Summary of Investigation Results

Tirabrutinib hydrochloride

July 17, 2024

Non-proprietary name

Tirabrutinib hydrochloride

Brand name (marketing authorization holder)

Velexbru Tablets 80 mg (Ono Pharmaceutical Co., Ltd.)

Japanese market launch

May 2020

Indications

•Recurrent or refractory primary central nervous system lymphoma

•Waldenström's macroglobulinaemia and lymphoplasmacytic lymphoma

Summary of revisions

1. Regarding skin disorders in the table of a guide for temporary/permanent drug discontinuation or dose reduction in the event of adverse reactions in the 7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION section, the item of "oculomucocutaneous syndrome (Stevens-Johnson syndrome) or toxic epidermal necrolysis (TEN)" should be newly added, and the statement that "Administration should be permanently discontinued." should be added.

2. "Toxic epidermal necrolysis (TEN)" and "oculomucocutaneous syndrome (Stevens-Johnson syndrome)" should be added to the item of "severe skin disorders" in the 11.1 Clinically Significant adverse Reactions section of 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving toxic epidermal necrolysis and oculomucocutaneous syndrome were evaluated. Cases for which a causal relationship between tirabrutinib hydrochloride and toxic epidermal necrolysis or oculomucocutaneous syndrome was reasonably possible have been

reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases* and patient mortalities involving toxic epidermal necrolysis and oculomucocutaneous syndrome reported in Japan

<**Toxic epidermal necrolysis** >

A total of 6 cases have been reported to date (including 4 cases for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

<**Oculomucocutaneous syndrome** >

A total of 13 cases have been reported to date (including 10 cases for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

*Cases collected in the PMDA's database for adverse drug reactions, etc. reports

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008)