Drug Shortage: Iohexol (Omnipaque) and Iodixanol (Visipaque)

This document provides mitigation strategies for handling ongoing drug shortages to participants in the Vizient® Pharmacy Program. Information is compiled from mitigation strategies of institutions that serve on the Vizient Clinical Pharmacy Council and is reviewed by a panel of pharmacists. For more information, contact pharmacyquestions@vizientinc.com

Situation

This mitigation strategy is to serve as a resource if iohexol (Omnipaque) and/or iodixanol (Visipaque) experience supply disruptions due to shortages.

Background

According to communication from GE Healthcare, a shortage of iohexol (Omnipaque) is occurring as a result of the Chinese government lockdowns related to COVID-19. Secondarily to the iohexol (Omnipaque) shortage, the alternative agent, iodixanol (Visipaque), is in short supply due to an increase in demand.

At the recommendation of GE Healthcare, distributors have implemented an approximate 20% allocation on iohexol (Omnipaque) that is expected to continue through the remainder of this shortage. Nearly all of the US supply for this product comes from the Shanghai plant. According to GE Healthcare, the supply impact is not related to quality, raw material supply, or supply chain issues. GE Healthcare will utilize their secondary manufacturing facility in Ireland to supplement US labeled iohexol (Omnipaque) supply. Additionally, it has been communicated that the impact is temporary, and the Shanghai facility is re-opened and ramping up production as allowed by local COVID-19 mitigation protocols. Appendix 1 contains the only 3 SKUs GE Healthcare will focus on in order to optimize production and get supply back in the system. Others will be added as capacity is regained.

Total global production of iodine, excluding US production data, was estimated at 32,000 metric tons in 2021 which is equivalent to pre-pandemic levels. GE Healthcare expects to have intermittent supply of iohexol (Omnipaque) and does not have additional information on iodixanol (Visipaque) availability at this time. This mitigation strategy is intended to provide guidance for present and future shortages.

Products affected[a]

Omnipaque 140	▪ 140 mg iodine/mL, 50 mL polymer bottle
Omnipaque 180	▪ 180 mg iodine/mL, 10, 20 mL vials
Omnipaque 240	▪ 240 mg iodine/mL, 10, 20 mL vials ▪ 240 mg iodine/mL, 50, 100, 150, 200 mL polymer bottles
Omnipaque 300	▪ 300 mg iodine/mL, 10, 125 mL vials ▪ 300 mg iodine/mL, 30, 50, 75, 100, 125, 150, 200 mL ▪ 300 mg iodine/mL, 500 mL polymer bottles (pharmacy and imaging bulk)
Omnipaque 350	▪ 350 mg iodine/mL, 125 mL vials ▪ 350 mg iodine/mL, 50, 75, 100, 125, 150, 200 mL ▪ 350 mg iodine/mL, 500 mL polymer bottles (pharmacy and imaging bulk)
Omnipaque Oral solution 9	▪ 9 mg iodine/mL, 500 mL polymer bottle
Omnipaque Oral solution 12	▪ 12 mg iodine/mL, 500 mL polymer bottle
Visipaque 270	▪ 270 mg iodine/mL, 50, 100, 150, 200 mL polymer bottles ▪ 270 mg iodine/mL, 500 mL polymer bottle (pharmacy bulk)
Visipaque 320	▪ 320 mg iodine/mL, 50, 100, 150, 200 mL polymer bottles ▪ 320 mg iodine/mL, 500 mL polymer bottle (pharmacy bulk)

[a] Review ASHP Drug Shortages for the most current information

Assessment

Iohexol (Omnipaque) is an iodinated contrast media, specifically a low-osmolality contrast media (LOCM). Iodixanol (Visipaque) is an iso-molar contrast media (IOCM). Both are utilized in computed tomography (CT) scans, X-rays, interventional radiology, and the cardiac catherization lab. Other FDA-approved LOCMs on the market include iopamidol (Isovue), iopromide (Ultravist), and ioversol (Optiray). Iopromide (Ultravist) and ioversol (Optiray) are manufactured by Bayer and Guerbet, respectively, and account for approximately ≤ 5% of the market share combined. Iopamidol (Isovue), manufactured by Bracco Diagnostics, accounts for the second largest national market share at ~45%. Bayer, Guerbet, or Bracco Diagnostics have communicated that they are currently not able to take on new accounts; however, iomeprol (Iomeron) imported by Bracco and international iopromide (Ultravist) imported by Bayer will be available in limited supply. Iohexol (Omnipaque) and iodixanol (Visipaque), manufactured by GE Healthcare, account for the largest market share at > 50%. These contrast agents are necessary for imaging studies to determine the appropriate diagnosis and subsequent treatment of patients for a variety of disease states. Hospitals and health systems are advised to have a mitigation strategy available, to conserve inventory, in the event of a shortage of these contrast agents. Refer to additional national guidance publications found in Appendix 2 for additional information.

