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## Safe Handling of Hazardous Drugs to Protect Healthcare Workers

### Situation

Healthcare personnel who transport, prepare, administer, and dispose of hazardous drugs can be exposed to these toxic agents in the air or on work surfaces, clothing, medical equipment, and other surfaces. As a result, both clinical and nonclinical workers are at risk for exposure when they create aerosols, mix liquids, generate dust, or touch contaminated surfaces if safe handling precautions are not followed. Frequent exposures to even very small concentrations of powerful drugs used for cancer chemotherapy, antiviral treatments, hormone regimens, and other therapies can have serious health consequences for workers who come in contact with them.<sup>1</sup>

Drugs defined as hazardous exhibit one or more of the following characteristics: carcinogenicity, teratogenicity, reproductive toxicity, organ toxicity at low doses, and genotoxicity.<sup>2</sup> These hazardous drugs, which include antineoplastics, are primarily drugs used to treat cancer. Antineoplastic agents were initially developed from chemical agents introduced as nitrogen mustard during World War I. The same mechanisms that kill cancer cells can be damaging to healthy cells. Hazardous drugs are not limited to antineoplastics; they include antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs.<sup>3</sup> The National Institute for Occupational Safety and Health (NIOSH) revised the American Society of Health-System Pharmacists (ASHP) definition of hazardous drugs. It identified approximately 150 drugs as hazardous, including 30 International Agency for Research on Cancer (IARC) known carcinogens.<sup>4, 5, 6</sup>

In the United States alone, approximately 8 million healthcare workers are involved in nursing, pharmacy, transport, and the cleanup of chemotherapy waste.<sup>7</sup> Many of these workers are not properly trained to handle exposures to hazardous drugs. In addition, some healthcare personnel experience barriers to accessing

proper engineering controls and protective equipment. The volume of hazardous drug use will increase over time. In fact, the World Health Organization predicts a 50 percent increase in cancer cases over the next 20 years as the population ages.<sup>8</sup> The increasing number of cancer cases will also require more potent chemotherapy drugs and will elevate the risk of exposure for healthcare workers. In addition to use in chemotherapy, investigational and experimental drugs are considered hazardous until proven otherwise. In addition, chemotherapy drugs and other hazardous drugs are used to treat non-malignant diseases, such as arthritis and multiple sclerosis, and their use is expanding in the veterinary field.

A study conducted by the University of Michigan on U.S. ambulatory oncology nurses discovered that the overall rate of exposure to the skin or eyes over a one-year period among 1,339 nurses surveyed was 16.9 percent.<sup>9</sup> In addition, a study conducted by NIOSH demonstrates that the surfaces in healthcare facilities are typically contaminated with antineoplastic drugs, and that contamination may lead to worker exposure.<sup>10</sup> This is consistent with studies published in the United States and many other countries around the world. In response to this information, the Joint Commission, the Occupational Safety and Health Administration (OSHA), and NIOSH issued a joint letter to healthcare facilities in the United States urging them to re-evaluate their safe handling practices related to hazardous drugs, and alerting them to the 2010 updated NIOSH hazardous drug list. However, adherence to national guidelines remains sporadic, and comprehensive standards are required to adequately protect healthcare personnel from hazardous drugs.

### Effects of Exposure to Hazardous Drugs

Results show that coming into contact with hazardous drugs can cause numerous problems. Exposed healthcare workers experienced higher rates of spontaneous abortions and potential

fetal malformations. Lawson et al. recently reported a statistically significant, nearly twofold increase in risk for spontaneous abortions among nurses exposed to antineoplastic agents during the first trimester.<sup>11</sup> Workers reported that they were experiencing side effects similar to those of a chemotherapy patient (hair loss, vomiting, mouth sores, and skin rashes).<sup>12, 13</sup> Additionally, the incidence of cancer in these workers was higher, especially for leukemia and bladder cancer.<sup>14, 15</sup> The Kaiser Permanente Center for Health Research published a study showing that exposure of pregnant women handling antineoplastic agents during pregnancy was associated with an increased risk for spontaneous abortions and stillbirth. In 2005, a survey of 7,500 members of the Oncology Nursing Society found a significant increased risk for infertility and miscarriage among U.S. nurses under 25 years of age working with chemotherapy.<sup>16</sup>

### **Current Policy**

In the 2012 medical fee revision, the technical fee for mixing of anticancer agents in a sterile setting was raised; though this was a positive step, the technical fee does not cover the cost of closed system transfer devices (CSTD) enough, and there are only three agents which have higher points. The result has been that many institutions use CSTDs only when mixing involves one or more of these three agents, while other agents are still prepared without CSTDs. This limited usage differs from the situation in the United States and elsewhere, where CSTDs are used for all potentially hazardous drugs.

