Bayer HealthCare
Bayer Schering Pharma

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Bayer Ltd, Ireland
The Atrium
Blackthorn Road
Dublin 18
Ireland

Tel: +353 1 299 9313
Fax: +353 1 206 1456
www.bayer.ie

IMPORTANT AVELOX® (MOXIFLOXACIN) INFORMATION REGARDING SERIOUS ADVERSE REACTIONS AND SAFETY MEASURES

Dear Healthcare Professional,

In agreement with EU regulatory authorities, including the Irish Medicines Board, Bayer would like to inform you of important safety information. A recent assessment of adverse reactions associated with the use of moxifloxacin resulted in the following information and recommendations:

- Treatment with moxifloxacin is associated with a risk of developing fulminant hepatitis potentially leading to life threatening liver failure and risk of potentially life threatening bullous skin reactions like Stevens-Johnson-Syndrome (SJS) or toxic epidermal necrolysis (TEN).

- Due to limited clinical data, moxifloxacin is contraindicated in patients with impaired liver function (Child Pugh C) and in patients with transaminases increased > 5 fold the upper limit of normal (ULN).

- Patients should be advised to stop treatment and to contact their physician if early signs and symptoms of these reactions occur.

- The product information has been appropriately updated.

- Healthcare professionals are encouraged to report any suspected adverse reactions associated with the use of moxifloxacin.

Background
Moxifloxacin is known to impair liver function, and the product information was updated to include Stevens-Johnson-Syndrome (SJS) in 2002. A review of worldwide serious, including fatal, cases of both hepatotoxicity and bullous skin reactions such as SJS and toxic epidermal necrolysis (TEN) reported for moxifloxacin was recently performed.

Safety Concern
The liver injuries possibly related to moxifloxacin were more frequently of cholestatic or mixed hepatocellular-cholestatic than of hepatocellular type. Onset of symptoms was usually between 3 and 10 days. Isolated cases of delayed hepatotoxic effects were also identified and usually occurred 5 to 30 days after cessation of moxifloxacin therapy. Eight reports of fatal hepatic injuries were considered as possibly related to moxifloxacin therapy. Cases of positive re-challenge gave further evidence of a causal relationship. However, the majority of patients experiencing serious liver injuries where the outcome was reported improved or recovered.

TEN was reported in several cases where a causal relationship was considered possible; this included two cases with fatal outcome. Additionally, a total of 35 individual cases of SJS were reported, including three cases where there was a fatal outcome and seven cases which were considered life-threatening. In these 10 cases of severe SJS, a progression to TEN was documented in three patients.

Based on the large patient exposure, the incidence of both life threatening liver injuries and TEN is very low, although a definite frequency cannot be calculated from these reports.

As a consequence of this review, Bayer has revised the product information for both the 400mg tablets and the 400mg/250ml solution for infusion for moxifloxacin across the EU (see annex for revised summary of product characteristics and package leaflet for the tablet formulation).

Recommendations to Healthcare Professionals
We would like to remind you that moxifloxacin is contraindicated in patients with impaired liver function (Child Pugh C) and in patients with transaminases increased > 5 fold ULN.

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We would like to further remind you to be vigilant for the early signs and symptoms of severe liver injury and bullous skin reactions like SJS or TEN. Patients should be advised to stop treatment immediately and to contact a physician if relevant signs or symptoms occur, including rapidly developing asthenia associated with jaundice, dark urine, bleeding tendency and hepatic encephalopathy.

When prescribing moxifloxacin, consideration should be given to official guidance on the appropriate use of antibacterial agents which is especially relevant with regard to treatment of less severe infections.

Call for reporting
If you have observed similar cases, please report adverse reactions to Bayer Limited or to the Irish Medicines Board in the usual way.

Communication information
If you have any further questions please do not hesitate to contact our Medical Information department at Bayer Limited, tel. 01 2999313. Additionally, the Irish Medicines Board has issued information on their website at www.imb.ie under publications.

Annexes:
Text of the revised Avelox 400 mg film-coated tablets SmPC and, if applicable, Avelox 400 mg/250 ml Solution for Infusion SmPC (with changes made visible). Updated PILs can be found on www.medicines.ie

Yours sincerely

Dr. Brona O'Neill
Medical Affairs Manager, Bayer Limited