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Pharmaceuticals and Medical Devices Agency

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Summary of Investigation Results

Bosentan hydrate

November 26, 2025

Non-proprietary name

Bosentan hydrate

Brand name (marketing authorization holder)

[1] Tracleer 62.5 mg film-coated tablets

[2] Tracleer 32 mg dispersible tablets for pediatric (Janssen Pharmaceutical K.K.), etc.

Japanese market launch

[1] June 2005

[2] January 2016

Indications

[1]

○ Pulmonary arterial hypertension (WHO functional class II, III, and IV).

○ Inhibition of development of digital ulcer in patients with systemic scleroderma (only for patients who currently have digital ulcers or have a history of digital ulcer.)

[2]

Pulmonary arterial hypertension

Summary of revisions

“Autoimmune hepatitis” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS section.

In association with relevant addition, adjustment in descriptions should be made to additionally include autoimmune hepatitis in precautions concerning hepatic function disorder in the 1. WARNINGS section and 7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION section.

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Investigation results and background of the revision

Cases of autoimmune hepatitis were evaluated. Cases*1 in which a causal relationship between bosentan hydrate and autoimmune hepatitis 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*2 and patient mortalities involving autoimmune hepatitis reported in Japan and overseas

No cases have been reported in Japan to date.

A total of 30 cases have been reported overseas to date (including 12 cases in which a causal relationship between the drug and the event was reasonably possible)
One instance of patient mortality has been reported overseas to date. (A causal relationship between the drug and the death following the event could not be established for this case.)

*1: Including the following case reports.
· Taefi A, et al. Am J Gastroenterol. 2014;109:S365-366
· de Araujo A, et al. J Gastrointestin Liver Dis. 2018;27 (1):89-92
*2: Among the cases collected in the PMDA's safety database for drugs, the cases that fell under MedDRA v28.0 PT “autoimmune hepatitis” were retrieved (however, cases for which the outcomes of the related events could not be identified from the information in the column of outcomes or clinical courses were excluded)

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).

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