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

Flunitrazepam (injections)

March 22, 2016

Non-proprietary name

Flunitrazepam (injections)

Brand name (Marketing authorization holder)

Rohypnol Intravenous Injections 2 mg (Chugai Pharmaceutical Co., Ltd.), Silece Intravenous Injections 2 mg (Eisai Co., Ltd.)

Indications

Induction of general anesthesia

Sedation during topical anesthesia

Summary of revision

1. Need for preparation of emergency analeptic drugs and flumazenil prior to administration as well as need for continuous monitoring of cardiorespiratory dynamics should be added in the Important Precautions section.
2. Reports of serious outcomes and need for appropriate measures should be added in the “Apnoea, respiratory depression, and glossoptosis” subsection of the Clinically significant adverse reaction section.

Background of the revision and investigation results

Although precaution for respiratory depression is described in the current package insert, cases of respiratory depression have been reported in patients treated with flunitrazepam including serious outcomes in Japan, and cases of insufficient monitoring and delayed therapeutic measures have been reported.

Pharmaceuticals and Medical Devices Agency
Office of Safety I
3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

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 reactions and fatal cases in the last 3 fiscal years in Japan

A total of 11 cases associated with respiratory depression have been reported (including 8 cases for which a causal relationship to the product could not be ruled out; however, 6 of these cases used the drug for a condition which was not included in the approved indication). Of the 11 cases, 4 fatal cases have been reported (the causal relationship between the product and the fatal outcome could not be established for these cases).

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