White Paper

Ready-To-Use Products Now, the Future: Safety and Advantages

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The Institute for Safe Medication Practices (ISMP) Guidelines for Safe Preparation of Compounded Sterile Preparations that was first published in 2013 recommends "To the maximum extent possible, Commercially-Prepared, premixed parenteral products and unit dose syringes are used versus manually compounded sterile products."[1]

The American Society of Health-System Pharmacists (ASHP), Joint Commission (JC) and ISMP have all made recommendations that, as much as possible, medications should be available to those administering to patients in unit-of-use or ready-to-administer packaging so no further manipulation takes place. Despite these recommendations, ISMP found in a 2018 survey that only one-quarter (25%) of participant receive more than half of adult IV push medications in pharmacy-prepared or commercially available ready-to-administer syringes.[2] Just 6% always receive ready-to-administer syringes.[2] The percentage is likely higher for infusions; however, this tells us there is still much room for improvement.

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The use of premixed or ready-to-administer medications is of such importance that the U.S. Food & Drug Administration (FDA) and International Medication Safety Network (IMSN) hosted a meeting for international drug regulators in June 2018 to discuss medication safety issues with regulated pharmaceutical products.[3] The meeting's objectives included discussions on ensuring the availability of ready-to-use products such as prefilled syringes and premixed IV solutions, as well as, other safe packaging methods aimed at decreasing nursing/pharmacy workloads and errors.[3]

When you hear ready-to-use product what do you think of? When we think of ready-to-use, there are different categories of products available on the market.

First, there are premixed products which we will refer to as the ready-to-administer products. The definition of a ready-to-administer product, according to ISMP, is an injectable product containing the active drug in solution at the required concentration and volume, presented in the final container (syringe, infusion bag, or elastomeric device), and ready to be administered to the patient.[4] You may sometimes find in the market that they use the term ready-to-use for these products.

These premixed products come from the manufacturer ready-to-administer without any further manipulation by pharmacy or nursing personnel. They provide the most benefits and are, therefore, the most preferred ready-to-administer/ready-to-use type of product.

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The benefits include but are not limited to:

- Depending on storage requirements, ready-to-administer/ready-to-use products can be stored on nursing units within automated dispensing machines since they usually have an extended shelf life compared to medications compounded in the pharmacy.
    - This allows for increased ease of access and more on-time administration of medications to patients. A medication that must be compounded in the pharmacy will end up in a queue of orders before it is prepared. Once prepared, the nurse will have to wait for the medication to be delivered.
    - Storage in the machines allows for better tracking, inventory control and, therefore, reduced waste.
    - The premix becomes even more advantageous for drugs that are required for emergent use, especially, in the intensive care unit and emergency room.
- There is a reduction in preparation time for pharmacy and/or nursing which allows more time to focus on other vital patient care concerns.
- Since no compounding is required for a true premix, there is no risk of preparing the product wrong or contaminating it during preparation.

There are the ready-to-use products that come from the manufacturer but require activation before administering, such as CLINIMIX by Baxter or cephalosporins in the DUPLEX® container from B. Braun. These offer all the same benefits like the above, however, they need to be activated prior to use.

There are other products a pharmacy may consider as ready-to-use as you may find them labeled that way in the market. They are products that can be used to produce ready-to-mix preparations that do not require traditional compounding with a syringe and needle. The United States Pharmacopeia (USP) refers to these as proprietary bag and vial systems. These require some assembly and activation by the pharmacy and/or nursing staff prior to administration. Some examples include the ADD-Vantage® by Pfizer, MINI-BAG Plus® by Baxter, Vial2Bag® by West Pharma, and addEASE® by B. Braun.

Although these are still preferred over traditional compounding, they do present challenges. If they are assembled and stored prior to use, it is considered compounding. Thus, beyond use dates are shortened which will present challenges with waste and stocking on nursing units.

These require pharmacy personnel to label and are, therefore, not immune to labeling mistakes.

In addition, these products require activation which introduces potential risk for not adequately transferring concentrated medication from the vial. This has been a problem since their introduction and results in the patient either not receiving the medication or not receiving the proper dose of medication.

