Statement from the Pediatric Endocrine Society Drug & Therapeutics Committee Regarding Regulations on Handling of GnRH agonists in Medical Settings

The PES Drug and Therapeutics Committee has received many inquiries regarding new regulations that will affect the handling and administration of GnRH agonists, specifically Lupron Depot. In response, we have gathered information from pharmacists and from pharmaceutical manufacturers and have prepared the following information for our members. *This document is for informational purposes only and should not be construed as guidance.* We encourage members to speak with their institutions’ pharmacists and consult their own institutional safety guidelines for further information. We anticipate that further information from the manufacturers of GnRH agonists may also be forthcoming.

**What are the new regulations?**

In February, 2016, The United States Pharmacopeial Convention (USP) published a new general chapter, <800> *Hazardous Drugs – Handling in Healthcare Settings*, that is expected to take effect December 1, 2019. (Implementation has been delayed from the initial 7/1/2018 date.) Because gosarelin, histrelin, leuprolide, and triptorelin are classified as Group 1 Antineoplastic Drugs in the 2016 National Institute for Occupational Safety and Health (NIOSH) list, these drugs are considered hazardous and are covered by the regulations in USP General Chapter <800>. USP <800> applies to all healthcare personnel who handle hazardous drug preparations and all entities that store, prepare, transport, or administer hazardous drugs. Although <800> does not become official until December, 2019, healthcare facilities may begin preparing for or implementing changes at any time, as compliance is expected starting on December 1, 2019.

**What do the regulations require for GnRH agonists?**

USP General Chapter <800> includes requirements for containment, receipt, storage, compounding, and administration of hazardous drugs. Antineoplastic drugs that require hazardous drug manipulation fall under the most stringent set of requirements, whereas some forms of hazardous drugs that do not pose significant risk of direct occupational exposure may not need to follow all of the containment requirements if a risk assessment is performed and appropriate safeguards are implemented. *Our understanding is that certain formulations of GnRH agonists, including Lupron Depot, may fall in a “gray area” regarding whether manipulation is required.* Because instructions for reconstitution of Lupron Depot include expelling air from the syringe, some have interpreted this to mean that USP <800> will require reconstitution/preparation to be performed in a biological safety cabinet within a negative pressure room. However, the following information is currently on the USP “Frequently Asked Questions” website for <800> ([http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings accessed 11/11/17](http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings accessed 11/11/17)):

“**NEW - If a NIOSH Group 1 HD is supplied as a ready to administer intramuscular injection, does expelling air from the syringe prior to administration require following all of the containment requirements in the chapter?”**

“No. If the NIOSH Group 1 HD is a final dosage form that is being prepared for immediate administration, an assessment of risk may be performed to determine alternative containment strategies and/or work practices. Section 14 of the chapter (“Administering”) states that CSTDs [Closed-system drug-transfer devices] must be used for administration of antineoplastic HDs when the dosage form allows.”
This suggests that Depot Lupron formulations may not need to follow all of the containment requirements in USP <800> and that a risk assessment by each institution will be required along with implementation of appropriate safeguards.

We encourage pediatric endocrinologists and primary care physicians who administer GnRH agonists to consult their pharmacists and institutional safety guidelines for guidance regarding safe storage and reconstitution of these drugs as well as use of Personal Protective Equipment during their administration. Based on the information currently on the USP website, as quoted above, it is not clear to us that use of a biological safety cabinet in a negative pressure room will be required for formulations that are reconstituted within the pre-filled syringe, such as Lupron Depot, but each institution must make its own determination regarding this issue.

Finally, as pediatric endocrinologists, we know that many children and adults with various conditions are treated with periodic Lupron injections, and we feel strongly about maintaining access to these medications in settings that are both safe for healthcare workers and reasonably accessible for patients.

**Further information:**
A copy of USP General Chapter <800> is available here [http://www.usp.org/usp-chapter-800-download](http://www.usp.org/usp-chapter-800-download)


For the 2016 NIOSH list of hazardous drugs, please see [https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf](https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf)

Takara Stanley, MD, and Brad Miller, MD, PhD, on behalf of the Drug and Therapeutics Committee of the Pediatric Endocrine Society

Version 11/11/2017