Iodixanol was added as a generic contract to Vizient's portfolio, effective July 18, 2022. Generic iodixanol will be available as iodixanol 270 (270 mg iodine/mL) and iodixanol 320 (320 mg iodine/mL) by Fresenius Kabi. Utilize generic iodixanol when available. Additionally, Vizient has compiled a list of FAQs to address the allocation methodology, communication methods, product and direct order questions, and FDA efforts of GE Healthcare's temporary supply disruption.

Recommendation

Must know information

- Iodixanol was added as a generic contract to Vizient's portfolio, effective July 18, 2022. Generic iodixanol will be available as iodixanol 270 (270 mg iodine/mL) and iodixanol 320 (320 mg iodine/mL) by Fresenius Kabi. Utilize generic iodixanol when available.
- Evaluate and assess purchasing iomeprol (Iomeron) imported by Bracco and international iopromide (Ultravist) imported by Bayer when it is available.
- Reschedule non-emergent imaging studies or interventional studies which require iohexol (Omnipaque), iodixanol (Visipaque), or other LOCM agents to conserve available inventory.
- Reserve iohexol (Omnipaque) and iodixanol (Visipaque) for critically ill patients requiring CT studies and interventional studies, or cardiac catherization lab interventions.
- If clinically appropriate, in coordination with radiologists, utilize other imaging study modalities such as magnetic resonance imaging (MRI), ultrasound, or nuclear studies.
- For oral administration, diatrizoate meglumine sodium (Gastrografin) or diatrizoate meglumine sodium (MD-Gastroview) can be utilized as alternatives. For genitourinary administration, alternatives may include diatrizoate (Cystografin), iothalmate (Cysto-Conray II), or iothalmate (Conray 43).
- Assess and evaluate imaging bulk package (IBP) transfer sets for transfer of contrast media to empty, single-use, sterile syringes on syringe-based contrast injection systems to maximize usage and reduce wastage (see specifics in the operational recommendations).

Clinical

1) Reserve iohexol (Omnipaque) and iodixanol (Visipaque) for critically ill patients requiring CT and interventional studies, or cardiac catheterization lab interventions.
    - Determine which patients qualify as critically ill with input from the appropriate hospital and pharmacy leadership bodies, in coordination with radiologists.
    - If clinically appropriate, in coordination with radiologists, utilize other imaging study modalities such as magnetic resonance imaging (MRI), ultrasound, or nuclear studies.
        - To determine if alternative studies are appropriate, please refer to the American College of Radiology (ACR) Appropriateness Criteria guidelines (Scroll down to the AC Portal and use the "Explore by scenario" icon.)
2) If utilizing iodixanol (Visipaque) in the catherization lab, consider reserving for patients with renal insufficiency or cardiac issues.
3) Use alternatives to nonionic contrast for oral, rectal, and genitourinary administration. For oral administration, diatrizoate meglumine sodium (Gastrografin) or diatrizoate meglumine sodium (MD-Gastroview) can be utilized as alternatives. For genitourinary administration, alternatives may include diatrizoate (Cystografin), iothalmate (Cysto-Conray II), or iothalmate (Conray 43).

Operational

1) To maximize usage and reduce wastage, assess and evaluate imaging bulk package (IBP) transfer sets for transfer of contrast media to empty, single-use, sterile syringes on syringe-based contrast injection systems.
    - Transfer sets on the market include the Bayer/Medrad IBP transfer set (Bayer), ulrich transfer set (GE), Liebel-Flarsheim IBP transfer set (Guerbet), and Injeneering transfer set (Bracco).
        - Bayer/Medrad IBP transfer set is approved for use with iopromide (Ultravist), iopamidol (Isovue), and iohexol (Omnipaque).
        - ulrich transfer set is approved for use with iohexol (Omnipaque) only.
        - Liebel-Flarsheim IBP transfer set is approved for use with ioversol (Optiray) only.
        - Injeneering transfer set is approved for use with iopamidol (Isovue) only.
    - Consult with the contrast injection system supplier at your institution for more information. The available systems are manufactured by Bayer, Bracco, GE (brand is ulrich), and Guerbet.
    - Transfer set duration of use is unique to each product, please refer to product-specific information to determine duration of use.
2) Evaluate and assess purchasing iomeprol (Iomeron) imported by Bracco and international iopromide (Ultravist) imported by Bayer when it is available.
3) Implement electronic health record changes to notify the ordering provider of the iohexol (Omnipaque) and iodixanol (Visipaque) shortage, provide an option to complete the imaging study without contrast, as clinically appropriate, and provide an option to defer the decision of contrast usage to the radiologists.
4) Pull available stock to inpatient pharmacy for inventory control, as able with imaging needs.
5) If inventory becomes critically low, reschedule non-emergent imaging or interventional studies which require iohexol (Omnipaque), iodixanol (Visipaque), or other LOCM agents to conserve available inventory.
6) Consider implementing strategies to reduce contrast dose and/or minimize waste. Strategies may include:
    - Utilize weight-based dosing (vs. fixed dosing) for CT and aliquot to avoid waste.
    - Reduce contrast dose in conjunction with low kVp protocols that improve contrast conspicuity.
    - Reduce dose and acquire studies with dual-energy protocols (where available) that improve contrast conspicuity.

