Japan Council for Quality Health Care

Project to Collect Medical Near-Miss/ Adverse Event Information

Medical Safety Information

No.129, August 2017

Contraindicated Combined Administration of Drugs (1st Follow-up Report)

Information about the contraindicated combined administration of drugs was provided in Medical Safety Information No.61 (December 2011). As 9 similar events have been reported since then, information about this issue is provided here again (information collection period: from November 1, 2011 to June 30, 2017). The information is compiled based on "Recurrence of Events and Occurrence of Similar Events" in the 44th and 49th Quarterly Reports.

Cases of the combined administration of a drug listed on the package insert as being contraindicated for combined administration (i.e. it should not be administered in combination with the other drug) have been reported again.

Combination of Drugs Contraindicated for Combined Administration		Number of Cases
Imuran Tablets (azathioprine)	Feburic Tablets (febuxostat)	3
Warfarin (warfarin potassium)	FLORID Oral gel (miconazole)	2
Warfarin (warfarin potassium)	Careram (iguratimod)	1
Rythmodan (disopyramide)	Avelox (moxifloxacin)	1
FP-OD (selegiline hydrochloride)	PETHILORFAN INJECTION* (pethidine hydrochloride)	1
Orap Tablets (pimozide)	Clarith tab. (clarithromycin)	1

*The active ingredients in PETHILORFAN INJECTION also include levallorphan tartrate.

◆ The package inserts for Warfarin and Florid Oral gel were amended in October 2016 to change the warning about combined use into a contraindication for combined administration.

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Case 1

The uric acid level of a patient taking Imuran Tablets became elevated, so the physician decided to issue a new prescription for Feburic Tablet. When the physician entered the prescription on the ordering screen, an alert stating that the drugs were contraindicated for combined administration was displayed. To issue the prescription, it was necessary to enter a comment, so the physician entered “Continue” in the comment field and issued the prescription. The health insurance pharmacy did not make an inquiry about the prescription, so the patient began taking both Imuran Tablets and Feburic Tablet. Two months later, the patient developed symptoms including dizziness and lightheadedness. The patient’s hemoglobin fell to 6.8g/dL and it was discovered that the patient had bone marrow suppression caused by combined use of Feburic Tablet while taking Imuran Tablets.

Case 2

The patient had venous thrombosis, so the physician in the department of cardiovascular medicine prescribed Warfarin 3mg. Two days after starting the Warfarin, the patient was prescribed Florid Oral gel by a dermatologist, due to oral candidiasis. The drug reference table had last been updated the month before the package insert had been amended to state that the drugs were contraindicated for combined administration, so no alert was displayed when the dermatologist prescribed the drug. The pharmaceutical department did not make an inquiry about the prescription. On the second day of using Florid Oral gel, the patient’s PT-INR could not be measured. The patient’s hemoglobin fell to 4.3g/dL and an endoscopy found bleeding from the gastric cardia.

Preventive measures taken at the medical institutions in which the events occurred

- **If information is received that the package insert for a drug has been amended with a new contraindication for combined administration:**
  - ○ **The pharmacist will notify all clinical departments of this information.**
  - ○ **The drug reference table will be updated without delay so that an alert is displayed.**
- **The physician will check whether the content of the prescription is appropriate if an alert is displayed when prescribing a drug.**
- **A warning label stating “Contraindications for Combined Administration” will be placed on the drug storage cabinet.**
- **If a drug contraindicated for combined administration is prescribed, the pharmacist will make an inquiry about the prescription.**

* As part of the Project to Collect Medical Near-Miss/Adverse Event Information (a Ministry of Health, Labour and Welfare grant project), this medical safety information was prepared based on the cases collected in the Project as well as on opinions of the “Comprehensive Evaluation Panel” to prevent the occurrence and recurrence of medical adverse events. See quarterly reports and annual reports posted on the Japan Council for Quality Health Care website for details of the Project.
http://www.med-safe.jp/

* Accuracy of information was ensured at the time of preparation but cannot be guaranteed in the future.

* This information is intended neither to limit the discretion of healthcare providers nor to impose certain obligations or responsibilities on them.

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