April 2025

Educational materials are not advertising

Direct Healthcare Professional Communication:

Name of the medicinal products:
1. Moximac, film-coated tablets, 400 mg,
RC No. UA/17579/01/01.
2. MOXIFLOXACIN (IN THE FORM OF HYDROCHLORIDE) 400 MG TABLETS
RC No. UA/18989/01/01
3. MOXIFLOXACIN HYDROCHLORIDE DISPERSIBLE TABLETS 100 MG dispersible tablets 100 mg
RC No. UA/18263/01/01.
4. LEVOMAC 750, film-coated tablets, 750 mg,
RC No. UA/15561/01/01
5. LEVOMAC I/V, solution for infusions, 500 mg/100 ml
RC No. UA/13772/01/01
6. LEVOMAC, film-coated tablets, 250 mg and 500 mg,
RC No. UA/8637/01/01, UA/8637/01/02
7. LEVOFLOXACIN 100 MG DISPERSIBLE TABLETS, dispersible tablets, 100 mg,
RC No. UA/18977/01/01
8. LEVOFLOXACIN 250, LEVOFLOXACIN 500, LEVOFLOXACIN 750, film-coated tablets, 250 mg, or 500 mg, or 750 mg,
RC No. UA/15003/01/01, UA/15003/01/02, UA/15003/01/03

Systemic and inhaled fluoroquinolones: risk of heart valve regurgitation/incompetence

Dear Healthcare professional,

Marketing authorization holders of fluoroquinolone antibiotics products in agreement with the European Medicines Agency and the Macleods Pharmaceuticals Limited would like to inform you of the risk of heart valve regurgitation/incompetence associated with fluoroquinolones for systemic and inhalation use.

Summary:

- **Systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.**

- **Conditions predisposing to heart valve regurgitation/incompetence include congenital or pre-existing heart valve disease, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, hypertension, rheumatoid arthritis, and infective endocarditis.**

- **In patients at risk for heart valve regurgitation/incompetence, systemic and inhaled fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options.**

- **Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.**

Background on the safety concern

Fluoroquinolones are antibiotics approved in the European Union for the treatment of certain bacterial infections, including life-threatening ones. Because they can have serious and long lasting side effects, their use is generally restricted to infections where it is considered inappropriate to use other antibiotics commonly recommended for these infections. Fluoroquinolones should only be used after carefully assessing its likely benefits and its risks including that of aortic aneurysm and dissection.

A recent epidemiological study [1] reported an about 2-fold increase in risk of mitral and aortic regurgitation in patients taking systemic fluoroquinolones compared with patients taking other antibiotics (amoxicillin or azithromycin).

Several medically confirmed cases of heart valve regurgitation/incompetence affecting any heart valve have been reported in patients receiving fluoroquinolones with probable or possible causal association. These data indicate that fluoroquinolones can cause heart valve regurgitation/incompetence. Additionally, a laboratory study [2] reported that exposure to ciprofloxacin led to collagen degradation in aortic myofibroblasts cells donated from patients with aortopathy, including aortic regurgitation. This finding provides insight into how fluoroquinolone-associated degradation of connective tissue may be associated with heart valve regurgitation/incompetence. Collagen degradation has also been postulated for fluoroquinolone-associated disorders of tendons and the aorta.

Factors that increase the risk for heart valve regurgitation/incompetence include congenital or pre-existing heart valve disease, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, hypertension, rheumatoid arthritis, and infective endocarditis.

In patients at risk for heart valve regurgitation/incompetence, systemic and inhaled fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic treatment options. Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.

Call for reporting

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Reporting suspected adverse reactions after registration of a medicinal product is important. This ensures continuous monitoring of the benefit/risk ratio of the medicinal product. We ask healthcare professionals to report any suspected adverse reactions after the use of fluoroquinolones through the state reporting system of the State Expert Center of the Ministry of Health of Ukraine by filling out the adverse reaction report card at **https://aisf.dec.gov.ua**.

Company contact point

If you have any questions or need additional information about medicines, you can contact the Contact Person responsible for pharmacovigilance in Ukraine of MACLEODS PHARMACEUTICALS LIMITED, located at: Ukraine, 02081, Kyiv, Zdolbunivska St., 7-D.
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Sincerely, Representative Office Director

Vijay Badekar

References

[1] Etminan M, Sodhi M, Ganjizadeh-Zavareh S, Carleton B, Kezouh A, Brophy JM. Oral Fluoroquinolones and Risk of Mitral and Aortic Regurgitation. J Am Coll Cardiol. 2019 Sep 17; 74(11):1444-1450.
[2] Guzzardi DG, Teng G, Kang S, Geeraert PJ, Pattar SS, Svystonyuk DA, Belke DD, Fedak PWM. Induction of human aortic myofibroblast-mediated extracellular matrix dysregulation: A potential mechanism of fluoroquinolone-associated aortopathy. J Thorac Cardiovasc Surg. 2019 Jan; 157(1):109-119.