- Repackage commercially available containers per FDA guidance or USP Chapter <797> (as applicable to the situation). Refer to Appendix 3 for repackaging considerations.

7) Coordinate direct orders with local GE Healthcare representatives.
   - Provide GE Healthcare with current days on-hand of inventory and the quantity needed to provide care for critically ill patients when ordering.
   - GE Healthcare has indicated that health systems sharing this level of transparency will allow for optimization of the allocation process to prioritize immediate needs and bi-weekly requirements for critically ill patients.
8) Ensure orders are placed for the 3 SKUs noted in Appendix 1. Orders placed for other Omnipaque and Visipaque SKUs will not be fulfilled currently.

Advocacy

Vizient regularly engages with the FDA and other federal agencies and policymakers as appropriate, to communicate the various supply chain challenges that our members are facing. The challenges Vizient members are facing regarding the Contrast Media category have been a high priority in recent FDA meetings with information continually being communicated.

Further Information

- Product availability questions can be directed to GE Healthcare Customer Service (800-292-8514 or ci.weborders@ge.com).
- If challenges working with local representatives, contact Steve Hines, GE national account manager (303-489-0638 or steven.hines@ge.com).
- Questions regarding information outside of the package insert can be directed to GE Medical Affairs (800-654-0118 or medical.affairs@ge.com).
- For more information, contact pharmacyquestions@vizientinc.com.

Appendix 1. GE Healthcare production focused only on these SKUs

NDC	Product	Item No.	SKU	Description
0407-1414-91	Omnipaque	Y-542	1123762	Omnipaque 350 mg iodine/mL, 100 mL
0407-1414-98	Omnipaque	Y-548B	1133990	Omnipaque 350 mg iodine/mL, 500 mL
0407-2223-17	Visipaque	V-562	1123772	Visipaque 320 mg iodine/mL, 100 mL

Appendix 2. National published guidance

Organization	Title
American College of Radiology (ACR)	Statement from the ACR Committee on Drugs and Contrast Media
American College of Radiology (ACR)	ACR Manual on Contrast Media
American Society of Health System Pharmacists (ASHP)	Considerations for Imaging Contrast Shortage Management and Conservation
Institute for Safe Medication Practices (ISMP)	Inappropriate Use of Pharmacy Bulk Packages of IV Contrast Media Increases Risk of Infections

Appendix 3. Considerations for repackaging[a]

Product	Single dose vial (SDV) or bottle	Pharmacy bulk packages	Imaging bulk packages
Iohexol (Omnipaque)	Note: SDVs should be used for a single patient. If a SDV must be used for more than a single patient, organizations must follow USP Chapter <797> Pharmaceutical Compounding – Sterile Preparations. • Per PI, no "in-use" time listed other than a 4-h limit for use with automated contrast injection system or contrast management system. • With no "in-use" time, BUD assignment is based on USP Chapter <797>. • Repackaging is considered medium risk compounding under the current version of USP Chapter <797>. • The maximum BUD for medium-risk compounding repackaged in a fully compliant pharmacy cleanroom is 30 h stored at controlled room temperature or 9 d stored in refrigeration. • Ensure storage of repackaged product is at a suitable temperature and in a compatible container.	• Per PI, "in-use" time of 8 h. In-use time is defined as the "time within which the opened product is to be used." • FDA repackaging guidance states BUD of a repackaged product may not exceed in-use time in PI.	
Iodixanol (Visipaque)	• Per PI, no "in-use" time listed. • Will be the same as Omnipaque specifications above, but these are single-dose bottles not vials.	• Per PI, "in-use" time of 8 h. In-use time is defined as the "time within which the opened product is to be used." • FDA repackaging guidance states BUD of a repackaged product may not exceed in-use time listed in PI.	n/a

Abbreviations: BUD = beyond use dating; PI = product labeling

[a] For additional considerations, please refer to ASHP's Considerations for Imaging Contrast Shortage Management and Conservation

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United States Pharmacopeia (USP-797). United States Pharmacopeial Convention; 2021. Accessed May 3, 2022.

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