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# Telithromycin: visual disorders

● ***Telithromycin*** **is a macrolide antibiotic with a negative risk-benefit balance. Its efficacy is no better than that of other macrolides.** ***Telithromycin*** **carries a risk of serious adverse effects, including loss of consciousness, QT prolongation, severe liver damage, aggravation of myasthenia gravis, and a high risk of drug interactions.**

● **In Finland, a 7-year pharmacovigilance review identified 20 reports of visual disorders among patients taking** ***telithromycin,*** **including blurred vision, accommodation disorder and diplopia, mainly in young patients and women.**

● **Visual disorders occurred in about 1% of patients receiving** ***telithromycin*** **in clinical trials. They were generally moderate, brief and reversible.**

● **These visual disorders may result from reversible paralysis of the ciliary body due to** ***telithromycin*****.**

● **In practice, these visual disorders, which can be dangerous when driving or operating heavy machinery, add to the already long list of adverse effects of** ***telithromycin*****. They are yet another reason not to use** ***telithromycin*****, but rather a safer macrolide such** ***spiramycin*****.**

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*Telithromycin* is a macrolide antibiotic (**a**)(1-3). There is no evidence that it is more effective than other macrolides, regardless of the bacterial species involved (1). *Telithromycin* shares the adverse effects of all macrolides, mainly including gastrointestinal disorders (diarrhoea, nausea and vomiting, abdominal pain and dyspepsia) and neurological disorders (headache and dizziness). It can also prolong the QT interval when used at the standard oral doses, and also provoke severe liver damage, aggravate myasthenia gravis, as well as cause loss of consciousness (1-4). In addition, like other macrolides, with the exception of *spiramycin*, *telithromycin* can interact with many other drugs, with potentially serious clinical consequences (1-3).

Visual disorders were first observed during clinical trials of *telithromycin* (1-4).

A Finnish review of pharmacovigilance reports published in 2009 examined the frequency, characteristics and reversibility of these ocular adverse effects (5).

**A Finnish review: generally reversible visual disorders.** The Finnish drug regulatory agency has published a 7-year review of pharmacovigilance reports concerning *telithromycin* since its market introduction in 2002. It mentions 20 reports of visual disorders out of a total of 52 reports involving *telithromycin* (5). Most of the patients were young (20 to 40 years) and female (16 cases).

Eight patients had blurred vision and 6 had miscellaneous visual disorders including loss of near or distant visual acuity, image distortion, and visual field disorders. Diplopia, ocular pain and oculogyric episodes were occasionally reported, sometimes associated with general symptoms such as headache, nausea, malaise, and dizziness (5).

In 15 cases the visual disorders occurred within 24 hours after treatment initiation. Outcome was known in 12 cases and was generally favourable. Four patients had not yet recovered normal vision when the disorder was reported. The doses of *telithromycin* are not specified in this review.

**Visual disorders in 1% of patients.** In clinical trials, reversible visual disorders were more frequent with *telithromycin* than with comparator antibiotics (5,6). According to the US Food and Drug Administration (FDA), visual disorders occurred in 0.7% of patients taking *telithromycin* (5). The European Medicines Agency (EMA) estimated that 1.1% of patients treated with *telithromycin* experienced visual disorders, versus 0.4% of patients in comparator groups (6). Blurred vision, other unspecified visual disorders, and abnormal accommodation were reported (1).

Between April 2004 and July 2006, FDA recorded 390 cases of visual disorders associated with *telithromycin*, 71 of which were serious (**b**)(4).

The Finnish review mentions a study based on an Italian register of visual adverse effects attributed to macrolides.

Nearly half of the reports involved *telithromycin* and blurred vision and/or diplopia occurred in about half of the cases linked to *telithromycin* (5).

**Ciliary body dysfunction?** Ophthalmological findings were normal in patients with visual disorders due to *telithromycin* (3).

The underlying mechanism is not entirely clear. One possibility is a reversible effect of *telithromycin* on the ciliary body, delaying ciliary muscle relaxation and thus affecting accommodation (6).

**In practice.** *Telithromycin* is sometimes associated with visual disorders. Even if they are usually moderate and transient, they can be troubling and may make driving or operating heavy machinery dangerous (7).

This is yet another reason to avoid using *telithromycin*, a drug with a clearly unfavourable risk-benefit balance (1).

It is time for the regulatory agencies or the manufacturer to withdraw *telithromycin* from the market.



*a- In 2006 and 2007, certain indications were restricted to second-line use due to numerous adverse effects (ref 8). The licensed indications of telithromycin are worded as follows in the EU summary of product characteristics: "In patients of 18 years and older:*
*-Community-acquired pneumonia, mild or moderate*
*-When treating infections caused by known or suspected beta-lactam and/or macrolide resistance (…): acute exacerbation of chronic bronchitis, acute sinusitis.*
*In patients of 12 years and older:*
*-Tonsillitis/pharyngitis caused by Streptococcus pyogenes, as an alternative when beta-lactam antibiotics are not appropriate in countries/regions with a significant prevalence of macrolide resistant S. pyogenes (…)" (ref 7).*

*b- The European SPC was modified in 2007 to recommend taking the drug at bedtime, in order to reduce the potential impact of visual disorders and loss of consciousness (ref 8).*

**Selected references from Prescrire's literature search.**

**1-** Prescrire Editorial Staff "Telithromycin" *Prescrire Int* 2003; **12** (63): 8-12.
**2-** Prescrire Rédaction "16-1-8. Patients sous macrolide" *Rev Prescrire* 2009; **29** (314 suppl. interactions médicamenteuses).
**3-** "Telithromycin". In: "Martindale The Complete Drug Reference" The Pharmaceutical Press, London. www.medicinescomplete.com accessed 12 June 2009: 6 pages.
**4-** Prescrire Editorial Staff "Telithromycin: visual disorders, myasthenia" *Prescrire Int* 2008; **17** (94): 67.
**5-** Vuorio A and Rajaratnam R "Telithromycin and visual disturbances" *TABU* 2009; **17** (2): 44-46.
**6-** EMA - CHMP "European Public Assessment Report - Ketek (revision 13) - Scientific discussion" 29 pages; posted on EMEA website 9 June 2009.
**7-** Commission européenne "Résumé des caractéristiques du produit - Ketek" 2 June 2009: 14 pages.
**8-** Prescrire Rédaction "Télithromycine: trop de risques graves, mais des agences frileuses" *Rev Prescrire* 2007; **27** (283): 347.