Considerations for Imaging Contrast Shortage Management and Conservation

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Introduction

This fact sheet summarizes the status of the current acute shortage of iohexol and provides an outline of potential actions for organizations to consider in managing the shortage. Healthcare professionals should use their professional judgment in deciding how to use the information in this document, taking into account the needs and resources of their individual organizations.

Background

Iohexol injection is currently unavailable or available in limited supply due to the shutdown of a production facility in Shanghai, China during a COVID-19 lockdown. The facility is open and production has resumed; however, the shortage is expected to continue until late-June, 2022. As a result of the iohexol shortage, other contrast agents may be affected as organizations seek suitable alternatives.

ISMP Medication Error Reporting

ASHP encourages the reporting of any medication errors related to drug shortages to the Medication Error Reporting page on the Institute for Safe Medication Practices (ISMP) website.

Conserving contrast

- Organizations should develop a policy or protocol to guide clinicians in selecting and prioritizing imaging scans. Organizations must consider the clinical appropriateness of each individual patient's needs, but may consider:
    - Using alternative imaging techniques such as ultrasound or MRI.
    - Performing scans without the use of contrast.
    - Delaying scans that are not clinically urgent.
    - Using alternative contrast agents.
- Organizations may consider prioritizing patients for imaging scans requiring contrast based on clinical acuity and the nature of the imaging procedure (i.e., interventional vs. diagnostic).
- The American College of Radiology (ACR) has issued a Statement from the ACR Committee on Drugs and Contrast Media in response to the shortage. The statement includes more detailed considerations for conserving contrast.

Repackaging contrast

ASHP has received several inquiries about the repackaging of commercially available containers of contrast. Products may be available as imaging bulk packages, pharmacy bulk packages, and single-dose containers (see Appendix A for listing of product types).

Organizations should be aware of the risks of inappropriate use of pharmacy bulk packages and single-dose vials. ISMP published an article in 2012 citing a CDC *MMWR* report of bacterial infections following the use of a single container of contrast used for multiple patients. The ISMP article reinforces the need for repackaging or multiple uses of a container, other than through the use of a contrast injection system, to be handled in a pharmacy's cleanroom according to USP Chapter <797>.[1]

Organizations may choose to refrigerate repackaged contrast to allow a longer beyond-use-date (BUD) according to USP Chapter <797>. While the labeled storage information for iohexol and iodixanol do not include refrigerated temperatures, they do reference "controlled room temperature" storage. According to USP Chapter <659>:

> "An article for which storage at *Controlled room temperature* is directed may, alternatively, be stored and shipped in a cool place or refrigerated, unless otherwise specified in the individual monograph or on the label."[2]

While refrigeration is an option based on USP Chapter <659>, organizations should be very careful not to freeze syringes. Consider including DO NOT FREEZE on the repackaged label.

Administering repackaged contrast

Organizations may find that patients require multiple containers of contrast, either multiple repackaged syringes or a combination of commercially available containers and repackaged syringes. To maintain sterility and a closed system, organizations may consider employing a three-way stopcock to allow the connection of two containers to the contrast management system.

Repackaging iohexol

Pharmacy bulk packages

- The product labeling for the pharmacy bulk packages contains an "in-use" time of 8 hours, defined as the "time within which the opened product is to be used."[3,4]
- FDA repackaging guidance for state-licensed pharmacies or federal facilities establishes the BUD of a repackaged product may not exceed the in-use time of the product labeling.[4]
- Per the FDA guidance, the BUD of a repackaged pharmacy bulk package of iohexol should not exceed **8 hours**.

Imaging bulk packages

- The imaging bulk package label states that it is only cleared for use with "automated contrast injection systems, contrast management systems, or contrast media transfer sets cleared for use with the contrast agent in this Imaging Bulk Package."[5]
- The product labeling for the imaging bulk packages also contains an in-use time of 8 hours, limiting the BUD of repackaged product to **8 hours**.

Single-dose vials

- Single-dose vials should be used for a single patient as part of a single injection.[6]
- If a single-dose vial must be used for more than one patient, either by splitting the dose or by repacking, organizations must follow USP Chapter <797> Pharmaceutical Compounding – Sterile Preparations.[6]
- The labeling for single-dose containers does not list an in-use time other than a 4-hour limit for use with automated contrast injection system or contrast management system. Therefore, FDA guidance for BUD assignment refers to USP Chapter <797>.[7,4]
- When assigning BUDs and determining storage, organizations must consider stability in the repackaged container and suitable temperature for the repackaged product.
    - Iohexol labeling requires storage at controlled room temperature; therefore, organizations should assign the maximum BUD per room-temperature storage conditions.
    - Iohexol is available in polypropylene bottles and therefore should remain stable in polypropylene syringes.
    - Repackaging should not occur in polycarbonate syringes without more information from the manufacturer or results of stability indicating assays confirming suitability of polycarbonate containers.
- Repackaging is a form of batching and is considered medium-risk compounding under the current version of USP Chapter <797>.
    - At controlled room temperature, the maximum BUD that can be assigned to iohexol repackaged per <797> medium-risk requirements is **30 hours**.[8]
    - If stored in a refrigerator, the maximum BUD that can be assigned to iohexol repackaged per <797> medium-risk requirements is **9 days.**[8]
- Note that in April, 2020, the USP Compounding Expert Committee issued the document *Operational Considerations for Sterile Compounding During COVID-19 Pandemic* that includes some additional information in response to staff, drug, and personal protective equipment shortages.[9]
    - The document supports risk-based enforcement discretion related to USP compounding standards and reflects options developed by the expert committee based on their expertise.
    - For the assignment of BUDs, the document establishes that a BUD of **4 days** for medium-risk preparations stored at room temperature or **10 days** stored in a refrigerator. These BUDs are based on the draft revision to USP Chapter <797> that also establishes a 4-day BUD for Category 2 compounded sterile preparations stored at room temperature.[9]
    - Organizations may consider adopting the BUD in the draft revision to USP Chapter <797> and *Operational Considerations* document after checking with their state board of pharmacy or other regulatory bodies to determine whether the extended BUD is allowed.

