*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

## Preparations containing hydrochlorothiazide

November 16, 2022

**Non-proprietary name**

a. Hydrochlorothiazide
b. Losartan potassium/hydrochlorothiazide
c. Candesartan cilexetil/hydrochlorothiazide
d. Valsartan/hydrochlorothiazide

**Brand name (marketing authorization holder)**

a. Hydrochlorothiazide Tablets 12.5 mg “Towa”, Tablets 25 mg “Towa”, Hydrochlorothiazide OD Tablets 12.5 mg “Towa” (Towa Pharmaceutical Co., Ltd.)
b. Preminent Tablets LD, HD (Organon K.K.), and the others
c. Ecard Combination Tablets LD, HD (Teva Takeda Yakuhin Ltd.), and the others
d. Co-Dio combination Tablets MD, EX (Novartis Pharma K.K.), and the others

**Indications**

a. Hypertension (essential, renal, etc.), malignant hypertension, cardiac induced oedema (congestive heart failure), renal induced oedema, hepatic induced oedema, premenstrual tension, oedema caused by drugs (corticosteroids, phenylbutazone, etc.)

b-d. Hypertension

**Summary of revisions**

“Acute respiratory distress syndrome” should be added to the Clinically Significant Adverse Reactions section.

**Investigation results and background of the revision**

Considering that the European summaries of product characteristics (SPCs) for preparations containing hydrochlorothiazide were revised based on the reported cases, and the incidence



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

of acute respiratory distress syndrome is considered to be very rare in the revised European SPCs, etc., cases involving acute respiratory distress syndrome in Japan and overseas were evaluated.

Cases for which a causal relationship between the preparations and acute respiratory distress syndrome was reasonably possible have been reported overseas since the market launch of preparations containing hydrochlorothiazide, and acute respiratory distress syndrome may lead to serious outcome. As a result of these, MHLW/PMDA in consultation with expert advisors concluded that revision of Precautions was necessary.

**Number of cases and patient mortalities involving acute respiratory distress syndrome reported in Japan and overseas during the previous 3 fiscal years**

a.-d.

No cases have been reported in Japan to date.

1 case has been reported overseas* to date. (A causal relationship between the drug and event was reasonably possible for this case†.)

No patient mortalities have been reported overseas to date.

*: Extracted with a preparation containing “hydrochlorothiazide” in the non-proprietary name

†: 1 case of hydrochlorothiazide

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).