

Assessment of Oral Chemotherapeutic Agents Safe Handling Among Healthcare Professionals in Saudi Arabia

Nagwa Ibrahim^{1*}, Meznah Al Mutairi², Mona Al Onazi²

How to cite this article: Ibrahim N, Al Mutairi M, Al Onazi M. Assessment of Oral Chemotherapeutic Agents Safe Handling Among Healthcare Professionals in Saudi Arabia. *Glob J Med Therap.* 2019;1(2):14-19.

Copyright: This is an open access journal published under the Creative Commons Attribution Non-Commercial License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction, provided the original work is properly cited and its authors credited.

Abstract-- Introduction: Traditionally, chemotherapeutic agents are administered as an intravenous infusion. Over the past decade, oral chemotherapy drugs are used increasingly as a treatment modality. The risk of harm and toxicities of oral chemotherapy compared to intravenous dosage form are the same. Application of best practice to ensure safe storage, handling, administration and disposal of oral chemotherapeutic agents is necessary to prevent exposure of the environment, healthcare professionals, patients, family members and caretakers to hazardous substances. **Objectives:** The objectives of this study are to assess the knowledge of pharmacy staff and oncology nurses about safe handling of oral chemotherapy and to establish recommendations based on study results. **Materials and Methods:** A descriptive survey design was developed. Data was collected through a structured questionnaire consisting of 5 sections (demographic data, storage, handling, disposal & cleaning of contaminated materials and training & education). Data was analyzed using IBM SPSS Statistics for Windows, version 17. **Results:** We collected 1000 surveys from four major tertiary care hospitals in Riyadh, Saudi Arabia. Most of the surveys were completed by pharmacists (52.6%), pharmacy technicians (26.7%) and oncology nurses (20.7%). The majority of participants had 2-5 years of experience (36.8%). Females composed 58.9% of the study population with five hundred eighty-nine participants. Most of participants were working in the inpatient pharmacy (42%). Separating oral anticancer agents (OACAs) from non-chemotherapeutic agents was acknowledged by 93.8%. On the other hand, only 16.8% of the participants reported that OACAs should not be stored in alphabetical order with other non-chemotherapeutic drugs. Less than half of the participants (42.9%) confirmed the equal risk of harm of OACAs versus intravenous form of chemotherapy. **Conclusions:** Our results demonstrated lack of knowledge among pharmacists, pharmacy technicians and oncology nurses regarding the risk of harm related to OACAs versus intravenous form of chemotherapy. Therefore, we recommend further education, awareness, development, and implementation of best practice guidelines about oral chemotherapy drugs safe handling in order to

prevent any harmful effects to healthcare professionals and caregivers dealing with chemotherapy.

Keywords: oral chemotherapy, safe handling, best practice, healthcare professionals.

1. INTRODUCTION

Cancer incidence is dramatically rising worldwide with an expected increase reaching up to 22.2 million in 2030 [1]. Anti-cancer agents (ACAs) are used for the treatment of different types of cancer including solid tumors and hematological malignancies. They belong to different classes of medications with different mechanisms of action and different toxicity profiles. These drugs are available in different dosage forms. Traditionally ACAs are administered as intravenous infusion. However, over the past 10 to 15 years, oral dosage forms became available in the market and are considered as a standard treatment in many cancer management protocols which might be used as a single agent or in combination with other anti-cancer drugs [2-4].

Oral anti-cancer agents (OACAs) have many potential advantages compared to intravenous forms. It does not need hospital admission or long stay in the oncology outpatient unit, cost of the utilization resources such as beds, preparation and administration equipment as well as healthcare provider's time is expected to be reduced. It is also preferred by the majority of patients as it is more convenient due to the ease of administration and reduced staying time in the clinic compared to intravenous infusion agents, as well as minimized need and risks of invasive devices [5-6].

ACAs including the oral dosage form are classified by the National Institute for Occupational Safety and Health (NIOSH) as hazardous drugs which mean that they possess at least one of the following characteristics: genotoxicity, carcinogenicity, teratogenicity, fertility impairment or reproductive toxicity and serious organ toxicity at low doses. OACAs have a chemical structure and toxicity profile that mimic existing drugs determined to be hazardous. Both oral

¹Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

²Princess Nourah Bint Abdul Rahman University, Riyadh, Saudi Arabia

*Corresponding Author: Nagwa Ibrahim, Pharm D, PhD.

