

Summary of Investigation Results

Ibuprofen L-Lysine

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	Ibuprofen L-Lysine	Ibulief I.V. Injection 20 mg (Recordati Rare Diseases Japan K.K.)
Japanese market launch	June 2018	
Indications	The following disease when conservative treatment (fluid restriction, diuretic use, etc.) is not sufficiently effective Patent ductus arteriosus in premature infants	
Summary of revisions	"Toxic epidermal necrolysis (TEN)" and "oculomucocutaneous syndrome (Stevens-Johnson syndrome)" should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.	
Investigation results and background of the revision	Cases involving severe cutaneous adverse reactions were evaluated. Cases in which a causal relationship between Ibuprofen L-Lysine and a severe cutaneous adverse reaction was reasonably possible have not been reported. However, precautions have already been issued for toxic epidermal necrolysis and oculomucocutaneous syndrome in the Japanese package inserts of ibuprofen products ^{*1} . For this reason, as a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.	
Reference: Number of cases* involving severe cutaneous adverse reactions ^{*2} reported in Japan and overseas	Japan	Overseas
	A total of 0 cases have been reported to date (including 0 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date.	< Toxic epidermal necrolysis > A total of 2 cases have been reported to date (including 0 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date. < Oculomucocutaneous syndrome > A total of 2 cases have been reported to date (including 0 cases in which a causal relationship between the drug

		and the event was reasonably possible). No deaths have been reported to date.
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*1: Electronic package insert of Brufen Tablets 100, 200, and Brufen Granules 20%

*: Cases collected in PMDA's safety database for drugs.

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).