Drug Safety Update

Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

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Contents

The Medicines and Healthcare products Regulatory Agency is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

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Following a review of the cardiac safety of simeprevir for hepatitis C, concomitant use of amiodarone for heart-rhythm disorders with simeprevir and sofosbuvir combination therapy should be avoided unless other antiarrhythmics cannot be given. This advice is due to a risk of severe bradycardia and heart block if taken together—see article 1.

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1 **Simeprevir with sofosbuvir: risk of severe bradycardia and heart block when taken with amiodarone**

Avoid concomitant use of amiodarone with simeprevir (Olysio▼) and sofosbuvir (Sovaldi▼) combination therapy, unless other antiarrhythmics cannot be given.

When treating patients with both heart rhythm disorders and hepatitis C:

- closely monitor patients taking amiodarone if they start taking the combination simeprevir and sofosbuvir; sofosbuvir and daclatasvir; and the fixed-dose combination of sofosbuvir and ledipasvir (particularly during the first weeks of treatment)
- only start amiodarone in patients taking any of these antiviral combinations when other antiarrhythmics are not tolerated or contraindicated; monitor closely (particularly during the first weeks of treatment)
- monitor patients at high risk of bradyarrhythmia continuously for 48 hours in an appropriate clinical setting after starting concomitant amiodarone and antiviral treatment
- monitor patients who have stopped amiodarone within the last few months and need to start taking any of these antiviral combinations—this is due to the long half-life of amiodarone
- advise patients taking amiodarone with any of these antiviral combinations to watch out for signs and symptoms of bradycardia and heart block, and to get medical help urgently if they experience any of these symptoms:
    - shortness of breath
    - light-headedness
    - palpitations
    - fainting
- please continue to report any suspected adverse reactions to any medicine on a Yellow Card

Simeprevir is a direct-acting antiviral medicine licensed to treat hepatitis C in combination with other medicines, including sofosbuvir. Amiodarone is licensed to treat severe heart-rhythm disorders in patients not responding to other treatments or when other treatments cannot be used.

In May's issue of Drug Safety Update, we issued advice on the use of some sofosbuvir combination therapy with amiodarone. We are now extending that advice to simeprevir.

MHRA and other EU medicines regulators have reviewed the cardiac safety of simeprevir, after a similar review of bradycardia events with sofosbuvir, daclatasvir, and ledipasvir with amiodarone use. Two EU cases of bradycardia events after the use of simeprevir with sofosbuvir and concomitant amiodarone use were identified. The recommendations from the review are outlined above.

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2 **Letters sent to healthcare professionals in July 2015**

Last month, letters were sent regarding:

- SGLT2 inhibitors: risk of diabetic ketoacidosis (see also June Drug Safety Update)
- Xgeva▼ (denosumab): contraindication in patients with unhealed lesions from dental or oral surgery; introduction of patient reminder card for risk of osteonecrosis of the jaw (see also July Drug Safety Update)

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