PQI IN ACTION

TRILACICLIB (COSELA™) MANAGEMENT

NCODA'S POSITIVE QUALITY INTERVENTION IN ACTION

INTRODUCTION

To promote higher quality patient care, NCODA created the NCODA Positive Quality Intervention (PQI) as a peer-reviewed clinical guidance document for healthcare providers. By providing Quality Standards and effective practices around a specific aspect of cancer care, PQI's equip the entire multidisciplinary care team with a sophisticated yet concise resource for managing patients receiving cancer treatment. This PQI in Action is a follow up to the Trilaciclib (COSELA™) PQI and explores how the medically integrated teams at Blue Ridge Cancer Care and Cone Health incorporate PQIs as part of their daily workflow. It will discuss how utilizing the **Trilaciclib (COSELA™) Management** PQI elevates patient care.

Cone Health, located in Greensboro, North Carolina, is a private, not-for-profit healthcare system that includes five hospitals, six ambulatory care centers, three outpatient surgery centers, six urgent care centers, two retirement communities and more than 120 physician practices. Cone Health offers personalized cancer treatment options including chemotherapy, clinical trials, hormone therapy, immunotherapy, radiation therapy and surgery, each care plan customized to the patient's specific type of cancer, health status, treatment goals and personal preferences.

Blue Ridge Cancer Care is a private practice that serves patients in nine locations throughout Southwest Virginia. This multi-physician practice offers state-of-the-art technologies and comprehensive care for every patient. In an effort to advance cancer research, Blue Ridge Cancer Care participates in clinical trials through US Oncology Research, and it houses the only oncology phase I unit in Southwest Virginia.

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TRILACICLIB (COSELA™) AND THE MIP: IMPROVING PATIENT QUALITY OF LIFE

Trilaciclib is used to protect against and decrease the incidence of chemotherapy-induced myelosuppression when a patient is receiving an etoposide-containing regimen or a topotecan-containing regimen for the treatment of extensive-stage small cell lung cancer (ES-SCLC)[1,2]. Myelosuppression, a common dose-limiting side effect of many chemotherapeutic drugs[3], poses a burden for cancer patients as they face an increased risk of excessive bleeding and life-threatening infections[4]. This side effect is a result of the destruction of non-cancerous proliferating progenitor cells of red blood cells, white blood cells and platelets[3]. Trilaciclib helps protect these hematopoietic stem and progenitor cells by arresting them in the G1 phase of the cell cycle, where cells are actively growing, before being exposed to the chemotherapy[2]. Trilaciclib has shown a significant reduction in the incidence and duration of chemotherapy-induced myelosuppression[5,6], and can be dispensed by the Medically Integrated Team, thus improving the patient's experience and quality of life.

Administration of trilaciclib (COSELA™) may also signify a potential relief to the patient's economic burden associated with myelosuppression and related adverse events. An economic assessment of trilaciclib based on clinical data from the pivotal Phase II trial (G1T28-05) estimated health and economic outcomes in the group of patients with ES-SCLC that received a platinum/etoposide-containing or topotecan-containing chemotherapy regimen with prior administration of trilaciclib, and compared these outcomes to the group that did not receive trilaciclib prior to their platinum/etoposide-containing or topotecan-containing regimen. Results showed correlation between the use of trilaciclib and a reduced cost of adverse event management and G-CSF prophylaxis. The cost of adverse event management with trilaciclib was $13,833, versus $64,139 without this pre-medication. Additionally, the difference in cost of G-CSF prophylaxis with trilaciclib was $2,541, versus $5,082 without trilaciclib. Overall, the total cost saving per patient was $18,840 when trilaciclib was administered before receiving myelosuppressive chemotherapy regimen. These results suggest that administering trilaciclib prior to first-line chemotherapy for ES-SCLC can be a cost-saving approach for cancer patients, showing economic benefit in addition to the clinical benefit of reducing the incidence of chemotherapy-induced myelosuppression. However, there are some limitations with this study. The rates of adverse events were based on only one clinical trial, assuming that every patient would complete four treatment cycles, which might not be reflective of real-world practice, and no real-world data was available to compare and validate the results of this first economic analysis. In this Phase II trial, patients were recruited from the United States and Europe, and differences in health care and finance systems were not taken into account to determine the economic impact of adverse event management. Additionally, G1 Therapeutics sponsored the editorial process for this manuscript, and unintentional bias cannot be ruled out. Future prospective studies are needed to determine the cost effectiveness of trilaciclib in real-world practice.

Nurses administering medication at Cone Health.

