

▼ Moxifloxacin – a new fluoroquinolone antibacterial

▼ Moxifloxacin (Avelox – Bayer plc), the latest fluoroquinolone antibacterial to be launched in the UK, is licensed for the oral treatment of adults with community-acquired pneumonia, acute exacerbation of chronic bronchitis or acute sinusitis. The company claims that the drug provides “rapid relief from chest infections”. Here we review the place of moxifloxacin in treating patients with respiratory tract infections.

Antimicrobial activity

Like other fluoroquinolones, moxifloxacin (pronounced *moks-i-floks-a-sin*) works by interfering with the replication, transcription and repair of bacterial DNA.¹ It is active in vitro against respiratory pathogens such as methicillin*-sensitive *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*.² Moxifloxacin is more active in vitro against *S. pneumoniae* and *Streptococcus pyogenes* than other fluoroquinolones available in the UK.² The drug is not active against *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus*. The emergence of strains of *S. pneumoniae* resistant to fluoroquinolones including moxifloxacin has been reported in England³ and Asia.⁴

Licensed indications and dose

In the UK, moxifloxacin is available only as a 400mg tablet for the oral treatment of adults, although an i.v. formulation is available in other countries. The licensed dose is 400mg once daily for 10 days for non-severe community-acquired pneumonia; for 5–10 days for acute exacerbation of chronic bronchitis; or for 7 days for “adequately diagnosed” acute bacterial sinusitis.⁵

Use in community-acquired pneumonia

Standard therapy

Amoxicillin* (or a macrolide for patients who are allergic to penicillin) is the treatment of choice for patients with non-severe community-acquired pneumonia (i.e. those who can be managed in the community or with brief inpatient treatment).^{6,7} For those with more severe community-acquired pneumonia, who require hospital admission, infection with an atypical pathogen is more likely, so combined use of amoxicillin and a macrolide is recommended; an oral fluoroquinolone with enhanced pneumococcal activity (e.g. levofloxacin, moxifloxacin) may be an alternative.

Clinical efficacy of moxifloxacin

Three published double-blind randomised controlled trials have compared oral moxifloxacin (400mg daily) with oral amoxicillin (1g three times daily),⁸ oral clarithromycin (500mg twice daily),⁹ or a combination of these two regimens,¹⁰ in a total of 1,447 adults with community-acquired pneumonia, most of whom were treated in the community. Clinical cure rate after 10 days’ treatment (the primary outcome measure) did not differ significantly between moxifloxacin and the comparator in the only study to report

an intention-to-treat analysis (86.5% with moxifloxacin vs. 82.2% with amoxicillin)⁸ or in the other two trials.^{9,10}

Use in chronic bronchitis

Standard therapy

Patients with chronic obstructive pulmonary disease (the term that has superseded labels such as ‘chronic bronchitis’) who experience an acute exacerbation with increased sputum purulence should be treated with a penicillin, macrolide or tetracycline.¹¹

Clinical efficacy of moxifloxacin

Five published double-blind randomised controlled trials have assessed oral moxifloxacin in patients with acute exacerbations of chronic bronchitis who had increased purulent or mucopurulent sputum.^{12–16} The primary outcome measure in all the trials was the rate of clinical cure or improvement (assessed at 0–21 days after treatment ended).

In a study involving 733 adults, there was no difference between moxifloxacin (400mg daily for 5 days) and oral standard therapy (7 days of amoxicillin 500mg three times daily, clarithromycin 500mg twice daily or cefuroxime axetil 250mg twice daily) on the primary outcome measure (87.6% vs. 83%, respectively).¹² In another study, 926 adults received moxifloxacin (400mg daily for 5 days or 10 days) or oral clarithromycin (500mg twice daily for 10 days).¹³ The three groups did not differ significantly on the primary outcome measure (95% with moxifloxacin for 5 days vs. 95% with moxifloxacin for 10 days vs. 94% with clarithromycin). Also, in the other three studies, involving a total of 1,910 patients, moxifloxacin (400mg daily for 5 days) did not differ significantly from oral clarithromycin (500mg twice daily for 7 days),¹⁴ oral azithromycin (500mg for 1 day then 250mg daily for 4 days)¹⁵ or oral levofloxacin (500mg daily for 7 days)¹⁶ on the primary outcome measure.