One problem in Japan has been that the concept of a hazardous drug is not widely recognized. Medical professionals handling hazardous drugs should be aware that they are at health risk and take extra precautions when handling such potentially hazardous drugs.

In the 2014 medical fee revision, despite strong advocacy from hospital pharmacist and

healthcare professionals, there was no expansion of technical reimbursement funding beyond the scope mentioned above. This resulted in the continued limitation of CSTD usage. In order to fully enforce the safe handling of hazardous drugs, the NIOSH hazardous drugs list should be widely recognized and shared with Japanese authorities as well as healthcare professionals and if necessary the technical fee for mixing with CSTD further increased to incentivize safe handling practices and enhanced healthcare worker safety.

### **Recommendations**

- Evaluate the healthcare workplaces to identify and assess hazards. All healthcare settings, places dispensing veterinary medicine, research laboratories, retail pharmacies, and home healthcare agencies must catalogue the types of drugs, their volume, the frequency of shipment, and the form of the drugs being handled at the facility. In addition, facilities should complete a work environment inventory that includes a catalogue of equipment designed to reduce exposure to hazardous drugs as well as the physical layout of work areas.
- Set up management policies and training programs to handle hazardous drugs. Administrative controls must be established at facilities that handle hazardous drugs, in order to address preparing, administering, and disposing of the agents. Policies and training programs should be instituted to address: the presence of hazardous drugs, labeling, storage, spill control, personnel issues (exposure of pregnant workers), and detailed procedures for preparing, administering, testing for surface contamination, and disposing of hazardous drugs.
- Require comprehensive use of equipment designed to reduce exposure to hazardous drugs. The use of personal protective equipment (PPE), ventilated cabinets (Class II or

III biological safety cabinets [BSC] or compounding aseptic containment isolators [CACI] that meet USP 797 requirements), and engineering controls that are clinically proven (such as CSTDs) are recommended by NIOSH, the International Society of Oncology Pharmacy Practitioners (ISOPP), the ASHP, the Oncology Nursing Society (ONS), and the U.S. Pharmacopeia 797 (USP 797)<sup>17, 18, 19, 20, 21</sup> and should be required to help prevent occupational exposure to hazardous drugs.

- Increase and standardize efforts to survey and report exposures to hazardous drugs. All incidents in healthcare settings related to hazardous drug exposure, spills, and splashes should be reported to management, report data should capture the worker's past exposure, medical history, and ongoing monitoring of blood and urine tests should

be conducted to help determine linkage to exposure and facilitate long-term epidemiological review. Prefectural cancer registries must capture the occupation of cancer patients to assist in efforts to identify the cause of the cancer nationally.

- Increase technical fee incentives for the use of CSTDs.

The current technical fee rate is not enough to cover purchases of CSTDs and furthermore, the current regime only allows for coverage of preparation only on a "per patient per day" basis.

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- Antineoplastic agents and other hazardous drugs are powerful drugs. As there is evidence that many of them **can cause cancer, and evidence that they may cause reproductive and developmental problems, fetal malformations, genotoxicity, and organ damage, it is prudent to be aggressive about safe handling and the use of closed system transfer devices (CSTD).**
- In the 2012 medical fee revision, the technical fee for mixing of antineoplastic agents in a sterile setting was raised; however, this applies to only three agents. Therefore in Japan, **many institutions use closed system transfer devices (CSTD) only for these three agents,** while other agents are still prepared without CSTDs, as opposed to the situation in the U.S. and elsewhere, where CSTD are used for any hazardous agents.

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### Medical Fee Revision in 2012

- **Reward for handling volatile drugs**  
“It has been pointed out that among anti-cancer drugs, there are agents that show carcinogenicity. In addition to skills needed for handling other agents, additional high level of different skills and safety control are required particularly for **handling agents with high volatility** in order to prevent exposure to the agents and environmental pollution, and therefore, the techniques should be rewarded.”