Medically Integrated Pharmacy is a model that promotes a patient-centered, multidisciplinary team approach. The MIP is an outcome-based collaborative and comprehensive model that involves oncology health care professionals and other stakeholders who focus on the continuity of coordinated, quality care and therapies for cancer patients.[7] The MIP model can improve management of patients on therapies like trilaciclib in several ways including improved communication across the practice, efficient management of regimen changes, quicker speed to therapy initiation, increased patient satisfaction, more robust financial assistance services, cost avoidance and producing less waste.[8] NCODA offers multiple tools to aid the MIP practice in managing anti-cancer therapies. This toolbox contains a Patient Survey that is practice-customizable, a Cost Avoidance and Waste Tracker, a Financial Assistance database, Treatment Support Kits, Patient Education sheets, and the Positive Quality Intervention clinical resource.

THE POSITIVE QUALITY INTERVENTION: CONCISE INFORMATION THAT GUIDES PATIENT-CENTERED DECISIONS

This article will explore the benefits of PQI utilization as a core standard of the MID and how adoption can benefit any practice. The PQI: **Trilaciclib (COSELA™) Management** is an evidence-based resource created for healthcare providers for managing patients at high risk for myelosuppression who will be receiving trilaciclib as a protective agent when undergoing treatment for ES-SCLC with a platinum/etoposide or topotecan-based regimen. It serves as an easy-to-read guide that walks the healthcare provider through the MID process from ordering, to reviewing patient criteria and risk factors, to managing adverse reactions at the time of infusion. Blue Ridge Cancer Center's Autumn Alvarez, PharmD, states that "the PQI is very concise and gives me the basics of all the information that I'm going to need to decide what I am going to tell the patient."

"THE PQI IS VERY CONCISE AND GIVES ME THE BASICS OF ALL THE INFORMATION THAT I'M GOING TO NEED TO DECIDE WHAT I AM GOING TO TELL THE PATIENT."

Autumn Alvarez, PharmD

Blue Ridge Cancer Care and Cone Health have both found successful ways to incorporate clinical resources, like the PQI, into practice. Each practice positions their Medically Integrated Teams in a way to ensure appropriate treatment, increased compliance, and maximize clinical outcomes. We will take a look specifically at their MID settings, how implementing the PQI: Trilaciclib (COSELA™) Management benefits their staff and patients, and how they advance patient care on a daily basis. When questions arise within the Medically Integrated Team, such as laboratory concerns or dose-related issues, Brandy Persson, PharmD, BCOP Oncology Pharmacist from Cone Health states that "often, answers are found in PQIs, especially when managing toxicities" and Debra McCorkindale, RN from Blue Ridge Cancer Center agrees that "the adverse reactions section is very valuable and helpful".

CLICK HERE TO VIEW PQI

"OFTEN, ANSWERS ARE FOUND IN PQIs, ESPECIALLY WHEN MANAGING TOXICITIES"

Brandy Persson, PharmD, BCOP

THE INTEGRATED PHARMACY MODEL

The Integrated Pharmacy Model addresses the challenges and limitations that other pharmacy models face, such as delays in treatment due to processing and transit times[10]. Autumn Alvarez, PharmD, from Blue Ridge Cancer Center says that "With a Medically Integrated Pharmacy here on site, we are more efficient than other pharmacies. We can turn around things to get the medication to the patient quicker." At Cone Health, the multidisciplinary team recognizes that "nursing is probably one of the most important parts of the Medically Integrated Pharmacy Team. They are with the patient all the time, and this helps to overcome obstacles before they are there. They have knowledge about the administration process, lines, compatibility and how to decrease wait time and total time at infusion, which is really important to the patients as well", as expressed by Persson.

Communication is essential to ensure an effective and safe infusion process. Debra McCorkindale, RN, safety nurse at Blue Ridge Cancer Center, walked us through the steps of the infusion process at their facility, and emphasized the importance of effective communication within the team. She explai-

ned that there is constant messaging between the physician, pharmacist, and nurses via a private patient chart messaging system. Similarly, at Cone Health the interdisciplinary team communicates with each other through a secure instant messaging feature in their Electronic Health Record in addition to numerous calls that the pharmacists receive each day from the members of the MIP team to ensure that all patient safety concerns are addressed, as described by Persson.

PUTTING THE TRILACICLIB (COSELA™) MANAGEMENT PQI INTO ACTION

The **Trilaciclib (COSELA™) Management** PQI provides the reader with background information, with the purpose of describing the indication, pharmacology and dosing of trilaciclib. This evidence-based guide presents a brief summary of the results from clinical trials, including the pivotal study (GIT28-05) used for FDA approval of the medication, which showed significant decrease in the incidence and duration of severe neutropenia versus placebo, and in the need for supplemental granulocyte colony-stimulating factor (GCS-F)[1]. Results from the pivotal study showed a decrease in the incidence of severe neutropenia in patients that received treatment with trilaciclib versus those that received placebo (2% vs 49%, P<0.0001), and a decrease in the mean duration of severe neutropenia in cycle 1 (1 day vs 4.7 days, P<0.0001)[1]. This and other studies have shown a decrease in the need for GCS-F support in patients that received trilaciclib versus placebo (1.149 events/cycle vs 0.280 events/cycle respectively, P=0.0145). Additionally, trialciclib decreased the need for platelet transfusions, although these results were not statistically significant[11].