Use in acute bacterial sinusitis

Standard therapy

Antibacterial therapy is not necessary for most patients with acute sinusitis.¹⁷ However, treatment with a penicillin, macrolide or cephalosporin may increase cure rates for those with radiologically or bacteriologically confirmed acute maxillary sinusitis.¹⁸

Clinical efficacy of moxifloxacin

Two double-blind randomised controlled trials compared oral moxifloxacin (400mg daily for 7 days¹⁹ or 10 days²⁰) with oral cefuroxime axetil (250mg twice daily for 10 days)

* This new spelling reflects the use of recommended International Non-proprietary Names (rINNs) instead of former British Approved Names (BANs), as required by European law. For more information, see the *British National Formulary*, or <http://medicines.mhra.gov.uk/inforesources/productinfo/banslist.pdf>

in 1,035 patients with acute bacterial sinusitis confirmed radiologically or bacteriologically. The rates of clinical resolution of symptoms did not differ significantly between moxifloxacin (89–90%) and cefuroxime axetil (87–90%).

“Rapid relief from chest infections”?

Promotional materials state that oral moxifloxacin provides “rapid relief from chest infections”. However, this claim is based on patients’ self-reported secondary-outcome data from one unblinded randomised controlled trial²¹ and on unblinded, non-randomised observational studies.^{22–24} Because of their design, these studies cannot provide convincing evidence that moxifloxacin relieves respiratory tract infections as quickly as, or faster than, do standard antibacterial treatments for these conditions.

Unwanted effects

In trials, the commonest unwanted effects (occurring in up to half of patients) were gastrointestinal disturbances and headache.^{11,14} Other common effects include dizziness, taste disturbance, abdominal pain, and raised serum levels of liver enzymes.⁵ Rarely, moxifloxacin causes tendonitis.

Precautions and contraindications

Prolongation of the QT_c interval on ECG is uncommon with moxifloxacin but may be more likely in patients who are hypokalaemic or taking concomitant medication known to prolong the QT_c interval (e.g. erythromycin, mizolastine, tricyclic antidepressants). Absorption of moxifloxacin is reduced by aluminium, iron or magnesium and so there should

be about 6 hours between taking moxifloxacin and any preparations containing these ions (e.g. antacids). Moxifloxacin is contraindicated in pregnant and breast-feeding women; children and growing adolescents; patients with a history of tendon disease related to quinolone therapy; and patients with QT_c interval prolongation, electrolyte disturbances, clinically relevant bradycardia or heart failure, or previous symptomatic arrhythmias. Moxifloxacin is excreted in the bile and faeces (about 65% of a dose) and via the kidneys (about 35%), and is contraindicated in patients with impaired liver function, severe renal dysfunction (creatinine clearance below 30mL/min) or undergoing renal dialysis.

Approximate drug costs* for typical oral courses

Drug	Dose	Cost
▼moxifloxacin	400mg daily for 5–10 days	£11.00–£21.90
amoxicillin	500mg–1g three times daily for 7 days	£1.90–£2.20
azithromycin	500mg once daily for 3 days	£13.40
clarithromycin	500mg twice daily for 7 days	£23.60
erythromycin	500mg four times daily for 7 days	£8.40
levofloxacin	500mg once daily for 7 days	£19.50

* Based on information in *Drug Tariff* and *Chemist & Druggist*.

Conclusion

Oral ▼moxifloxacin is a new quinolone antibacterial licensed for treating adults with various respiratory infections often managed in primary care. On published clinical evidence, it offers no compelling advantages over established treatments for these conditions. In our view, claims that oral moxifloxacin provides “rapid relief from chest infections” are unsubstantiated, may mislead prescribers and should be withdrawn.

[M=meta-analysis; R=randomised controlled trial]

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