Email address: nag_ibrahim@hotmail.com

Received: 19 August 2019

Accepted: 23 September 2019

Published: 29 September 2019

and injection forms of ACAs are considered high alert medications by the institute for Safe Medication Practices (ISMP) and NIOSH as they have the same risk of harm in terms of toxicities and potential harm from medication error [7-10].

Hazardous drugs require careful handling to minimize the possible adverse effects of exposure and to decrease contamination. Personnel who might be exposed to ACAs are healthcare professionals such as nurses, pharmacy technicians, pharmacists, cleaners, store personnel and porters as well as patients and caregivers [11-12]. Accidental exposure to ACAs might occur at different stages during handling such as preparation, administration, packing, transport and storage. It is essential to ensure the implementation of safe handling best practice in order to prevent additional exposure of hazardous substances to the environment, healthcare professionals, patients and their families [13-15].

There are several challenges associated with the increasing use of OACAs pertinent to healthcare providers, patients and caregivers. Healthcare providers, mainly pharmacists, are concerned with the challenges of updating their knowledge, safe handling, minimizing medication error and managing side effects as well as educating patients and caregivers. Moreover, the challenges for patients and caregivers include adherence, understanding possible side effects and interaction with food and other drugs. The safe handling policies and procedures of OACAs are not well established compared to injectable forms.

The objectives of this study are to assess the knowledge of pharmacists, pharmacy technicians and oncology nurses about the best practice of safe handling of OACAs and to establish recommendations based on the study results.

2. MATERIALS AND METHODS

A multicenter cross-sectional descriptive study was conducted from July 2014 to September 2014 in four major tertiary care hospitals with oncology services in Riyadh, Saudi Arabia. The study was approved by the Ethical and Research Committee.

We designed a structured questionnaire that consisted of 33 questions evaluating 5 sections: (1) Demographic data section: included hospital name, participant position, years of experience, gender and location; (2) Storage section: included 4 questions; (3) Handling section: included 21 questions; (4) Disposal and cleaning of contaminated materials section: included 3 questions; (5) Training and Education section: included 5 questions.

Pharmacists and pharmacy technicians dealing with chemotherapy as well as oncology nurses in the assigned hospitals were invited to participate in the study. Participation was voluntary. Answers included yes, not sure and no. All answers were expressed in percentages.

The face value of the questionnaire was validated by 15 participants and revised by an oncology consultant clinical pharmacist. Data was analyzed using IBM SPSS Statistics for Windows version 17.

3. RESULTS

3.1 Demographic data

We distributed 1,300 surveys. We were able to collect 1,000 surveys. The response rate is 76.9%. Most of the surveys were completed by pharmacists (52.6%), followed by pharmacy technicians (26.7%) and oncology nurses (20.7%). The majority of participants had 2-5 years of experience (36.8%). Most of the participants were female (58.9%). The highest numbers of surveys were collected from the in-patient pharmacy (42%). The characteristics of participants are presented in **Table 1**.

Table 1. Demographic Data

Demographic Data	Total Number of Participants = 1000	
	Participants	Percentage (%)
Position		
<i>Pharmacists</i>	526	52.6
<i>Pharmacy technician</i>	267	26.7
<i>Oncology Nurse</i>	207	20.7
Years of experience		
<i>< 2 years</i>	272	27.2
<i>≥2-5 years</i>	368	36.8
<i>≥ 5-10 years</i>	203	20.3
<i>≥ 10 years</i>	157	15.7
Gender		
<i>Male</i>	411	41.1
<i>Female</i>	589	58.9
Location		
<i>Ward – inpatient</i>	212	21.2
<i>Out-patient pharmacy</i>	368	36.8
<i>In-patient pharmacy</i>	420	42.0

3.2 Storage

This section assessed the storage of OACAs with 4 questions as demonstrated in **Table 2**. The overall correct answer in this section was 72.4%. Although 93.8% acknowledged they separate OACAs from non-chemotherapeutic agents, only 16.8% acknowledged OACAs should not be stored in alphabetical order with other non-chemotherapeutic drugs.

