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Summary of Investigation Results

Gadobutrol

July 17, 2024

Non-proprietary name

Gadobutrol

Brand name (marketing authorization holder)

Gadovist iv injection 1.0 mol/L Syringe 5 mL, 7.5 mL, 10 mL, Gadovist iv injection 1.0 mol/L 2 mL (Bayer Yakuhin, Ltd.)

Japanese market launch

Gadovist iv injection 1.0 mol/L Syringe 5 mL, 7.5 mL, 10 mL: June 2015

Gadovist iv injection 1.0 mol/L 2 mL: August 2018

Indications

Magnetic resonance imaging of the following parts

•Brain and spinal cord

•Trunk and extremities

Summary of revisions

“Acute respiratory distress syndrome” and “pulmonary oedema” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11 ADVERSE REACTIONS. The language concerning pulmonary oedema described in “shock, anaphylaxis” should be deleted.

Investigation results and background of the revision

Cases involving acute respiratory distress syndrome and pulmonary oedema were evaluated. Cases for which a causal relationship of gadobutrol to acute respiratory distress syndrome or pulmonary oedema not associated with shock or anaphylaxis was reasonably possible

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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* and patient mortalities involving acute respiratory distress syndrome and pulmonary oedema reported in Japan

<Acute respiratory distress syndrome>

A total of 19 cases have been reported to date (including 6 cases for which a causal relationship between the drug and event was reasonably possible).

One instance of patient mortality has been reported to date. (A causal relationship between the drug and death subsequent to the event could not be established for this case.)

<Pulmonary oedema>

A total of 19 cases have been reported to date (including 11 cases for which a causal relationship between the drug and event was reasonably possible).

One instance of patient mortality has been reported to date. (A causal relationship between the drug and death subsequent to the event could not be established for this case.)

*Among cases collected in the PMDA's database for adverse drug reactions, etc. reports, those that reported as adverse drug reaction names (PT) "acute respiratory distress syndrome," "acute pulmonary oedema," "pulmonary oedema," and "non-cardiogenic pulmonary oedema" and that included a description concerning chest imaging findings within the report were retrieved.

Considering possibilities such as assessment of acute respiratory distress syndrome being difficult due to lack of diagnostic information but assessment of pulmonary oedema being possible in some of the cases, a causality assessment of the retrieved cases was conducted as "acute respiratory distress syndrome" and "pulmonary oedema," respectively. Cases of pulmonary oedema associated with shock or anaphylaxis were excluded from those retrieved cases for which a causal relationship between the drug and event was reasonably possible, since it is a known event for which precautions have already been included in the package insert.

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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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