Amanda Skeen,CPhT, Pharmacy Technician from Cone Health describes the PQI as a "short and condensed version of the package insert". When evaluating trilaciclib's safety and efficacy, the **Trilaciclib (COSELA™) Management** PQI can be used as a quick reference.

THE PQI IS A "SHORT AND CONDENSED VERSION OF THE PACKAGE INSERT."

Amanda Skeen, CPhT

THE PQI PROCESS

The first step in the Trilaciclib (COSELA™) PQI Process is identifying the patients that are at high risk of myelosuppression who will receive treatment for ES-SCLC with a platinum/etoposide or topotecan based regimen. To identify patients eligible to receive trilaciclib, Dr. Goldschmidt from Blue Ridge Cancer Center says, "I stick with the FDA indication – small cell carcinoma of the lung receiving platinum, etoposide or topotecan based therapy". The PQI Process gives readers a step-by-step process to follow after identifying an appropriate candidate for treatment, laying out the intervention, clinician directed guidance, and critical clinical criteria that could be potentially overlooked in practice. This section is where the MIP should begin upon receipt of an order for trilaciclib. After confirming appropriateness of the therapy, a medication review is recommended to identify potential interactions with agents such as cisplatin, dofetilide and dalfampiridine, as well as reviewing the adverse effects associated with trilaciclib and recommending actions based on the supplemental information included in the PQI. The most common adverse reactions for trilaciclib are infusion-site reactions, fatigue, hypocalcemia, hypophosphatemia, increased aspartate aminotransferase, headache, and pneumonia.

At Cone Health, the pharmacy team utilizes PQIs as "confirmation that we are doing a good job", as Brandy Persson, PharmD commented. Dr. Mohamed added that "we work together to prevent and treat injection site reactions, monitor and treat electrolyte abnormalities, as well as facilitate appropriate COSELA™ and chemotherapy timing particularly in instances when a COSELA™ dose is missed or discontinued."

The PQI Process for COSELA™ includes dosing and administration details that can guide pharmacy technicians in the preparation process, pharmacists in the verification process, and nurses at the time of infusion. Trilaciclib 240 mg/m2 is administered over 30 minutes within 4 hours prior to starting the chemotherapy infusion. The 300mg vial is reconstituted in 19.5 mL NS or D5W, resulting in a concentration of 15 mg/mL. The **Trilaciclib (COSELA™) Management** PQI includes important details to keep in mind when diluting the medication, such as making sure that the final solution is clear yellow. Further dilution with NS or D5W will yield a concentration between 0.5-3 mg/mL[2].

"WE WORK TOGETHER TO PREVENT AND TREAT INJECTION SITE REACTIONS, MONITOR AND TREAT ELECTROLYTE ABNORMALITIES, AS WELL AS FACILITATE APPROPRIATE COSELA AND CHEMOTHERAPY TIMING PARTICULARLY IN INSTANCES WHEN A COSELA DOSE IS MISSED OR DISCONTINUED."

Mohamed K. Mohamed, MD, PhD

PATIENT-CENTERED ACTIVITIES: PRIORITIZING PATIENT SAFETY

The Patient Centered Activities section follows the PQI Process and gives specific patient centered guidance for the team. The first points of the Trilaciclib (COSELA™) Management PQI Patient Centered Activities revolve around patient education, to be provided to the patient in written and verbal form, followed by instructing the patient to notify the infusion nurse of any signs of infusion-related toxicity, such as irritation, swelling, pain, redness, or itchy skin around the injection site during the infusion, and any worsening respiratory issues. When it comes to counseling patients, Dr. Goldschmidt, Medical Oncologist from Blue Ridge Cancer Center, reiterated that it is important to "educate them about the chemical phlebitis, pneumonitis and hypersensitivity issues." The Patient Centered Activities also include educating patients of childbearing potential on the possible harms to the unborn baby, and guides the provider through patient counseling, focusing on the treatment regimen and verifying the patient's understanding.

As part of the medication administration process, patient education is an important task that involves everyone in the Medically Integrated Team. At Blue Ridge Cancer Center, most of the patient education on intravenous chemotherapy regimens is done by the physician. Patients are scheduled to come in for an in-person teaching appointment with the physician, physician assistant or nurse practitioner, sometimes on the same day of treatment, to go over the patient's chemotherapy regimen, the expected side effects during the infusion, and ensuring that the patient receives an on-call number for guidance on the management of other potential complications. Dr. Mohamed, medical oncologist at Cone Health, feels strongly about working with a medically integrated team, saying that "I enjoy the collaboration with our integrated pharmacy team. Our team and our patients benefit from their knowledge and experience."

