

**Dear Healthcare Professionals Letter
of Rapid Safety Communication
BLUE LETTER**

SOVRIAD Capsules 100 mg and Hyperbilirubinaemia

From the launch of SOVRIAD on December 6, 2013 till October 10, 2014, a total of 3 cases of remarkable increase in blood bilirubin levels followed by hepatic dysfunction and/or renal impairment, *etc.* leading to death have been reported in patients treated with SOVRIAD (simeprevir sodium). The estimated number of users is approximately 18 900 patients. Considering this situation, it has been decided to update the Warnings subsection in Precautions section in the package insert of the drug for requiring further attention.

Please pay attention to the following points for the use of SOVRIAD

Cases of remarkable increase in blood bilirubin levels followed by hepatic dysfunction and/or renal impairment, *etc.* leading to death have been reported in patients treated with this drug. Pay attention to the followings:

- Blood bilirubin tests should be performed regularly during the treatment courses with this drug.
- If any abnormalities are observed including persistently increase in blood bilirubin levels, administration of this drug should be discontinued and appropriate measures should be taken.
- Blood bilirubin levels may be increased even after discontinuation of this drug. Therefore the patients' condition should be carefully observed.
- Patients should be advised to see their doctor immediately when colouring yellow of ocular and/or skin, brown urine, and/or general malaise, *etc.* are observed after the treatment courses.

Please be informed that Warnings section, Precautions for Indications, Important precautions, and Clinically significant adverse reactions section have been updated.

Contact information is available in Page 3.

Revisions of PRECAUTIONS in the Package Insert

Revised	Current
<p>Warnings</p> <ol style="list-style-type: none"> 1. This drug must be administered under supervision of a physician with sufficient knowledge and experience in the treatment of viral liver disease only to patients in whom treatment with this drug is deemed appropriate. 2. <u>Cases of remarkable increase in blood bilirubin levels followed by hepatic dysfunction and/or renal impairment, etc. leading to death have been reported in patients treated with this drug. Pay attention to the followings:</u> <ol style="list-style-type: none"> (1) <u>Blood bilirubin tests should be performed regularly during the treatment course with this drug.</u> (2) <u>If any abnormalities are observed including persistent increase in blood bilirubin levels, administration of this drug should be discontinued and appropriate measures should be taken.</u> (3) <u>Blood bilirubin levels may be increased even after discontinuation of this drug. Therefore the patients' condition should be carefully observed.</u> (4) <u>Patients should be advised to see their doctor immediately when colouring yellow of ocular and/or skin, brown urine, and/or general malaise, etc. are observed after the treatment courses.</u> 	<p>Warnings</p> <p>This drug must be administered under the supervision of a physician with sufficient knowledge and that experience in the treatment of viral liver disease only to patients in whom treatment with this drug is deemed appropriate.</p>
<p>Precautions for Indications</p> <p>Prior to initiate the administration of this drug to patients, healthcare professionals should check that blood hepatitis C virus –ribonucleic acid is positive and that <u>hepatic cirrhosis is ruled out</u> based on histology, residual function of the liver, platelet count, etc.</p>	<p>Precautions for Indications</p> <p>Prior to initiate the administration of this drug to patients, healthcare professionals should check that blood hepatitis C virus-ribonucleic acid is positive. and that chronic hepatitis is diagnosed based on histology, residual function of the liver, platelet count, etc.</p>
<p>Precautions</p> <p>2. Important Precautions</p> <p>No related information</p>	<p>Precautions</p> <p>2. Important Precautions</p> <p>(3) Increased blood bilirubin levels have been reported in the treatment with this drug. Blood bilirubin levels, liver function test values and/or patients' condition should be carefully monitored during the treatment courses with this drug. If hepatic function is aggravated, appropriate measures should be taken.</p>
<p>4. Adverse reactions</p> <p>(1)Clinically significant adverse reactions</p> <p><u>Hyperbilirubinaemia (incidence unknown)</u></p> <p><u>Blood bilirubin levels may be remarkably increased. Cases of remarkable increase in blood bilirubin levels followed by hepatic dysfunction and/or renal impairment, etc. leading to death have been reported. Blood bilirubin tests should be performed regularly during the treatment courses with this drug. Patients' condition should be carefully observed. If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken. (See Warnings section)</u></p>	<p>4. Adverse reactions</p> <p>(1)Clinically significant adverse reactions</p> <p>No related information</p>

Hepatic dysfunction (incidence unknown)

Hepatic dysfunction accompanied by increased aspartate aminotransferase (glutamate oxaloacetate transaminase), alanine aminotransferase (glutamate pyruvate transaminase), alkaline phosphatase, gamma-glutamyl transpeptidase, etc. may occur. Patients should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken.

_____ : revision, _____ : Deletion

[Inquiry]

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Toll Free: 0120-23-6299 Open: 9:00 - 17:40 (weekday only)

From 24 October 2014 through 7 November 2014: 9:00 – 17:40 (including weekend and holiday)