

Questions and answers on the referral for Augmentin (amoxicillin and clavulanic acid)

The European Medicines Agency has completed a review of Augmentin. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that there is a need to harmonise the prescribing information for Augmentin in the European Union (EU). The review was carried out under an 'Article 30' referral¹.

What is Augmentin?

Augmentin is an antibiotic. It is used for the short-term treatment of a number of common infections:

- infections of the respiratory tract (airways and lungs) such as tonsillitis, sinusitis, otitis media (infection of the middle ear), exacerbation (flare up) of bronchitis and pneumonia;
- infections of the urinary tract (the structures that carry urine in the body);
- infections of the skin and soft tissues (the structures just below the skin);

It can also be used for more serious infections, such as bone or intra-abdominal infections. It can be used in the prevention of some infections.

Augmentin, also known as 'coamoxiclav', contains two active substances: amoxicillin, which is an antibiotic belonging to the beta-lactam family (the same family as penicillins), and clavulanic acid, which is a 'beta-lactamase inhibitor'. When Augmentin is absorbed in the body, the amoxicillin component kills the bacteria that are causing the infection, while the clavulanic acid component blocks an enzyme, betalactamase that enable the bacteria to destroy amoxicillin. As a result, the antibiotic can work for longer, and is more effective in killing bacteria. The ratio of amoxicillin to clavulanic acid can vary from 16:1 (one gram of amoxicillin to 62.5 mg clavulanic acid) to 2:1 (250 mg of amoxicillin to 125mg of clavulanic acid).

Augmentin is available as tablets, oral suspensions and solutions for injections or infusion (drip into vein). It is also available under other trade names, such as Augmentan, Augmentine, Clavamel, Clavamox, Clavepen, Clavulin, Clavumox, Clavurion, Neoduplamox, Noprilam, Pangamox, Penilan and Spektramox.

Why was Augmentin reviewed?

Augmentin is authorised in the EU via national procedures. This has led to divergences in the way the medicine can be used across Member States in which this medicine is approved, as seen in the differences in the Summaries of Product Characteristics (SPCs), labelling and package leaflets in the countries where the medicines are marketed.

On 28 January 2008, the European Commission referred the matter to the CHMP in order to harmonise the marketing authorisations for Augmentin in the EU.

¹ Article 30 of Directive 2001/83/EC as amended, referral on the grounds of divergent decisions adopted by Member States

What are the conclusions of the CHMP?

The CHMP, in the light of the data submitted and the scientific discussion within the Committee, was of the opinion that the SPCs, labelling and package leaflets should be harmonised across the EU. The areas harmonised include:

Therapeutic indications

The indications (the diseases the medicine can be used to treat) for the tablets and oral suspensions depend on the ratio of the active substances and have been harmonised to include: acute bacterial sinusitis (adequately diagnosed), acute otitis media, lower respiratory tract infections (such as acute exacerbations of chronic bronchitis and community acquired pneumonia), cystitis, pyelonephritis, and skin and soft tissue infections in particular cellulites, animal bites, severe dental abscess with spreading cellulitis, and bone and joint infections.

The Committee agreed that the tablets and oral suspensions containing amoxicillin and clavulanic acid as a 2:1 ratio should not be used in lower respiratory tract infections or in otitis media. This is because the total daily dose of amoxicillin these formulations provide using the standard dosages is not sufficient to kill effectively the bacteria while higher dosages may result in patients receiving too much clavulanic acid.

The Committee also restricted the use of oral suspensions containing amoxicillin and clavulanic acid as a 14:1 ratio to the treatment of children with acute otitis media and community acquired pneumonia likely to have been caused by penicillin-resistant *Streptococcus pneumoniae*.

Tablets containing amoxicillin and clavulanic acid as a 16:1 ratio should only be used for the treatment of community-acquired pneumonia that is likely to have been caused by penicillin-resistant *Streptococcus pneumoniae*. The 16:1 ratio is for patients aged at least 16 years.

The CHMP harmonised the indications for Augmentin used as an intravenous injection (into a vein) to include certain diseases for which oral treatment is not appropriate: severe infections of the ear, nose and throat, intra-abdominal infections and female genital infections. The Committee agreed that the injection can always be used at the start of treatment, before switching to the tablets or oral suspension, for all the disease for which oral treatment is appropriate. The CHMP also agreed that the injection can be used to prevent infections in major surgeries involving the gut, pelvic cavity, head and neck and the biliary tract.

The CHMP recommended that the indication of tonsillitis for Augmentin be removed.

Posology and method of administration

The Committee harmonised the text of the posology section of the SPC to highlight to prescribers the need to check the appropriateness of the amoxicillin:clavulanic acid ratio to use, looking in particular at the type of bacteria that may be causing infections, the severity and site of infection, and the age, weight and kidney function of the patients.

The CHMP harmonised the posology for children, using the patient's weight as the cut-off point to distinguish the dosage for 'adults and adolescents' (weighing more than 40 kg) from the dosage for children (below 40 kg).

Previously, Augmentin tablets and suspensions using a 4:1 ratio had been taken twice daily, however the CHMP agreed that a twice-daily dosage was not appropriate as a standard dosage. The Committee's recommended dosage is now three times daily. However, the twice-daily dosage can still be used in patients for whom a reduced dose of Augmentin is needed, such as those with problems with their liver or kidneys.

The Committee also recommended that in situations where a higher dose of amoxicillin is required, another preparation of Augmentin should be chosen in order to avoid the patient taking too much clavulanic acid.

Contra-indications

The Committee harmonised the contra-indications for Augmentin to two contra-indications: in case of hypersensitivity to penicillins, or allergic reaction to other beta-lactam antibiotics, and in case of jaundice or liver problems previously caused by amoxicillin/clavulanic acid.

Other

The CHMP harmonised the information in the SPC on the potential interaction of Augmentin with other medicines, and with some laboratory tests. The Committee also harmonised the section listing the types of bacteria against which the medicines is active, and the concentration at which it is effective.

Suitability of different types of Augmentin in EU countries

The Committee also agreed that the formulations of Augmentin that are made available in each EU country must be tailored to the types of bacteria that are 'prevalent' in the country, especially their ability to resist the action of certain antibiotics. The CHMP emphasized that the availability of a medicine containing a certain ratio of amoxicillin:clavulanic acid in one country did not mean that this medicine should also be used in another country. This applies in particular to medicines with a 2:1 or 4:1 ratio, as these, taken at the recommended dose, may not provide a dose of amoxicillin that is sufficient to kill locally prevalent bacteria in areas where there is a high level of resistance to penicillins.

The amended information to doctors and patients is available [here](#).

The European Commission issued a decision on 19 October 2009.

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