# Direct Healthcare Professional Communication

**Systemic and inhaled fluoroquinolones: warning about new risk of heart valve regurgitation/incompetence.**

## Date: 05-Nov-2020

## Systemic Fluoroquinolones

| Trade Name | Generic Name | Registration No. |
|---|---|---|
| TARIVID 200MG F-C TAB | OFLOXACIN | 37-23-94 |
| TARIVID I.V2MG-MLSOLUTION FOR INFUSION | OFLOXACIN | 38-23-96 |
| TAVANIC 250MG F.C TAB | LEVOFLOXACIN | 43-23-02 |
| TAVANIC 500MG F.C TAB | LEVOFLOXACIN | 44-23-02 |
| TAVANIC 5 MG -1 ML SOLUTION I.V INFUSION | LEVOFLOXACIN | 46-23-03 |

**Dear Healthcare professional,**

SANOFI Saudi Arabi in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform of the new risk of heart valve regurgitation/incompetence associated with fluoroquinolones for systemic and inhalation use.

### *Summary*

- New data suggests that systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.
- 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.
- 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.
- Patients should be informed of the risk of heart valve regurgitation/incompetence associated with the use of fluoroquinolones and advised to seek immediate medical attention in case of onset of dyspnoea or heart palpitations, or development of oedema of the abdomen or lower extremities.

### *Background on the safety concern*

Fluoroquinolones are antibiotics approved for the treatment of certain bacterial infections, including life-threatening ones that were subject to a Direct Healthcare Professional Communication on 10-Jan-2019 about the risk of disabling and potentially irreversible serious

side effects and the risk of aortic aneurysm and dissection. Their use is restricted to severe infections or infections where it is considered inappropriate to use other antibiotics commonly recommended for these infections and the fluoroquinolones prescription shall be considered after a careful assessment of the benefits and risks.

A recent epidemiological study [1] reported an approximatively 2-fold increase in the 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 at least possible causal association.

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.

Healthcare professionals are informed that a careful assessment of the benefits and risks of fluoroquinolones use and consideration of other therapeutic options are advised in patients with risk factors or conditions predisposing to heart valve regurgitation/incompetence (such as Marfan syndrome, Ehlers-Danlos syndrome, Turner syndrome, Behçet's disease, hypertension, rheumatoid arthritis, and infective endocarditis). In addition, healthcare professionals are reminded of the already recommended careful consideration of fluoroquinolones use in patients with risk factors or conditions predisposing to aortic aneurysm or dissection.

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

The product information for fluoroquinolones-containing medicines will be updated accordingly.

## *Call for reporting for adverse reactions*

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to National Pharmacovigilance and Drug Safety Center in SFDA.

Website: https://ade.sfda.gov.sa/

E-mail: npc.drug@sfda.gov.sa

Fax: +966-11-2057662

***Company contact point***

For SANOFI Saudi Arabia Pharmacovigilance Center please contact us in the below contact information.

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Kind regards,

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Qualified Person for Pharmacovigilance (QPPV)

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 Cardial. 2019 Sep 17;74(11):1444-1450.
[2] Guzzardi DG, Teng G, Kang S, Geeraert PJ, Pattar SS, Svystonyuk DA, Belke DO, 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.