Medical Fee Revision 2012, Health Insurance Bureau, MHLW

- Additional Insurance Points for Sterile Preparation -

A. When “closed system connector” is used

→ (1) Volatile agents※: 150 insurance points

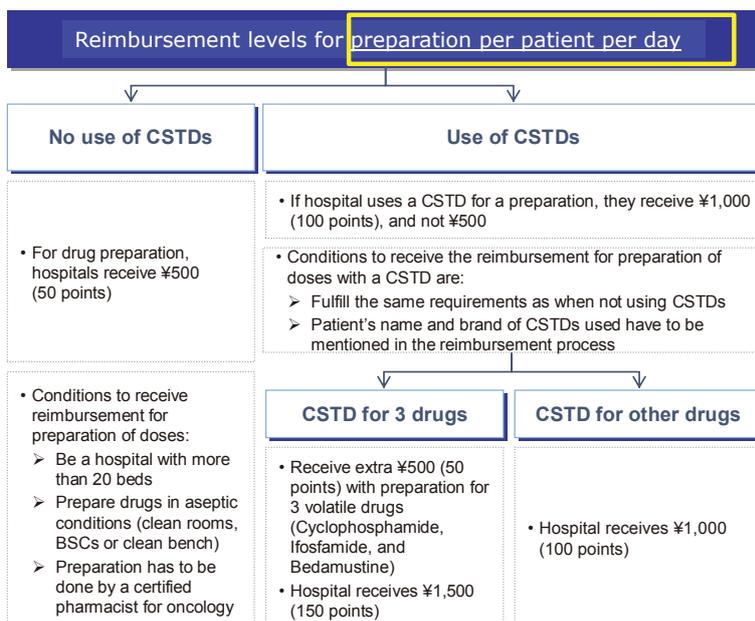
→ (2) Other than (1): 100 insurance points

Technical fee covers preparation per patient per day

※Ifosfamide, Cyclophosphamide, Bendamustine

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Japan Reimbursement policy - Use of CSTDs Category G020

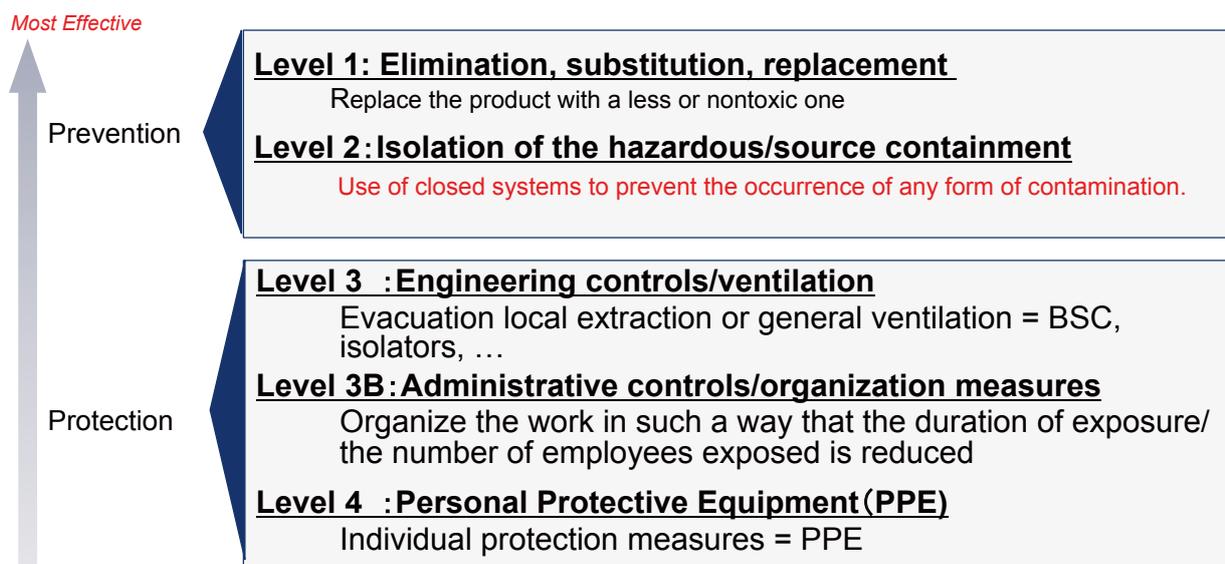


For preparation per patient per day, hospitals receive either ¥500 if they do not use CSTDs, ¥1,000 if they use CSTDs (¥500 more), or ¥1,500 if they use CSTDs for 3 volatile drugs. Source: Ministry of Health, Labour and Welfare [www.mhlw.go.jp/bunya/iryuhoken/iryuhoken15/dl/2-5.pdf](http://www.mhlw.go.jp/bunya/iryuhoken/iryuhoken15/dl/2-5.pdf) (in Japanese, Accessed 2013 Jan. 18)

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## Hierarchic order in protection measures

~ISOPP (International Society of Oncology Pharmacy Practitioner)~



Source: ISOPP standards and practice (2009) pp.18-19  
 ONS Safe Handling of Hazardous Drugs 2<sup>nd</sup> edition (2011)  
 EU Directive(90/394/EEG): Official Journal of the European Union L 158