Table 2. Storage of OACAs

Storage of OACAs Assessment Questions	Yes (%)	No (%)	Not sure (%)
<i>1- We ensure proper storage and handling of OACAs to prevent accidental exposure and to ensure the integrity.</i>	92.3	3.3	4.4
<i>2- We store OACAs in a designated area as per the manufacturer's instructions and separate them from non-chemotherapeutic agents.</i>	93.8	3	3.2
<i>3- We follow storage specification for OACAs that are air, moisture, and/or light-sensitive.</i>	86.8	5.8	7.4
<i>4- We store OACAs in alphabetical order with other non-chemotherapeutic drugs.</i>	74.9	16.8	8.3

Table 3. Handling of OACAs

Handling of OACAs Assessment Questions	Yes (%)	No (%)	Not sure (%)
5- We have a hospital wide policy regarding handling and administration of ACAs.	82.4	11.3	6.3
6- We have a hospital wide policy regarding handling and administration of OACAs.	81.7	10.6	7.7
7- The risk of harm by handling OACAs is as equal to injectable chemotherapy.	42.9	22.7	34.4
8- We handle and administer OACAs without precautions.	7.7	3.8	88.5
9- OACAs should be handled with same precautions recommended for intravenous chemotherapy.	54.7	16.8	28.5
10- We limit handling and administering OACAs to qualified trained personal.	70.9	11.2	17.9
11- Doses for oral chemotherapeutic agents in liquid form required to be dispensed in single dose oral syringe.	67.1	18.1	14.8
12- Oral chemotherapeutic agents are considered as a "High Alert Drugs".	90	5.7	4.3
13- Label with special handling precautions should be set with oral chemotherapy container.	92.1	4.5	3.4
14- Caution labels should be available in OACAs dispensing area.	91	5.4	3.6
15- We have "Spill Kit" available in all areas dealing with OACAs.	82.8	9.6	7.6
16- Package label of OACAs should indicate the agent is cytotoxic.	84.2	8.3	7.5
17- Proper use of personal protective clothing and equipment should be instituted to minimize exposure and health risks.	83.7	10.3	6
18- We do not dispense OACAs using automatic counting machines.	73.9	10.9	15.2
19- We use disposable gloves for dispensing OACAs.	86.4	8.6	5
20- We perform OACAs manipulations such as compounding, crushing, cutting, or splitting in a biological safety cabinet or isolators and we use personal protective equipment, which are disposable.	88.3	7	4.7
21- We use separate equipments for OACAs.	84.7	7.6	7.7
22- We have a written emergency plan in the event of a spill or accidental exposure to OACAs.	82.6	9.2	8.2
23- We have an updated list of hazardous medications which is readily accessible to all healthcare personnel involved in handling of OACAs.	64.7	19.3	16
24- We accept telephone orders for OACAs to be taken by nursing or pharmacy	29.7	16.7	53.6
25- If non-oncology nurses are permitted to administer OACAs, special training is provided regarding administration and handling of OACAs.	49.3	33.3	17.4
26- All chemotherapy orders, including oral chemotherapeutic agents, are reviewed by a pharmacist specialized in oncology.	51.5	22.2	26.3

3.3 Handling

This section evaluated proper handling of OACAs with 21 questions as mentioned in **Table 3**. The overall correct answer was 72.6%. Around 80% acknowledge the existence of a hospital wide policy regarding handling and administration of ACAs including oral forms. Less than half of the participants (42.9%) confirmed the equal risk of harm of OACAs versus intravenous form, while 34.4% were not sure. Although 88.5% were not sure if OACAs handling need special precautions, only 50% were confident about the handling precautions of OACAs versus intravenous form.

About 73.9% were confident that they do not need to use the automatic counting machines while counting and dispensing the OACAs. More than 50% were not sure if OACAs orders should not be accepted through phone calls. Half the participants thought non oncology nurses dealing with OACAs need special training and 50% acknowledged that OACAs orders should be reviewed by oncology pharmacists.

3.4 Disposal and Cleaning of Contaminated Materials

This domain assessed the disposal and cleaning of contaminated materials with 3 questions as reported in

Table 4. Disposal and Cleaning of Contaminated Materials

Disposal and Cleaning of Contaminated Materials Assessment Questions	Yes (%)	No (%)	Not sure (%)
27- All disposable materials used while handling OACAs are disposed of as chemotherapy wastage according to the local waste disposal guidelines.	79.5	6.4	14.1
28- All non-disposable materials exposed to oral chemotherapeutic agents, including counting trays, tools, surfaces, etc. are washed or decontaminated thoroughly after use.	83	7.7	9.3
29- Packaging and supplies for OACAs are disposed in specially designated chemotherapy buckets.	80.4	9.5	10.1

Table 4. The overall correct answer was 81%.

