Japan Council for Quality Health Care

Project to Collect Medical Near-Miss/ Adverse Event Information

Medical Safety Information

No.140, July 2018

Administration of an Antineoplastic Agent in Excess of the Total Dosage Limit

Two cases have been reported in which patients were affected by administration of an antineoplastic agent in excess of the total dosage limit specified on the package insert (information collection period: from January 1, 2014 to May 31, 2018). The information is compiled based on “Individual Theme Review” in the 46th Quarterly Report.

Cases have been reported in which patients were affected by administration of an antineoplastic agent in excess of the total dosage limit. The total dosage is the cumulative amount administered over the patient’s lifetime.

Name of Active Ingredient	Brand Name	Total Dosage Specified on Package Insert	Total Dosage	Effect on Patient
Doxorubicin hydrochloride	Adriacin Injection 10	No more than 500 mg (titer)/m^2 (body surface area)	620 mg/m^2	Cardiomyopathy
	Doxorubicin Hydrochloride for Injection		600 mg/m^2	Cardiomyopathy

Antineoplastic agents whose package insert specifies the total dosage (partial list)

Side-effect	Name of Active Ingredient	Brand Name	Package Insert Section
Cardiotoxicity	Doxorubicin hydrochloride	Doxil Injection 20 mg	Warnings
		Adriacin Injection 10/50	Usage and Dosage
		Doxorubicin Hydrochloride Injection 10 mg/50 mg	
		Doxorubicin Hydrochloride for Injection 10 mg/50 mg	
	Epirubicin hydrochloride	Epirubicin Hydrochloride Injection 10 mg/50 mg	Precautions for Use (Important Basic Precautions)
		Epirubicin Hydrochloride 10 mg/50 mg	
		Farmorubicin for Injection 10 mg/50 mg	
		Farmorubicin RTU Inj. 10 mg/50 mg	
	Pirarubicin	Therarubicin 10 mg/20 mg for Injection	
		Pinorubin for Inj. 10 mg/20 mg/30 mg	
	Aclarubicin hydrochloride	Aclacinon 20 mg for Injection	
	Daunorubicin hydrochloride	Daunomycin 20 mg for Injection	
Pulmonary toxicity	Bleomycin hydrochloride	Bleo for Inj. 5 mg/15 mg	Usage and Dosage
	Peplomycin sulfate	Pepleo for Inj. 5 mg/10 mg	

*From PMDA, Information on Package Inserts for Prescription Drugs (as of April 30, 2018)

*There are also other antineoplastic agents whose package inserts specify the total dosage in the Precautions for Use (Side-effects) section.

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Case

Six courses of AP therapy were carried out due to a recurrence of endometrial cancer two years earlier. Following tumor resection due to recurrence of the cancer a year earlier, three more courses of AP therapy were carried out. At this point, the total dosage of doxorubicin hydrochloride was 470 mg/m^2. Although the physician knew that the total dosage limit for doxorubicin hydrochloride was 500 mg/m^2, they ordered a further six courses of AP therapy, because there were no accurate records. The patient subsequently experienced onset of cardiomyopathy and checks revealed that the total dosage of doxorubicin hydrochloride was 620 mg/m^2.

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

- **Physicians will use referral letters from other medical institutions and information from patients, etc. to check the past treatment history and will record the details.**
- **The electronic medical record system will be improved so that an alert is generated at the time the physician prescribes the drug if the prescription will exceed the total dosage limit specified on the package insert.**
- **Pharmacists will record and check the total dosage on the Regimen Check Sheet.**
- **To provide patients with information, the total dosage will be noted on their medication notebook and this will be explained.**

Complementary comment by the Comprehensive Evaluation Panel

- **Medical institutions should consider mechanisms for ascertaining the total dosage of antineoplastic agents.**

* 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 the Project website for details.
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.

Department of Adverse Event Prevention
Japan Council for Quality Health Care
1-4-17 Kandamisaki-cho, Chiyoda-ku, Tokyo 101-0061 JAPAN
Direct Tel: +81-3-5217-0252 Direct Fax: +81-3-5217-0253
http://www.med-safe.jp/