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

Baloxavir marboxil

March 1, 2019

Non-proprietary name

Baloxavir marboxil

Branded name (Marketing authorization holder)

Xofluza Tablets 10 mg, 20 mg, Xofluza granule 2% portions (Shionogi & Co., Ltd.)

Indications

Influenza A and B viral infections

Summary of revisions

1. Language concerning instructions to patients and their families regarding contacting the attending physician if haemorrhage symptom appears as well as the necessary explanation that haemorrhage symptom may appear in some cases several days after administration of this drug should be added to the Important Precautions section.
2. A Precautions for Co-administration section should be newly added including language concerning the necessity of careful monitoring of patients when this drug is co-administered with warfarin, in light of reports of prolonged prothrombin time associated with the combination administration.
3. “Bleeding” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases of bleeding have been reported in patients treated with baloxavir marboxil in Japan and the necessity of revision of the package insert was accordingly considered. In the Expert Discussion, while the necessity of revision of the package insert at this time was supported by numerous expert advisors, there was an opinion that sought epidemiological analyses of haemorrhage events or detailed investigation of the trend of occurrence of such

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events with other antiviral agents against influenza as the basis for consideration of the revision. MHLW/PMDA concluded that revision of the package insert was necessary at this time based on the results of their investigation of the currently available evidence and in consultation with expert advisors.

Number of adverse reactions and patient mortalities reported in Japan during the previous 3 fiscal years

A total of 25 cases involving bleeding have been reported to date (including 13 cases for which a causal relationship with the product could not be ruled out.)

3 instances of patient mortality have been reported to date (a causal relationship with the product could not be established in these cases.)

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