3.5 Training and Education

This section assessed training and education using 5 questions as demonstrated in **Table 5**. The overall correct answer in this section was 71%. About 85.3% acknowledged that they have orientation and training programs specifically in handling of ACAs. Moreover, 62.9% acknowledged that they have education material in the related areas while 23.3% were not sure.

4. DISCUSSION

Currently, more than 25-50% of the newly approved ACAs are available as oral forms. OACAs have many advantages being more convenient for the patient, reduce both time and cost as it does not require hospitalization or insertion of invasive devices. OACAs are classified as high alert medications. Therefore, safe handling and strict adherence to the international/national/institutional guidelines are essential. The most comprehensive international guideline about safe handling and dispensing of OACAs is the American Society of Clinical Oncology and Oncology Nursing Society

Table 5. Education and Training

Education and Training Assessment Questions	Yes (%)	No (%)	Not sure (%)
30- We attend orientation programs and routine training courses specific to handle ACAs including oral form.	85.3	7.5	7.2
31- We have educational program within the institution about handling ACAs.	82.4	13.1	4.5
32- Healthcare workers involved in the handling of OACAs are trained and competent to treat individuals accidentally exposed to chemotherapeutic agents and on the disposal of ACAs.	62.9	13.8	23.3
33- We receive regular continuous education about safe handling and administration of ACAs in our institution.	62.9	13.8	23.3
34- Education material about safe handling of OACAs is available in the related areas.	61.7	19	19.3

(ASCO/ONS) guidelines for safe administration and management of oral chemotherapy [16]. In addition, a multinational study has been done in 2015 by the International Medication Safety Practice (ISMP) and International Medication Safety Practice Canada (ISPMC) addressing safeguards in oncology practice mainly OACAs [17]. Our study highlights the serious gaps about best practice in handling OACAs among healthcare professionals in hospitals mainly pharmacists, pharmacy technicians and oncology nurses.

OACAs can have just as many effects and harm on healthcare workers, patients and caregivers for long term exposure as intravenous chemotherapy. Unfortunately, most people do not realize this fact. The general misconception is that OACAs exposure risk is low and the necessary handling precautions are minimal. It is even important to know that uncoated tablets can pose a higher risk of exposure via inhalation or contact with skin. The fact is that the risk of potential harm from handling OACAs is equal to that for intravenous chemotherapy. Exposure could be at any point during preparation, administration, dispensing, transportation and disposal [18-21].

It has been proven that healthcare professionals not applying the safe handling measures are at higher risk of exposure to these cytotoxic agents. A measurable amount of these drugs has been detected in urine samples of about 40-60% of personal handling cytotoxic medications [22-23].

A study was conducted in USA to assess the community pharmacists' knowledge and attitudes toward OACAs demonstrating that pharmacists were least knowledgeable about special handling of OACAs (25%) [24]. Participants expressed their interest to know more about OACAs as it is important to their practice 3.7/5 score. In addition, they expressed their interest participating in additional continuous pharmacy education (CPE) programs on OACAs 4.2/5 score. Another study was conducted in Saudi Arabia to address the gaps in knowledge and safe handling of OACAs among pharmacists in hospitals-based cancer care [20]. The overall correct answers, incorrect answers and don't know that related to the knowledge about the application of general principles of dispensing and safe handling of OACAs were 48%, 32% and 20% respectively versus 72.6%, 13%, 18.3% in our study. 93% of pharmacists acknowledged the use of a separate counting tray versus 73.9% in our study and only one third of

the participants thought that protective gloves were needed during dispensing of OACAs versus 86.3% in our study. A higher percentage has attended orientation and education programs, counting for 85.3% in our study compared to 70% in the study conducted by Mekdad et al [20] and 16% in US pharmacist study [19].

We might refer the difference in results between the studies we mentioned compared to our study to involvement of community pharmacists in addition to hospital pharmacists, different types of questions to assess the knowledge such as dosing and side effects, and confidence in educating patients. In this study we focused on storage, handling, disposal and cleaning of contaminated materials, training and education in major tertiary hospitals. We emphasized more about best practice of safe handling of OACAs. The highest percentages of lack of knowledge were in the risk of harm while handling oral versus intravenous form and the need for special precautions while handling OACAs. Less than half (42.9%) were knowledgeable about the risk of harm being equal in oral and intravenous forms and 88.5% were not sure if handling OACAs requires special precautions.

