caused by bacteria known to be sensitive. The prevalence of resistance may vary geographically and with time for selected species of bacteria. Bacteria become resistant to antibiotics for many reasons, but by using antibiotics carefully the chance that bacteria becoming resistant to them can be reduced: use them at the right dose, time and number of days (finish the treatment course and do not use antibiotics prescribed to another person).

VI.2.2 Summary of treatment benefits

According to **Ferris** (2009) antibiotic therapy for acute bacterial sinusitis (inflammation of the sinus) is usually empiric, targeting the common pathogens. The first choice is first-line antibiotics including amoxicillin (**Holten** et al. 2000). The second choice is second-line antibiotics including the newer macrolides: clarithromycin, azithromycin or amoxicillin/clavulanic acid. For patients with uncomplicated acute sinusitis, the less expensive first-line agents appear to be as effective as the costlier second-line agents (**Ferris** 2009). However, according to **Wald** et al. (2013) amoxicillin (with or without clavulanate) is the first-line treatment of acute bacterial sinusitis.
In clinical situations in which there is increased development of beta-lactamase–producing organisms, amoxicillin may be the first choice for the treatment of otitis media (**Holten** et al. 2000). For most outpatient procedures, amoxicillin is the preferred agent for bacterial endocarditis prophylaxis. Orally administered amoxicillin and ampicillin are used primarily to treat mild infections such as otitis media, sinusitis, bronchitis, urinary tract infections and bacterial diarrhea (**Holten** et al. 2000). However, beta-lactam antibiotics (like amoxicillin) are usually not the first choice for empiric outpatient treatment of community-acquired pneumonia (**Holten** et al. 2000). For the diagnosis of streptococcal pharyngitis or tonsillitis a microbiological evaluation is needed. The first choice in treatment in European countries still remains amoxicillin or amoxicillin clavulanate (**Bonsignori** et al. 2010).
According to **Ferris** et al. (2009), for early-diagnosed Lyme disease (from a tick bite) the treatment of choice in children is amoxicillin (for 14 days). An adequate treatment for gastric ulcers caused by the bacterium *Helicobacter pylori* is a combination of clarithromycin, amoxicillin or metronidazole and a proton pomp inhibitor (an ulcer healing agent) (**Ferris** et al. 2009).

VI.2.3 Unknowns relating to treatment benefits

Amoxicillin has been in use for many years and the safety profile of the active ingredient is well established, therefore almost all different populations are exposed and the effects of amoxicillin on these different populations are known. However, limited data is available concerning amoxicillin during pregnancy and breastfeeding. Dosage adjustment are also applicable for patients with kidney problems (renal impairment) Therefore, as a precautionary measure, amoxicillin should only be used during pregnancy and breastfeeding and in patients with renal impairment if per the judgment of the physician the potential benefits outweigh the possible hazards.

VI.2.4 Summary of safety concerns

Summary of safety concerns – important identified risks

Risk	**What is known**	**Preventability**
Hypersensitivity (allergic reaction)	Allergic reactions and hypersensitivity reactions can occur with and without previous exposure to amoxicillin (or its excipients) or another penicillin or cephalosporin (a beta-lactam antibiotic). These reactions can be very serious reactions but also mild, dependent of the symptoms of the patient. The occurrence of the serious reaction anaphylactic shock (allergic reaction including rash, throat swelling and low blood pressure which can lead to a life-threatening situation) is rare (in 0.1% of patients or less, but in more than 0.01%). Treatment for hypersensitivity reactions is available and will result in a quick recovery of the patient.	When it is proven that the allergic/hypersensitivity reaction is due to amoxicillin or one of the excipients, it can be easily prevented by not taken the drug again. A previous allergic reaction to amoxicillin or another penicillin/cephalosporin is also a contraindication for the use of amoxicillin so this patient population will then be excluded from the use of amoxicillin. Patients who react allergically to other antibiotics should use amoxicillin with caution, since they could have an increased risk for allergic reactions.
Antibiotic-associated colitis including Clostridium difficile-associated diarrhoea (inflammation of the lining of the colon and diarrhoea)	Antibiotic-associated colitis (also called pseudomembraneous colitis: inflammation of the colon) is a known effect with antibiotics and may range in severity from mild to life threatening. Diarrhoea is a commonly reported adverse effect of antibiotic use (reported in 10% of patients or less, but in more than 1%). It can be causing just some inconvenience, but can also be more severe with the risk of dehydration.	When a patient is experiencing diarrhoea before treatment with amoxicillin, the physician should consider this in his diagnosis. When the diarrhoea is severe, dehydration may occur. A physician should be urgently contacted when severe diarrhoea with bleeding.

Risk	What is known	Preventability
	Therefore, it is important to contact a physician when suffering from severe persistent diarrhoea during or subsequent to the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a physician be consulted and an adequate therapy initiated.	
The product does not work due to resistance of bacteria to the product (Emergence of bacterial resistance)	Sometimes an infection caused by bacteria does not respond to a course of an antibiotic. One of the commonest reasons for this to occur is because the bacteria causing the infection are resistant to the antibiotic that is being taken. This means that they can survive and even multiply despite the antibiotic. Bacteria can become resistant to antibiotics for many reasons.	Using antibiotics carefully can help to reduce the chance of bacteria becoming resistant to them.

Summary of safety concerns – important potential risks

Risk	What is known
Acute generalized exanthemous pustulosis (serious skin condition)	The occurrence at the treatment initiation of a feverish generalized erythema (superficial reddening of the skin) associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction can be severe and requires amoxicillin discontinuation and contra-indicates any subsequent administration of amoxicillin.
Seizures (fits) in patients with kidney problems (Convulsions in renal impaired patients)	Seizures can occur in patients with an impaired kidney function. This is because the kidneys are involved in getting amoxicillin out of the body after intake. Therefore it may result in an unexpected increase of amoxicillin in the body. The dosage should therefore be adjusted for these patients. People with kidney problems should be dosed with caution and monitored at regular intervals. People with a history of seizures or treated epilepsy should be administered amoxicillin with caution.
Blood takes longer to clot (Prolongation of prothrombin time and bleeding time)	The blood may take longer to clot than it normally would when taking amoxicillin. Therefore nosebleeds can occur. This should also be kept in mind if you cut yourself; it may be necessary to contact a physician after cuts.

Summary of safety concerns –Missing information

Risk	What is known
Increased exposure in patients with kidney problems (Dose adjustments in renal impairment)	The kidneys are involved in getting amoxicillin out of the body after intake. Patient with kidney problems can have difficulty getting amoxicillin out of the body, this may result in an unexpected increase of amoxicillin in the body. The dosage should therefore be adjusted for these patients. People with kidney problems should be dosed with caution and monitored at regular intervals.
Exposure in pregnant women	Amoxicillin passes the placenta. Data on limited number of exposed pregnancies indicate no adverse event of amoxicillin on pregnancy or the health of the foetus or newborn child. As a precautionary measure, amoxicillin should only be used during pregnancy if in the judgment of the physician the potential benefits outweigh the possible hazards.
Experience in lactating women (exposure through human milk) (exposure through breast feeding)	Amoxicillin passes into the breast milk in small quantity. In rare cases this can lead to diarrhoea and/or fungal infections in the infant. Also the possibility of sensitisation of the infant to antibiotics should be considered. Therefore a physician should be consulted and in some cases it may be necessary to stop breastfeeding.

VI.2.5 Summary of additional 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.
This medicine has no additional risk minimisation measures.

VI.2.6 Planned post-authorisation development plan

No post-authorisation studies are planned and therefore this section is not applicable.