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

Tazobactam/Piperacillin Hydrate

January 12, 2016

Non-proprietary name

Tazobactam/Piperacillin Hydrate

Brand name (Marketing authorization holder)

Zosyn Intravenous Injections 2.25 g, 4.5 g, Zosyn Intravenous Infusions Bag 4.5 g (Taiho Pharmaceutical Co., Ltd.) , and the others

Indications

1. General 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, pneumonia, pyelonephritis, complicated cystitis, peritonitis, Intra-abdominal abscess, cholecystitis, and cholangitis.
2. Febrile neutropenia

Summary of revision

1. “Drug-induced hypersensitivity syndrome (DIHS)” should be newly added in the Clinically significant adverse reaction section.
2. “Acute generalised exanthematous pustulosis” should be added to the “toxic epidermal necrolysis, oculomucocutaneous syndrome” subsection in the Clinically significant adverse reaction section.

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Background of the revision and investigation results

- Drug-induced hypersensitivity syndrome

Cases of drug-induced hypersensitivity syndrome or drug rash with eosinophilia and systemic syndrome have been reported in patients treated with tazobactam/piperacillin hydrate both in Japan and overseas. In addition, the company core datasheet (CCDS)* has been updated. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

- Acute generalised exanthematous pustulosis

Cases of acute generalised exanthematous pustulosis have been reported in patients treated with tazobactam/piperacillin hydrate both in Japan and overseas. In addition, the CCDS* has been updated. Furthermore, cases of acute generalised exanthematous pustulosis have been reported in patients treated with piperacillin sodium in Japan. Following an investigation result based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

The number of reported adverse reaction and fatal cases in the last 3 fiscal years in Japan

1. A total of 3 cases with drug-induced hypersensitivity syndrome have been reported (including 2 cases for which a causal relationship to the product could not be ruled out). No fatality has been reported.
2. A total of 2 cases with acute generalised exanthematous pustulosis have been reported (the causal relationship to the product could not be ruled out for both cases). No fatality has been reported.

NOTE:

*CCDS is prepared by the marketing authorization holder and covers materials relating to safety, indications, dosing, pharmacology, and other information concerning the product.

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