

Questions and answers on the review of oral formulations of medicines containing norfloxacin

The European Medicines Agency (EMA) has completed a review of the safety and effectiveness of 'oral formulations' of medicines containing norfloxacin for the treatment of complicated pyelonephritis. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of these medicines do not outweigh their risks for this type of infection, and that this indication should be removed from the marketing authorisations for these medicines throughout Europe. The review was carried out under an 'Article 31' referral¹.

The use of other formulations of norfloxacin, such as injections, and its use for other diseases, were unaffected by the CHMP's review.

What is norfloxacin?

Norfloxacin is an antibiotic that is used to treat infections of the urinary tract (the structures that carry urine). One type of urinary infection is 'complicated pyelonephritis', a type of kidney infection. 'Complicated' means that there are other factors that are making the infection worse. Norfloxacin is currently used to treat 'acute' (sudden) and 'chronic' (long-term) complicated pyelonephritis.

Medicines containing norfloxacin have been available in all European Union (EU) Member States since the mid-1980s under various trade names. They are available as 'oral formulations' (medicines that are taken by mouth, such as tablets, capsules and solutions) as well as formulations for injection. They are authorised by regulatory authorities in Member States.

Norfloxacin belongs to the 'fluoroquinolone' family. It works by blocking an enzyme that bacteria use to make more DNA. By doing this, it stops the bacteria that are causing an infection from growing and multiplying.

Why were norfloxacin-containing medicines reviewed?

During the assessment of an application to renew the marketing authorisation for a norfloxacin-containing medicine, the Belgian medicines regulatory agency questioned the effectiveness of oral formulations of the medicine for complicated pyelonephritis, in comparison with other fluoroquinolones. In current practice, this disease is usually treated using either injectable antibiotics, or other fluoroquinolones taken by mouth or given by injection.

Consequently, the Belgian medicines regulatory agency asked the CHMP to carry out an assessment of the benefit-risk balance of oral formulations of all norfloxacin-containing medicines for complicated pyelonephritis, and to issue an opinion on whether this indication should be maintained, varied, suspended or withdrawn from the marketing authorisations for oral formulations of products containing norfloxacin across the European Union.

Which data has the CHMP reviewed?

The CHMP reviewed data supplied by the companies that make norfloxacin-containing medicines. This included the results of the small number of studies that have looked at the safety and effectiveness of oral formulations of norfloxacin when used to treat complicated pyelonephritis. Most

¹ Article 31 of Directive 2001/83/EC as amended, referral under Community interest.

of these studies were carried out in the 1980s. The CHMP also looked at information on the levels of norfloxacin in the blood and tissues.

What are the conclusions of the CHMP?

The CHMP noted that there is very little information available to support the effectiveness of oral formulations of norfloxacin-containing medicines in the treatment of complicated pyelonephritis. Most of the evidence supplied by the companies was weak, since the studies involved few patients, patients who also had other infections or patients who were taking other medicines.

Information on the levels of norfloxacin in the blood and tissues was also limited. However, this information showed that levels of alternative antibiotics taken by mouth tend to be higher and may persist for longer than norfloxacin, so they may be more useful in treating complicated pyelonephritis than norfloxacin.

Therefore, the CHMP concluded that the benefits of oral formulations of norfloxacin do not outweigh their risks for complicated pyelonephritis. The Committee therefore recommended that this indication should be removed from the marketing authorisations for these medicines.

What are the recommendations for patients and prescribers?

- Doctors should no longer prescribe oral formulations of norfloxacin-containing medicines for complicated pyelonephritis. They should consider switching patients already taking norfloxacin by mouth for this type of infection to alternative treatments.
- Patients who are taking norfloxacin-containing medicines for complicated pyelonephritis should discuss their treatment with their doctor if they continue to have symptoms or at their next scheduled visit.
- Patients who have any questions should speak to their doctor or pharmacist.

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