Repackaging iodixanol

The information for iohexol repackaging and BUDs also applies to iodixanol repackaging. Iodixanol is not available in an imaging bulk package.

Pharmacy bulk packages

- The product labeling for the pharmacy bulk packages contains an "in-use" time of 8 hours, defined as the "time within which the opened product is to be used."[10,4]
- Per the FDA repackaging guidance, the BUD of a repackaged pharmacy bulk package of iodixanol should not exceed **8 hours**.

Single-dose vials

- Single-dose vials should be used for a single patient as part of a single injection.[6]
- If a single-dose vial must be used for more than one patient, either by splitting the dose or by repacking, organizations must follow USP Chapter <797> Pharmaceutical Compounding – Sterile Preparations.[6]
- The labeling for single-dose containers does not list an in-use time other than a 4-hour limit for use with automated contrast injection system or contrast management system. Therefore, FDA guidance for BUD assignment refers to USP Chapter <797>.[11,4]
- When assigning BUDs and determining storage, organizations must consider stability in the repackaged container and suitable temperature for the repackaged product.
    - Iodixanol is available in polypropylene bottles and therefore should remain stable in polypropylene syringes.
    - Repackaging is a form of batching and is considered medium-risk compounding under the current version of USP Chapter <797>.
        - At controlled room temperature, the maximum BUD that can be assigned to iodixanol repackaged per <797> medium-risk requirements is **30 hours**.[8]
        - If stored in a refrigerator, the maximum BUD that can be assigned to iodixanol repackaged per <797> medium-risk requirements is **9 days.**[8]
- Note that in April, 2020, the USP Compounding Expert Committee issued the document *Operational Considerations for Sterile Compounding During COVID-19 Pandemic* that includes some additional information in response to staff, drug, and personal protective equipment shortages.[9]
    - The document supports risk-based enforcement discretion related to USP compounding standards and reflects options developed by the expert committee based on their expertise.
    - For the assignment of BUDs, the document establishes that a BUD of **4 days** for medium-risk preparations stored at room temperature or **10 days** stored in a refrigerator. These BUDs are based on the draft revision to USP Chapter <797> that also establishes a 4-day BUD for Category 2 compounded sterile preparations stored at room temperature.[9]
    - Organizations may consider using this extended BUD after checking with their state board of pharmacy or other regulatory bodies to determine whether the extended BUD is allowed.

References

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Appendix A

List of iohexol and iodixanol products by package type

Omnipaque™ (iohexol)		
Package size	**Concentration**	**NDC**
Imaging bulk package		
500 mL	300 mg/mL	0407-1413-72
500 mL	350 mg/mL	0407-1414-72
Pharmacy bulk package		
500 mL	300 mg/mL	0407-1413-68
500 mL	350 mg/mL	0407-1414-98
Single-dose vial		
50 mL	140 mg/mL	0407-1401-52
10 mL	180 mg/mL	0407-1411-10
20 mL	180 mg/mL	0407-1411-20
10 mL	240 mg/mL	0407-1412-10
20 mL	240 mg/mL	0407-1412-20
50 mL	240 mg/mL	0407-1412-30
100 mL	240 mg/mL	0407-1412-33
150 mL fill in 200 mL	240 mg/mL	0407-1412-34
200 mL	240 mg/mL	0407-1412-35
10 mL	300 mg/mL	0407-1413-10
30 mL fill in 50 mL	300 mg/mL	0407-1413-59
50 mL	300 mg/mL	0407-1413-61
75 mL fill in 100 mL	300 mg/mL	0407-1413-62
100 mL	300 mg/mL	0407-1413-63
125 mL fill in 150 mL	300 mg/mL	0407-1413-53
125 mL fill in 200 mL	300 mg/mL	0407-1413-69
150 mL fill in 200 mL	300 mg/mL	0407-1413-65
200 mL	300 mg/mL	0407-1413-66
50 mL	350 mg/mL	0407-1414-89
75 mL fill in 100 mL	350 mg/mL	0407-1414-90
100 mL	350 mg/mL	0407-1414-91
125 mL fill in 150 mL	350 mg/mL	0407-1414-76
125 mL fill in 200 mL	350 mg/mL	0407-1414-95
150 mL fill in 200 mL	350 mg/mL	0407-1414-93
200 mL	350 mg/mL	0407-1414-94

Visipaque™ (iodixanol)		
Package size	**Concentration**	**NDC**
Pharmacy bulk package		
500 mL	320 mg/mL	0407-2223-23
Single-dose vial		
50 mL	270 mg/mL	0407-2222-16
100 mL	270 mg/mL	0407-2222-17
150 mL	270 mg/mL	0407-2222-19
200 mL	270 mg/mL	0407-2222-21
50 mL	320 mg/mL	0407-2223-16
100 mL	320 mg/mL	0407-2223-17
150 mL	320 mg/mL	0407-2223-19
200 mL	320 mg/mL	0407-2223-21