

07 April 2015

IMPORTANT DRUG WARNING

Subject: Serious and Life-Threatening Cases of Symptomatic Bradycardia as well as One Case of Fatal Cardiac Arrest Reported with Co-administration of Amiodarone With Either Harvoni® (ledipasvir and sofosbuvir fixed-dose combination) or With Sovaldi® (sofosbuvir) in Combination with Another Direct Acting Antiviral.

Dear Health Care Provider,

Gilead Sciences Ireland UC (previously Gilead Sciences Limited) and its authorised representative in Saudi Arabia, Cigalah Group, by agreement with Saudi Food and Drug Authority would like to inform you of new important safety information for Harvoni and Sovaldi.

Summary

- Post marketing cases of symptomatic bradycardia, as well as one fatal cardiac arrest and cases requiring pacemaker insertion have been reported in patients taking amiodarone and Harvoni, or amiodarone and Sovaldi in combination with another Direct Acting Antiviral (DAA), for example, daclatasvir or simeprevir (Olysio).
- In patients receiving amiodarone, bradycardia was observed within hours to days of starting Harvoni or Sovaldi in combination with another DAA
- Risk factors for the development of symptomatic bradycardia in patients receiving amiodarone may include coadministration of a beta blocker, or those with underlying cardiac comorbidities and/or advanced liver disease.
- Coadministration of amiodarone with Harvoni or coadministration of amiodarone with Sovaldi in combination with another DAA is not recommended

Further Information

- Harvoni is indicated for the treatment of chronic hepatitis C (CHC) in adults (for hepatitis C virus (HCV) genotype-specific activity see the full prescribing information).
- Sovaldi is indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in adults.

Nine cases of symptomatic bradycardia have been reported during post marketing in patients receiving amiodarone with Sovaldi in combination with another DAA (daclatasvir, an investigational DAA, or Olysio (simeprevir)) or amiodarone with Harvoni. Seven patients were also receiving a beta blocker.

- Six cases occurred within the first 24 hours and the remaining three cases occurred within the first 2-12 days following HCV treatment initiation.
- One case was a fatal cardiac arrest and 3 cases required pacemaker intervention.
- In 3 cases, rechallenge with HCV treatment in the setting of continued amiodarone therapy resulted in recurrence of symptomatic bradycardia.
- In one case discontinuation of amiodarone followed by rechallenge of HCV treatment after 8 weeks did not result in recurrent bradycardia.
- Three of the 9 cases were in patients receiving Harvoni, 5 cases were in patients receiving Sovaldi plus an investigational agent (daclatasvir) and 1 case was in a patient receiving Sovaldi with Olysio (simeprevir).

Prescriber Action

Coadministration of amiodarone with Harvoni or Coadministration of amiodarone with Sovaldi in combination with another DAA is not recommended.

For patients taking amiodarone who have no other alternative, viable treatment options and who will be co-administered Harvoni, or for patient taking amiodarone who has no other alternative, viable treatment options and who will be co-administered Sovaldi in combination with another DAA:

- Counsel patients about the risk of serious symptomatic bradycardia
- Cardiac monitoring in an in-patient setting for the first 48 hours of coadministration is recommended, after which outpatient or self-monitoring of the heart rate should occur on a daily basis through at least the first 2 weeks of treatment.

Patients who are taking Harvoni or Sovaldi in combination with another DAA who need to start amiodarone therapy due to no other alternative, viable treatment options should undergo similar cardiac monitoring as outlined above.

Due to amiodarone's long half-life, patients discontinuing amiodarone just prior to starting Harvoni or Sovaldi in combination with a DAA should also undergo similar cardiac monitoring as outlined above.

Tell your patients if they develop signs or symptoms that might suggest symptomatic bradycardia they should seek medical evaluation immediately. Symptoms may include:

- Near-fainting or fainting
- Dizziness or lightheadedness
- Malaise
- Weakness
- Excessive tiredness
- Shortness of breath
- Chest pains
- Confusion or memory problems

Reporting Adverse Events

Please report all adverse events, following or coincident with the use of Harvoni or Sovaldi, to:

The National Pharmacovigilance and Drug Safety Center (NPC):

<https://ade.sfda.gov.sa/>

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

Fax: +966-11-205-7662

Call NPC at +966-11-2038222 Ext: 5729, 2356, 2317, 2340

Or

Cigalah Group on:

Email: drug-safety@cigalah.com.sa,

Fax: 00966- 12-6578861

Office: 00966- 12-6136740

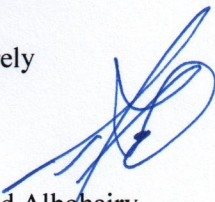
And

Email: khaled.kandeel@biopharma-mea.com

Fax: +966 12 6511040 Ext. 105

Mobile: +966 500594303

Sincerely



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