Drug Shortage: Oncology agents

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 oncology agents experience supply disruptions due to shortages.

Background

Previous shortages of oncology agents have caused concern. Certain oncology agents have been prone to shortages with a limited number of manufacturers in the marketplace and few clinical alternatives. This mitigation strategy is intended to provide guidance for present and future shortages.

Products affected

Review ASHP Drug Shortages for the most current information.
Review Vizient Drug Shortage Alerts for current Vizient-specific contracting information and shortage details.

Novaplus Enhanced Supply (NES), a program created by Vizient, was established to enhance resiliency of supply in times of drug shortages. Access to additional inventory of select essential medications is available to members who: **1)** participate in the pharmacy program, and **2)** lack essential medications because a wholesale distributor has depleted all inventory of a medication. Access to the inventory request form is available on the NES program webpage. Please note, the medications available via the NES program are subject to change, and not all medications for which a mitigation strategy is published are available. For more information, contact pharmacyquestions@vizientinc.com.

Assessment

Due to continuous evolution of guidance and recommendations surrounding oncology agents, it is not practical to create mitigation strategies for each shortage as they are subject to frequent change based on guideline recommendations. This document will serve as a repository of general recommendations for oncology shortages, as well as specific recommendations for select agents. Oncology agents are critical, life-saving medications which have been acutely impacted by national shortages. Those vulnerable to shortages, generally, are generic medications with few manufacturers. Several of these agents are backbone therapies of various regimens. Additionally, not all have a readily available clinical alternative, and some are required therapies for curative treatment regimens. Refer to the American Society of Clinical Oncology (ASCO) ethical guidance to develop institutional processes to ethically manage oncology agent shortages. Hospitals and health systems are advised to have a mitigation strategy available in the event of a shortage of oncology agents.

Recommendation

Must know information

- Recommendations vary by oncology agent, by patient population, and on a case-by-case basis. The following general strategies, as clinically appropriate, should be assessed for each shortage:
    - Reduce or round down dose
    - Extend dosing interval
    - Prioritize for treatment with curative regimens
    - Prioritize for ongoing therapy and evaluate other regimens for new starts
    - Utilize an alternative treatment regimen
    - Delay treatment
- Refer to the American Society of Clinical Oncology clinical guidance (in collaboration with the Society of Gynecologic Oncology) and the National Comprehensive Cancer Network guidelines to evaluate clinical alternatives, potential alternative regimens, and establish which regimens are curative vs salvage therapy.

- Refer to Appendix 1 for member recommendations of select oncology agents (ie, cisplatin, fluorouracil, fludarabine, liposomal doxorubicin, methotrexate, and topotecan). Refer to Appendix 2 for recommendations of select cancer types.
- Round to the nearest vial size to reduce waste and conserve inventory, as clinically appropriate.
- Schedule patients requiring the same oncology agent on the same day to maximize vial usage and reduce wastage.

Clinical

1) Recommendations vary by oncology agent, by patient population, and on a case-by-case basis. The following general strategies, as clinically appropriate, should be assessed for each shortage:
    - Reduce or round down dose
    - Extend dosing interval
    - Prioritize for treatment with curative regimens
    - Prioritize for ongoing therapy and evaluate other regimens for new starts
    - Utilize an alternative treatment regimen
    - Delay treatment
2) Refer to the American Society of Clinical Oncology clinical guidance (in collaboration with the Society of Gynecologic Oncology) and the National Comprehensive Cancer Network guidelines to evaluate clinical alternatives, potential alternative regimens, and establish which regimens are curative vs salvage therapy.
3) Refer to Appendix 1 for member recommendations of select oncology agents (ie, cisplatin, fluorouracil, fludarabine, liposomal doxorubicin, methotrexate, and topotecan). Refer to Appendix 2 for recommendations of select cancer types.
4) Consult with institutional oncology specialists to discuss alternatives and alternative regimens, as clinically appropriate.
5) Consult with investigational program and principal study investigators, if applicable, for protocol recommendations regarding shortages, substitutions, and processes for deviations from the study protocol.

Operational

1) Implement electronic health record changes to prompt evaluations of alternatives and appropriateness of use (ie, ongoing therapy vs new start).
2) Round to the nearest vial size to reduce waste and conserve inventory, as clinically appropriate.
3) Schedule patients requiring the same oncology agent on the same day to maximize vial usage and reduce wastage.

Appendix 1. Clinical recommendations for select oncology agents

Cisplatin injection

1) Utilize carboplatin as an alternative to cisplatin, as clinically appropriate.
2) Based on anecdotal evidence, consider adjusted body weight dosing for obese patients.
3) Refer to the cisplatin importation checklist.

Fluorouracil (5-FU) injection

1) Utilize capecitabine plus oxaliplatin as an alternative to fluorouracil for new start patients on mFOLFOX6, as clinically appropriate.

