IRISH MEDICINES BOARD

Fluoroquinolones and the risk of QT Prolongation

Fluoroquinolones are broad spectrum antibiotics, authorised for a wide range of indications. Those currently authorised in Ireland include: moxifloxacin, levofloxacin, ofloxacin and ciprofloxacin*.

The potential for fluoroquinolones to cause QT prolongation is recognised and has been previously considered on the basis of available data for the individual substances, as reflected in the product specific information. A further recent European review of study and postmarketing data in relation to QT prolongation and fluoroquinolones concluded that the risk of QT prolongation does not appear to be similar across this class of antibiotics, but that substances may be classified according to their potential to prolong QT interval and precipitate cardiac events (i.e. ventricular arrhythmia). As moxifloxacin has been associated with an established potential for increased risk of QT prolongation, prescribers are reminded to use moxifloxacin only when it is considered inappropriate to use antibacterial agents that are commonly recommended or when these have failed for the treatment of: acute bacterial sinusitis, acute exacerbations of chronic bronchitis, community acquired pneumonia (except severe cases) and mild to moderate pelvic inflammatory disease.

Following assessment of the available evidence, levofloxacin, ofloxacin and ciprofloxacin are considered to have a lower potential to induce QT interval prolongation. It is important to note that in the context of conditions which favour the development of QT prolongation e.g. hypokalaemia, hypomagnesaemia, bradycardia, patients with congenital or acquired QT prolongation, some fluoroquinolones have the potential to induce life-threatening Torsades de Pointes (e.g. moxifloxacin). The product information for fluoroquinolones will be updated and harmonised throughout Europe in relation to the updated assessment of the risk of QT interval prolongation for the individual substances.

For further information and the complete list of fluoroquinolones considered as part of the review please see the following link: **http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500100459.pdf**

Key message:

- The risk of QT interval prolongation with fluoroquinolone antibiotics varies across this class of antibiotics.
- Due to an increased risk of QT prolongation (in addition to the potential for other serious risks, i.e. serious hepatotoxicity), oral moxifloxacin should only be used when use of other antibacterial agents is inappropriate, or have failed.
- Consideration should be given to official guidance on the appropriate use of antibacterial agents.

*** Brands include:**
Moxifloxacin: Avelox – Levofloxacin: Tavanic, Tavager – Ofloxacin: Tarivid, Biravid – Ciprofloxacin: Truoxin, Ciproxin

Direct Healthcare Professional Communications

In the case of urgent and/or important safety issues about a medicinal product, a Direct Healthcare Professional Communication (DHPC) is used to notify healthcare professionals. A DHPC (also known as a 'Dear Doctor Letter') aims to ensure safe and effective use of a marketed medicine and is delivered directly to healthcare professionals by marketing authorisation holders or by competent authorities such as the IMB.

The initiative for issuing a DHPC can come from the European or National regulatory authorities or the marketing authorisation holder. Agreement is needed between the marketing authorisation holder and competent authorities on the content and format of the information with consideration of the supportive evidence, recipients, and distribution timetable. DHPCs are an important communication tool that can aid education and risk management for healthcare professionals. Situations where a DHPC should be considered as part of the risk-management process include:

- Suspension, withdrawal, revocation of a marketing authorisation with recall of the medicine from the market for safety reasons
- Important changes to the Summary of Product Characteristics (SmPC) e.g. new warnings or contraindications, reduced recommended dose, or restricted indications or availability
- A change in the balance of benefits and risks for a medicine

DHPCs are published on the IMB website (**www.imb.ie**) under 'Publications' once they have been distributed. Recent DHPCs published on the IMB website are listed in the Drug Safety Newsletter. Further information can be found on the IMB website and/or in Volume 9A of The Rules Governing Medicinal Products in the European Union – Guidelines on pharmacovigilance for medicinal products for human use – which outlines the obligations of marketing authorisation holders and national competent authorities for pharmacovigilance of licensed medicines including guidance on risk communication and DHPCs.

DHPCs published on IMB website in February 2011

Gadolinium containing contrast agents	Information on the risk of Nephrogenic Systemic Fibrosis (NSF)
Keppra (levetiracetam)	Calibration changes in dosing syringe and new presentations
Revlimid (lenalidomide)	Veneous and arterial thromboembolic event risk
Oruvail and Orugesic (ketoprofen)	Photosensitivity and supply information
Provigil (modafinil)	Change in indications
Lucentis (ranibizumab)	Blocked needles in some injection administration packs

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