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Direct Healthcare Professional Communication

Risk of clinically significant arrhythmias when Harvoni (sofosbuvir+ledipasvir) or Daklinza (daclatasvir) in combination with Sovaldi (sofosbuvir) are given concomitantly with amiodarone

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and Medicines Authority Gilead Sciences International would like to inform you of the following:

Summary

- Cases of severe bradycardia and heart block have been reported in patients taking amiodarone and Harvoni, or amiodarone and Sovaldi in combination with Daklinza
- Bradycardia was observed within hours up to 2 weeks after initiating HCV treatment
- Patients taking amiodarone should be closely monitored when initiating Harvoni or Sovaldi in combination with Daklinza (see below, Further recommendations)
- Amiodarone should only be initiated in patients treated with Harvoni, or Sovaldi in combination with Daklinza when other alternative anti-arrhythmic treatments are not tolerated or contraindicated. Similar close monitoring is required.
- Due to the long half-life of amiodarone, appropriate monitoring should also be carried out for patients who have discontinued amiodarone within the past few months and are to be initiated on Harvoni or Sovaldi in combination with Daklinza

Further information on the safety concern and the recommendations

- Eight cases of severe bradycardia or heart block have been reported postmarketing in patients receiving amiodarone with either Harvoni, or Sovaldi in combination with Daklinza.
- Three of the 8 cases were in patients receiving Harvoni and 5 cases were in patients receiving Sovaldi plus Daklinza.

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- Six cases occurred within the first 24 hours and the remaining 2 cases occurred within the first 2-12 days following Hepatitis C Virus (HCV) treatment initiation.
- One case was a fatal cardiac arrest and 2 cases required pacemaker intervention.
- In 2 cases, rechallenge with HCV treatment in the setting of continued amiodarone therapy resulted in recurrence of symptomatic bradycardia.
- In one case while after 8 days of amiodarone discontinuation, the rechallenge of HCV treatment resulted in recurrent bradycardia, this was no longer the case when rechallenge occurred after 8 weeks of amiodarone discontinuation.
- The mechanism behind such findings is not established and additional cases (involving the combined use of sofosbuvir with other direct-acting antiviral (DAA) than daclatasvir or ledipasvir or cases without amiodarone) are currently being further investigated.

Because the number of patients taking amiodarone who have been exposed to Harvoni or Sovaldi in combination with Daklinza is unknown, it is not possible to estimate the incidence of occurrence of these events.

Further recommendations

If combination of amiodarone and Harvoni or amiodarone and Sovaldi in combination with Daklinza cannot be avoided it is recommended that patients are closely monitored, particularly during the first weeks of treatment. Patients who are identified as being at high risk of bradyarrhythmia should be continuously monitored for 48 hours in an appropriate clinical setting after initiation of concomitant amiodarone and antiviral therapy.

Patients who have discontinued amiodarone within the past few months and are to be initiated on Harvoni or Sovaldi in combination with Daklinza should be monitored due to the long half-life of amiodarone.

All patients receiving Harvoni or Sovaldi plus Daklinza in combination with amiodarone with or without other drugs that lower heart rate should also be warned of the symptoms of bradycardia and heart block and should be advised to seek medical advice urgently should they experience them.

The Product Information for these products will be updated with the new knowledge and recommendations.

Call for reporting

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with these products in accordance with the national spontaneous reporting system.

These medicinal products, approved in the EU in 2014, are under additional monitoring.

Company contact points

If you have further questions or require additional information, please contact:

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Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gzira GZR 1368, www.medicinesauthority.gov.mt/adrportal

Suspected adverse drug reactions may also be reported to GILEAD SCIENCES INTERNATIONAL LTD via email to csafety@gilead.com or tel: +44(0)1223897500 or to AM MANGION Ltd via email to pv@ammangion.com.mt or tel (+356) 23976333

Yours sincerely,

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