Despite the existence of ACAs safe handling guidelines including oral dosage forms at the major tertiary hospitals dealing and caring for oncology/hematology patients, results from our study, as well as the study conducted by Mekdad et al indicate the suboptimal implementation of these guidelines. Accordingly, urgent need for interventions including more education and awareness are highly warranted based on the presented deficiencies and gaps in knowledge.

Our study had several limitations that should be addressed. We did not assess knowledge about possible side effects and patient education information. Community pharmacies weren't included in our study as OACAs are not provided by them based on the regional regulations. On the other hand, our study had several strengths. Our assessment was very specific to best practice of safe handling of OACAs within hospitals mainly evaluating the knowledge of pharmacists, pharmacy technicians and oncology nurses. Moreover, we conducted our study in four major tertiary care hospitals which allows us to fairly evaluate and assess their level of knowledge. This allows us to find the current gaps in knowledge in order to prevent further harmful risks by implementing educational and awareness programs for healthcare professionals.

5. CONCLUSIONS AND RECOMMENDATIONS

Our study demonstrates and highlights the significant gaps of knowledge and deficiencies among healthcare professionals including pharmacists, pharmacy technicians and oncology nurses concerning best practice of safe handling of OACAs in relation to the risk of harm related to OACAs versus intravenous form of chemotherapy. It is essential to ensure that our staff is implementing the guidelines.

We recommend conducting educational and awareness programs for healthcare professionals, mainly pharmacists, in order to practice proper safety measures. Providing education to healthcare professionals will lead to an improvement in dealing with OACAs, as well as to educate their patients and care givers accordingly. In addition, we highly recommend the development of well-established unified guidelines specific for OACAs that fill the knowledge gaps and match the needs of the region. Collaboration at the national level is highly warranted.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

Author Contributions: MM and MO designed the survey, drafted the tables, performed the statistical analysis and contributed in the manuscript writing. NI had the idea of the research, suggested methodology, reviewed the survey and wrote the manuscript. All authors revised the final manuscript and approved the final version.

Funding: No funding was obtained for this study.

