European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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QUESTIONS AND ANSWERS ON THE REVIEW OF KETEK (TELITHROMYCIN)

As part of its continuous monitoring of medicines, the European Medicines Agency (EMEA) has reviewed the available information on the safety and effectiveness of Ketek (telithromycin). It has concluded that the ways in which Ketek can be used must be restricted, that some of the warnings in the medicine's prescribing information must be strengthened, and that patients with myasthenia gravis (a disease of the nerves causing muscle weakness) should not be given the medicine.

What is Ketek?
Ketek contains the active substance telithromycin. Telithromycin is an antibiotic that belongs to the class called the 'ketolides', which kill bacteria by stopping them making proteins.

Ketek is used to treat adult patients with the following infections:

- community-acquired pneumonia (an infection of the lungs that is caught outside of hospital),
- acute exacerbation (flare-up) of chronic bronchitis (long-lasting inflammation of the airways in the lungs),
- acute sinusitis (short-lived infection of the sinuses, air-filled passageways in the bones around the nose and eyes).

Ketek is also used to treat patients aged 12 years or over who have tonsillitis or pharyngitis (infections of the tonsils or throat) caused by the bacterium *Streptococcus pyogenes*. Ketek is used when a class of antibiotics called 'beta-lactams' are not appropriate. Beta-lactams include penicillin, ampicillin and amoxicillin.

Ketek is authorised in the European Union/European Economic Area, and is marketed in Austria, Belgium, Cyprus, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Norway, Portugal, Slovenia, Spain, Sweden and the United Kingdom. Telithromycin is also authorised as Levviax, but this product is not marketed in the European Union.

Why has the EMEA reviewed the medicine?
The EMEA has been carrying out a comprehensive review of the safety and effectiveness of Ketek since January 2006, following reports of severe liver side effects in patients taking telithromycin. As part of this review, several updates relating to the safety of Ketek were made to the Product Information during 2006. These included strengthening the warnings on serious liver reactions and contraindicating the use of the medicine in patients with a previous history of serious liver disorders. In January 2007, the Agency's Committee for Medicinal Products for Human Use (CHMP) requested updated information from the company that makes Ketek on the safety and effectiveness of the medicine in each of its approved indications (listed above). The review of this information was finalised at the CHMP's meeting of 19-22 March 2007[1].

Which data has the CHMP reviewed?
The review included information on the safety and effectiveness of Ketek in each of its approved indications, as well as a comparison of the medicine's balance of benefits and risks with those of other antibiotic medicines that are used to treat infections of the respiratory tract (lungs and airways). The

[1] This procedure is described in Article 22 of Regulation (EC) No 726/2004 and results in a CHMP scientific opinion.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.europa.eu http://www.emea.europa.eu
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company also presented information on 'resistance' to other antibiotic medicines in European countries, and the activity of Ketek against infections that are resistant to these medicines. Resistance is where a bacterium is insensitive to a medicine, having developed ways of fighting its effects.

What were the conclusions of the CHMP?
The CHMP concluded that the effectiveness of Ketek has been demonstrated in its approved indications. This includes the treatment of infections caused by bacteria that are resistant to other types of antibiotic medicine, notably macrolides (including erythromycin and azithromycin) and beta-lactams.

The CHMP also found that, compared with other antibiotic medicines, the use of Ketek is associated with a greater risk of certain side effects. Some of these side effects may be serious, including a worsening of myasthenia gravis (which can be life-threatening) transient loss of consciousness, and temporary disturbances to vision, such as blurred vision, difficulty focusing and double vision. Severe problems with the liver are rare, but do not occur more frequently than with other antibiotic medicines. These side effects are already included in the European product information for Ketek.

The Committee noted that community-acquired pneumonia is a serious infection that carries a significant risk of death. This is not the case for the other infections that Ketek is used to treat. Therefore, based on the benefits and risks of the use of Ketek in each of the indications, the CHMP concluded that:

- the benefits of using Ketek to treat community-acquired pneumonia continue to outweigh its risks,
- for acute exacerbation of chronic bronchitis and acute bacterial sinusitis, the benefits of using Ketek only outweigh its risks when treating infections caused by bacteria that are known or suspected to be resistant to beta-lactams or macrolides,
- for tonsillitis/pharyngitis, the benefits of using Ketek outweigh its risks only when beta-lactams are not appropriate, in countries or regions where there are high levels of resistance to macrolides.

For most patients, this means that other antibiotic medicines are more likely to be used as first-line options for bronchitis, sinusitis and tonsillitis/pharyngitis in the future. Prescribers should consider official guidance on the appropriate use of antibiotic medicines and local levels of resistance to antibiotics.

The CHMP recommended that the prescribing information for Ketek be updated to reflect these restrictions. It also recommended that the existing warning over the use of Ketek in patients with myasthenia gravis be upgraded to a contraindication, meaning that patients with this disease should not take the medicine. It also recommended that the prescribing information be updated to strengthen warnings on transient loss of consciousness and effects on vision, including their impact on driving and using machinery, and to recommend that the medicine be taken at bedtime to reduce the impact of these side effects on daily life.

What is the advice to patients and prescribers?

- Doctors should prescribe Ketek according to the updated prescribing information, and consult official guidance on the use of antibiotics.
- Patients who are already taking Ketek should not stop their treatment unless they have been advised to do so by their doctor or pharmacist.
- Patients who have questions or concerns should talk to their doctor or pharmacist.

For further information, see the updated Product Information adopted by the CHMP on 22 March 2007.

A European Commission decision on this opinion will be issued in due course.