This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Tazobactam/piperacillin hydrate

February 14, 2023

Non-proprietary name

Tazobactam/piperacillin hydrate

Brand name (marketing authorization holder)

Zosyn I.V. injection 2.25, 4.5, Zosyn I.V. infusion bag 4.5 (TAIHO Pharmaceutical Co., Ltd.), and the others

Japanese market launch

I.V. injection: October 2008, I.V. infusion bag: June 2015

Indications

·Common infection

<Applicable microorganisms>

Tazobactam/piperacillin hydrate-susceptible strains of genus *Staphylococcus*, genus *Streptococcus*, genus *Pneumococcus*, genus *Enterococcus*, *Moraxella (Branhamella) catarrhalis*, *Escherichia coli*, genus *Citrobacter*, genus *Klebsiella*, genus *Enterobacter*, genus *Serratia*, genus *Proteus*, genus *Providencia*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, genus *Acinetobacter*, genus *Peptostreptococcus*, genus *Clostridium* (excluding *Clostridium difficile*), genus *Bacteroides*, and genus *Prevotella*

<Applicable conditions>

Sepsis, deep-seated skin infections, secondary infections following erosion or ulcer, pneumonia, pyelonephritis, complicated cystitis, peritonitis, intra-abdominal abscess, cholecystitis, and cholangitis

·Febrile neutropenia

Summary of revisions

"Haemophagocytic lymphohistiocytosis (haemophagocytic syndrome)" should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases involving haemophagocytic lymphohistiocytosis reported in Japan and overseas were evaluated. Cases for which a causal relationship between tazobactam/piperacillin hydrate and haemophagocytic lymphohistiocytosis was reasonably possible have been reported in Japan and overseas. 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*,† and patient mortalities involving haemophagocytic lymphohistiocytosis reported in Japan and overseas

A total of 15 cases have been reported in Japan to date (including 5 cases for which a causal relationship between the drug and event was reasonably possible).
A total of 2 patient mortalities have been reported in Japan to date. (A causal relationship between the drug and deaths subsequent to the event could not be established for any of these cases.)

A total of 26 cases have been reported overseas to date (including 3 cases for which a causal relationship between the drug and event was reasonably possible).
1 instance of patient mortality has been reported overseas to date. (A causal relationship between the drug and death subsequent to the event could not be established for this case.)

*: Cases collected in the PMDA's database for adverse drug reactions, etc. report
†: Cases reported on the old preparations (combination drugs with a tazobactam: piperacillin hydrate potency ratio of 1:4) are included.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

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).