REFERENCES

- Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008-2030): a population based study. *Lancet Oncol.* 2012; 13(8):790-801. DOI: 10.1016/S1470-2045(12)70211-5.
- Aisner J. Overview of the changing paradigm in cancer treatment: oral chemotherapy. *Am J Health Syst Pharm.* 2007; 64(9 Suppl 5):S4-S7. DOI:10.2146/ajhp070035.
- Weingart SN, Brown E, Bach PB, Eng K, Johnson SA, Kuzel TM, Langbaum TS, Leedy RD, Muller RJ, Newcomer LN, O'Brien S, Reinke D, Rubino M, Saltz L, Walters RS. NCCN Task Force Report: Oral chemotherapy. *J Natl Compr Canc Netw.* 2008; 6(Suppl 3): S1-S14. https://www.nccn.org/JNCCN/PDF/JNSU3_combined_Oral_Chemo_2008.pdf. Accessed October 5, 2019.
- Greco FA. Evolving role of oral chemotherapy for the treatment of patients with neoplasms. *Oncology (Williston Park).* 1998; 12(3 Suppl 4): 43-50. <https://www.cancernetwork.com/ovarian-cancer/evolving-role-oral-chemotherapy-treatment-patients-neoplasms>. Accessed October 5, 2019.
- Goodin S, Griffith N, Chen B, Chuk K, Daouphars M, Doreau C. Safe Handling of Oral Chemotherapeutic Agents in Clinical Practice: Recommendations From an International Pharmacy Panel. *J Oncol Pract.* 2011; 7(1): 7-12. DOI: 10.1200/JOP.2010.000068.
- Jacobson JO, Polovich M, Gilmore TR, Schulmeister L, Esper P, Lefebvre KB, Neuss MN. Revisions to the 2009 American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards: expanding the scope to include inpatient settings. *Oncol Nurs Forum.* 2012; 39(1): 31-8. doi: 10.1188/12.ONF.31-38.
- Johnson PE, Chambers CR, Vaida AJ. Oncology medication safety: a 3D status report 2008. *J Oncol Pharm Pract.* 2008; 14(4):169-80. doi: 10.1177/1078155208097634.
- Chan A, Leow YC, Sim MH. Patients' perspectives and safe handling of oral anticancer drugs at an Asian cancer center. *J Oncol Pharm Pract.* 2009; 15(3):161-5.
- Institute of Safe Medication Practices. ISMP list of high-alert medications in community/ambulatory healthcare. 2012. <https://www.ismp.org/sites/default/files/attachments/2017-11/highAlert-community.pdf>. Accessed October 5, 2019.
- NIOSH list of antineoplastic and other hazardous drugs in health care settings 2016. <https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf>. Accessed October 5, 2019.
- Carrington C, Stone L, Koczwara B, Searle C, Siderov J, Stevenson B, Michael M, Hyde S, Booth A, Rushton S, Clinical Oncological Society of Australia. The Clinical Oncological Society of Australia (COSA) guidelines for the safe prescribing, dispensing and administration of cancer chemotherapy. *Asia Pac J Clin Oncol.* 2010; 6(3):220-37. doi: 10.1111/j.1743-7563.2010.01321.x.
- Sessink PJ, Bos RP. Drugs hazardous to healthcare workers. Evaluation of methods for monitoring occupational exposure to cytostatic drugs. *Drug Saf.* 1999; 20(4):347-59. DOI:10.2165/00002018-199920040-00004
- Larson RR, Khazaeli MB, Dillon HK. "Monitoring method for surface contamination caused by selected antineoplastic agents", *Am. J. Health-Syst Pharm.* 2002; 59(3): 270-7. DOI:10.1093/ajhp/59.3.270.
- Valanis B, Vollmer W, Labuhn K, Glass A. Occupational exposure to antineoplastic agents and self-reported infertility among nurses and pharmacists. *J Occup Environ Med.* 1997; 39(6):574-80. DOI:10.1097/00043764-199706000-00013
- Beney J, Bero LA, Bond C. Expanding the roles of outpatient pharmacists: effects on health services utilisation, costs, and patient outcomes. *Cochrane Database Syst Rev.* 2000; (3): CD000336. DOI:10.1002/14651858.CD000336
- Michael N, Martha P, Kristen M, Peg E, Terry G, Kristine L, Lisa S, Joseph J. 2013 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards Including Standards for the Safe Administration and Management of Oral Chemotherapy. *J Oncol Pract.* 2013; 9(2 Suppl):5s-13s. doi: 10.1200/JOP.2013.000874
- ISMP 2018-2019 Targeted Medication Safety Best Practices for Hospitals. <https://www.ismp.org/sites/default/files/attachments/2019-01/TMSBP-for-Hospitalsv2.pdf>. Accessed October 5, 2019.
- Fransman W, Vermeulen R, Kromhout H. Occupational dermal exposure to cyclophosphamide in Dutch hospitals: a pilot study. *Ann Occup Hyg.* 2004; 48(3):237-244. <https://www.ncbi.nlm.nih.gov/pubmed/15059800>. Accessed October 5, 2019.
- O'Bryant C, Crandell B. Community pharmacists' knowledge of and attitudes toward oral chemotherapy. *JAPHA.* 2008; 48(5): 632-639. DOI: <https://doi.org/10.1331/JAPHA.2008.07082>.
- Mekdad S, AlSayed A. Towards safety of oral anti-cancer agents, the need to educate our pharmacists. *Saudi Pharmaceutical Journal,* 2017; 25(1): 136-140.

<https://doi.org/10.1016/j.jsps.2015.06.007>

21. Patel S. Safe handling of chemotherapy for pharmacists. *US Pharm.* 2014; 39(8):4-7. <https://www.uspharmacist.com/article/safe-handling-of-chemotherapy-for-pharmacists> . Accessed October 5, 2019.
22. Pethran A, Schierl R, Hauff KI. Uptake of antineoplastic agents in pharmacy and hospital personnel. Part1: monitoring of urinary concentrations. *Int. Arch. Occup. Environ. Health.* 2003; 76(1); 5-10. DOI:10.1007/s00420-002-0383-8
23. Schreiber C, Radon K, Pethran A. Uptake of antineoplastic agents in pharmacy personnel. Part II: study of work related risk factors. *Int. Arch. Occup. Environ. Health.* 2003; 76(1): 11-16. DOI: 10.1007/s00420-002-0385-6.
24. Schepel L. Strategies for medication safety: an organization based approach focusing on high alert medications and clinical pharmacy services in Helsinki University hospital. Helsinki 2018. <https://helda.helsinki.fi/bitstream/handle/10138/266766/Strategi.pdf?sequence=3&isAllowed=y>. Accessed October 5, 2019.