This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of investigation results

Hepatitis C Direct Acting Antivirals

May 18, 2016

Non-proprietary name

a. Telaprevir

b. Simeprevir Sodium

c. Daclatasvir Hydrochloride

d. Asunaprevir

e. Vaniprevir

f. Sofosbuvir

g. Ledipasvir Acetonate/Sofosbuvir

h. Ombitasvir Hydrate/Paritaprevir Hydrate/Ritonavir

Brand name (Marketing authorization holder)

a. Telavic Tablets 250 mg (Mitsubishi Tanabe Pharma Corporation)

b. Sovriad Capsules 100 mg (Janssen Pharmaceutical K.K.)

c. Daklinza Tablets 60 mg (Bristol-Myers Squibb K.K.)

d. Sunvepra Capsules 100 mg (Bristol-Myers Squibb K.K.)

e. Vanihep Capsules 150 mg (MSD K.K.)

f. Sovaldi Tablets 400 mg (Gilead Sciences, Inc.)

g. Harvoni Combination Tablets (Gilead Sciences, Inc.)

h. Viekirax Combination Tablets (AbbVie G.K.)

Indications

a. 1. Improvement of viremia in any of the following patients with serogroup 1 (genotype I [1a] or II [1b]) chronic hepatitis C virus infection

(1) Treatment-naïve patients with high blood HCV RNA load

(2) Patients who have failed to respond to, or have relapsed after, therapy including interferon

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2. Improvement of viremia in patients with serogroup 2 (genotype III [2a] or IV [2b]) chronic hepatitis C virus infection who have failed to respond to, or have relapsed after, interferon monotherapy or interferon and ribavirin combination therapy.

b and e. Improvement of viremia in any of the following patients with serogroup 1 (genotype I [1a] or II [1b]) chronic hepatitis C virus infection

(1) Treatment-naïve patients with high blood HCV RNA load
(2) Patients who have failed to respond to, or have relapsed after, therapy including interferon

c, d, g, and h. Improvement of viremia in patients with serogroup 1 (genotype 1) chronic hepatitis C virus infection or compensated cirrhosis type C

f. Improvement of viremia in patients with serogroup 2 (genotype 2) chronic hepatitis C virus infection or compensated cirrhosis type C

Summary of revision

a,b,d,e

1. “Patients currently infected with hepatitis B virus or patients with a history of hepatitis B virus infection” should be newly added in the Careful Administration section.
2. “Reactivation of hepatitis B virus” should be newly added in the Important Precautions section.

c,f,g,h

1. The Careful Administration section should be newly added in the package insert. In this new Careful Administration section, “Patients currently infected with hepatitis B virus or patients with a history of hepatitis B virus infection” should be added.
2. “Reactivation of hepatitis B virus” should be newly added in the Important Precautions section.

Background of the revision and investigation results

Cases of reactivation of hepatitis B virus have been reported in Japan and overseas due to increase in hepatitis B viral load in association with decrease in hepatitis C viral load after initiating treatment with hepatitis C direct acting antivirals, and there was a case of hepatic function disorder that ended up being fatal in Japan. Hepatitis C direct acting antivirals, for which there were no reports of reactivation of hepatitis B virus in Japan and overseas, may carry the same risk. Following an investigation result based on the opinions of expert

advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan

a. No case associated with hepatitis B virus reactivation has been reported.

b. A case associated with hepatitis B virus reactivation has been reported (the causal relationship to the product could not be ruled out for this case). No fatality has been reported.

c and d. A total of 9 cases associated with hepatitis B virus reactivation have been reported (including 8 cases for which a causal relationship to the product could not be ruled out). Of the 9 cases, 2 fatal cases have been reported (including 1 case for which a causal relationship to the product could not be ruled out).

e. No case associated with hepatitis B virus reactivation has been reported.

f. A case associated with hepatitis B virus reactivation has been reported (the causal relationship to the product could not be ruled out for this case). No fatality has been reported.

g. A total of 2 cases associated with hepatitis B virus reactivation have been reported (the causal relationship to the product could not be ruled out for both cases). No fatality has been reported.

h. No case associated with hepatitis B virus reactivation has been reported.