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Summary of investigation results

Bcr-Abl tyrosine kinase inhibitors

August 4, 2016

Non-proprietary name

a. Imatinib mesilate

b. Nilotinib hydrochloride hydrate

c. Dasatinib hydrate

d. Bosutinib hydrate

Brand name (Marketing authorization holder)

a. Glivec Tablets 100 mg (Novartis Pharma K.K.), and others

b. Tasigna Capsules 150 mg, 200 mg (Novartis Pharma K.K.)

c. Sprycel Tablets 20 mg, 50 mg (Bristol-Myers Squibb K.K.)

d. Bosulif Tablets 100 mg (Pfizer Japan Inc.)

Indications

a. 1. Chronic myeloid leukaemia
   2. KIT (CD117) - positive gastrointestinal stromal tumor
   3. Philadelphia chromosome - positive acute lymphocytic leukaemia
   4. The following FIP – 1 - like 1 – platelet - derived growth factor receptor alpha (FIP1L1 - PDGFRα) - positive diseases:
      Hypereosinophilic syndrome, chronic eosinophilic leukaemia

b. Chronic myeloid leukaemia in chronic or accelerated phase

c. 1. Chronic myeloid leukaemia
   2. Recurrent or refractory Philadelphia chromosome - positive acute lymphocytic leukaemia

d. Chronic myeloid leukaemia resistant or intolerant to prior drugs

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Summary of revision

a, b, and c

1. Precautions regarding reactivation of hepatitis B virus should be newly added in the Important Precautions section.
2. Potential reactivation of hepatitis B virus should be added in the “Infections” subsection of the Clinically significant adverse reaction section.

d. Precautions regarding 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 patients treated with imatinib mesilate, nilotinib hydrochloride hydrate, and dasatinib hydrate both in Japan and overseas. In addition, the company core datasheet (CCDS)* and the Summary of the product characteristics in Europe have been updated. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the Important Precautions section and the Clinically significant adverse reaction section in the package insert was necessary.

Although no case of reactivation of hepatitis B virus has been reported in patients treated with bosutinib hydrate, CCDS and the Summary of the product characteristics in Europe have been updated. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the Important Precautions section in the package insert was necessary.

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

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

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

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c. A case associated with the reactivation of hepatitis B virus has been reported (a causal relationship to the product could not be established for this patient). No fatality has been reported.

d. No case associated with the reactivation of hepatitis B virus has been reported.

Note:

*CCDS is prepared by the marketing authorization holder and covers materials relating to safety, indications, dosing, pharmacology, and other information concerning the product.

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