On January 23, 2019, West Pharmaceutical Services Inc. sent customers and distributors an "Amended Urgent Medical Device Recall" notice due to the possibility that the device may not adequately transfer concentrated medication from a vial to an IV bag before infusion into a patient's vein. If inadequate transfer occurs, the drug delivered to the patient may have variable or unpredictable dosing, which means that a patient may be infused with an overdose or under-dose of medication, leading to life-threatening adverse health consequences. The FDA received sixteen complaints of serious adverse health consequences related to the use of the 13mm device with oxytocin in pregnant women in connection with labor and delivery. Since this device may be used with many different types of medications in different patient care settings, all the Vial2Bag fluid transfer systems are being recalled while an investigation is underway." (FDA, https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm630325.htm)."[5]

Therefore, with these products, we need to educate those administering on proper activation and we need to ensure the actual device functions properly.

Wouldn't it be great if all compounded sterile preparations were commercially available as ready-to-administer? If there is an affordable ready-to-administer/ready-to-use product available, rest assured a pharmacy will purchase it. The less compounding that must be done, the more pharmacy and nursing can focus on other vital patient care concerns.

The challenges for producing such products include but are not limited to:

- Cost. Premixed and ready-to-use products usually cost more than the vials of drug alone.
- There is no standardization of concentrations throughout all facilities in the US and, therefore, many different concentrations would need to be produced.
- Drug stability/shelf life may not be practical.
- Drug usage volume may be too low to produce at a manufacturing level.
- For ready-to-use products requiring assembly and activation:
    - May not have all dose options available in a single vial
    - Adapters may not accommodate all sizes of vials

Many facilities may think if they can't get a commercially-prepared premixed solution then they could outsource a premixed solution from a 503B pharmacy. Although this is another route to consider for premixed solutions after the New England Compounding Center (NECC) national outbreak, we all know this may not come without risk.

ISMP recommends utilizing the ASHP Foundation's document, "Outsourcing Sterile Products Preparation: Contractor Assessment Tool" (http://www.ashpfoundation.org/sterileproductstool), as a resource to analyze the capabilities and quality of external compounding providers prior to selecting a vendor.[1]

Utilize the ASHP Vendor Assessment Tool if outsourcing premix products. Visit http://www.ashpfoundation.org/sterileproductstool

As with any new products and/or processes, there will be problems. There can be mix-ups just like with vials of drugs when packaging looks the same. Consider barcode scanning at all points where problems may occur, such as, during assembly and labeling, when adding to storage, and prior to administration.

Where activation is required, make sure those who administer these medications are trained and educated on how to properly activate the products. There have been many reported errors concerning the activation of these products. Do not dispense new types of products without first training and educating anyone involved in the administration of the product on how to use it.

There are many benefits to using ready-to-use products including a decreased workload on already overwhelmed compounders, increased ease of access which results in better patient care due to fewer delays in the delivery of medications, better inventory control, and less risk of administering an improperly prepared or contaminated medication with the use of these products. There are a lot of options available for premix/ready-to-administer/ready-to-use products. Hopefully, your facility is taking advantage of these product benefits and manufacturers can overcome some of the challenges so that we may see an increase in affordable commercially prepared premixes and other types of ready-to-use products.

References

1. ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations. Revised 2016.

2. Acute Care ISMP Medication Safety Alert. November 1, 2018. Volume 23 Issue 22. https://www.ismp.org/sites/default/files/attachments/2018-10/20181101.pdf

3. FDA U.S. Food & Drug Administration. FDA/IMSN Summit with international drug regulators to discuss medication safety issues. Accessed 1/12/2019. https://www.fda.gov/Drugs/NewsEvents/ucm603304.htm

4. ISMP Safe Practice Guidelines for Adult IV Push Medications. A compilation of safe practices from the ISMP Adult IV Push Medication Safety Summit. 2015. https://www.ismp.org/sites/default/files/attachments/2017-11/ISMP97-Guidelines-071415-3.%20FINAL.pdf

5. FDA U.S. Food & Drug Administration. West Pharmaceutical Services Inc. Recalls Vial2Bag Fluid Transfer Systems Due to Potential Malfunctions. Accessed 2/5/ 2019. https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm630325.htm