2) Hold fluorouracil boluses as part of mFOLFOX6 and FOLFIRI regimens.
3) For continuous infusions of fluorouracil, evaluate switching to bolus doses, as clinically appropriate.

Fludarabine injection

1) Prioritize fludarabine for patients undergoing hematopoietic stem cell transplantation and chimeric antigen receptor T-cell therapy.

Liposomal doxorubicin injection

1) Prioritize liposomal doxorubicin for patients with relapsed Hodgkin lymphoma receiving gemcitabine, vinorelbine, liposomal doxorubicin (GVD) plus pembrolizumab and ovarian or peritoneal cancer patients with paclitaxel intolerances or reactions.
2) Consider alternative therapies for other cancer types, except for recurrent, platinum-resistant ovarian cancer if liposomal doxorubicin is the only option.

Methotrexate injection

1) Prioritize preservative-free products for pediatric patients, intrathecal use, and treatment of central nervous system lymphoma with concern of benzyl alcohol toxicity. High-dose methotrexate compounded with preservative-containing products are of greatest concern.
2) Consider alternative formulations of methotrexate for maintenance of chronic immune disease.

Topotecan injection

1) Prioritize topotecan injection for patients on intrathecal therapy for leptomeningeal disease (LMD) and pediatric patients with high-risk neuroblastoma.
2) Limit new starts for solid tumors with neuroendocrine / small cell features to patients for which alternative therapies are not clinically appropriate.
3) Transition patients with small cell lung cancer (SCLC) to oral capsules, as clinically appropriate.
4) Refer to national guidelines such as NCCN for treatment of solid tumors and alternative recommendations. Prioritize topotecan injection for patients with no alternative agents available.

Appendix 2. Alternative recommendations for select cancer types

Site-specific cancer type[a]	American Society of Clinical Oncology / Society of Gynecologic Oncology general recommendations and alternatives	Link to guidance document
Breast cancer	• Carboplatin and cisplatin have no role in the treatment of hormone receptor-positive HER2-negative breast cancer in the curative setting. • Carboplatin and cisplatin have a limited role in the non-curative setting for all subtypes of breast cancer during national shortage given available alternatives. • Clinical trials remain an important option for any line of therapy for both early and late-stage breast cancer that may provide a platinum-free alternative approach.	Link
Gastrointestinal cancer	• Capecitabine is a reasonable substitute for 5-FU (refer to 5-FU prescribing information for potential contraindications). • Oxaliplatin is a reasonable substitute for cisplatin. • Oxaliplatin is a reasonable substitute for carboplatin but must be provided in conjunction with 5-FU (or capecitabine if 5-FU is unavailable). • 5-FU should be prioritized for patients with dysphagia.	Link

Bladder cancer	Refer to link for guidance	Link
Testicular germ cell tumors	There are no alternatives to cisplatin in the first-line setting. The goal of treatment for testicular germ cell tumors is curative.	Link
Ovarian germ cell tumors	While non-platinum regimens exist, the preference is to refer the patient to a center where platinum is available or obtain the drug for the individual patient.	Link
Cervical, vulvar, and vaginal cancers	Prioritize cisplatin and carboplatin for cervical cancer treatment with curative intent.	Link
Gestational trophoblastic neoplasia (GTN)	• Prioritize methotrexate for curative intent treatment in patients with high-risk GTN. • Prioritize cisplatin for curative intent treatment in patients who have not responded to, or relapsed, after multi-agent chemotherapy regimens.	Link
Gynecologic cancer clinical trials	Refer to link for guidance	Link
Ovarian, fallopian tube, and peritoneal cancers	Refer to link for guidance	Link
Head and neck cancer	• Platinum agents (and cisplatin specifically) play a major role for which there is no substitution in the treatment of head and neck cancer patients. • This clinical advisory group recommends prioritizing head and neck cancers because there are no curative alternatives or substitutions for this cancer type. • Platinum should not be used in combination with radiation for cutaneous squamous cell carcinoma and salivary carcinoma nor in the postoperative radiotherapy setting for anything except positive surgical margins or extranodal extension.	Link
Mesothelioma	• Cisplatin and carboplatin have similar activity, but carboplatin has less toxicity and can generally be substituted. • Chemotherapy is inferior for patients with non-epithelioid histology, and immunotherapy is recommended. • Neoadjuvant or adjuvant immunotherapy may have activity; however, referral to a clinical trial is currently recommended.	Link
Non-small cell lung cancer	While non-platinum regimens exist, the preference is to refer the patient to a center where platinum is available or obtain the drug for the individual patient.	Link
Small cell lung cancer	Refer to link for guidance	Link

[a] Refer to links for complete information of available alternatives and recommendations.

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