"I ENJOY THE COLLABORATION WITH OUR INTEGRATED PHARMACY TEAM. OUR TEAM AND OUR PATIENTS BENEFIT FROM THEIR KNOWLEDGE AND EXPERIENCE."

Mohamed K. Mohamed, MD, PhD

Additional supplemental information on the **Trilaciclib (COSELA™) Management** PQI provides recommended actions for the most pertinent adverse reactions that could occur when a patient is started on this medication.

ADVERSE REACTION	SEVERITY	RECOMMENDED ACTION
Injection-site reactions, including phlebitis and thrombophlebitis	Grade 3: Ulceration or necrosis; severe tissue damage; operative intervention indicated OR Grade 4: Life-threatening consequences; urgent interventions indicated	Stop infusion and permanently discontinue
Acute drug hypersensitivity	Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL)	Stop infusion and hold trilaciclib until recovery to ≤Grade 1 or baseline; then consider resuming trilaciclib If Grade 2 recurs, permanently discontinue
	Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL OR Grade 4: Life-threatening consequences; urgent intervention indicated	Permanently discontinue
ILD/ Pneumonitis	Grade 2: Symptomatic	Hold trilaciclib until recovery to ≤Grade 1 or baseline; consider resuming trilaciclib If Grade 2 recurs, permanently discontinue
	Grade 3: Severe symptoms; limiting self-care ADL; oxygen indicated OR Grade 4: Life-threatening respiratory compromise; urgent intervention indicated	Permanently discontinue
Other toxicities	Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL	Hold trilaciclib until recovery to ≤Grade 1 or baseline; consider resuming trilaciclib If Grade 3 recurs, permanently discontinue
	Grade 4: Life-threatening consequences; urgent intervention indicated	Permanently discontinue

IV INFUSION BAG MATERIAL	DILUENT	DILUTED STORAGE DURATION
Polyvinyl chloride (PVC), Ethylene vinyl acetate (EVA), Polyolefin (PO), or Polyolefin/polyamide (PO/PA)	D5W	Up to 12 hours at 20°C to 25°C (68°F to 77°F)
PVC, EVA, or PO	NS	Up to 8 hours at 20°C to 25°C (68°F to 77°F)
PO/PA	NS	Up to 4 hours at 20°C to 25°C (68°F to 77°F)

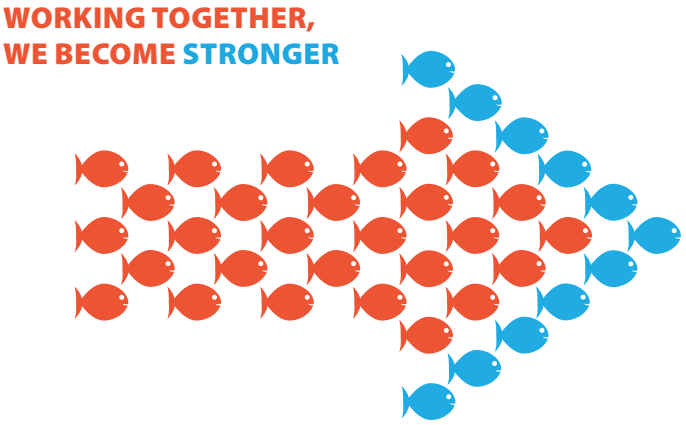
CONCLUSION: NCODA, THE MID AND PQI – COLLABORATION LEADS TO POSITIVE OUTCOMES

At Cone Health and Blue Ridge Cancer Center, safe and effective patient care is ensured by encouraging collaboration within the members of a Medically Integrated Team and utilizing evidence-based resources such as PQIs to support clinical decisions. Debra McCorkindale, RN is very passionate about her patients, and she shared her response when they point out their positive experience with the health care team at Blue Ridge Cancer Center: "It is easy to be nice when we have a really great group of patients to work with."

The MIP model was designed with patients and the medical professionals in mind, with the ultimate goal of obtaining positive outcomes for each patient. Accessibility, conciseness, and ease of use are three things that make PQIs stand out. These peer-reviewed documents can be utilized by any member of the team as a quick reference when questions arise at any step of the MIP process, bringing value to the patient care process at health care centers like Cone Health and Blue Ridge Cancer Center. NCODA is committed to improving cancer patient care by providing educational tools and resourced based on the most recent data with the highest quality of evidence. Pairing Medically Integrated Dispensing with the **Trilaciclib (COSELA™) Management** PQI meets NCODA's Guiding Values of being Patient-Centered and Always Collaborative.

"IT IS EASY TO BE NICE WHEN WE HAVE A REALLY GREAT GROUP OF PATIENTS TO WORK WITH."

Debra McCorkindale, RN



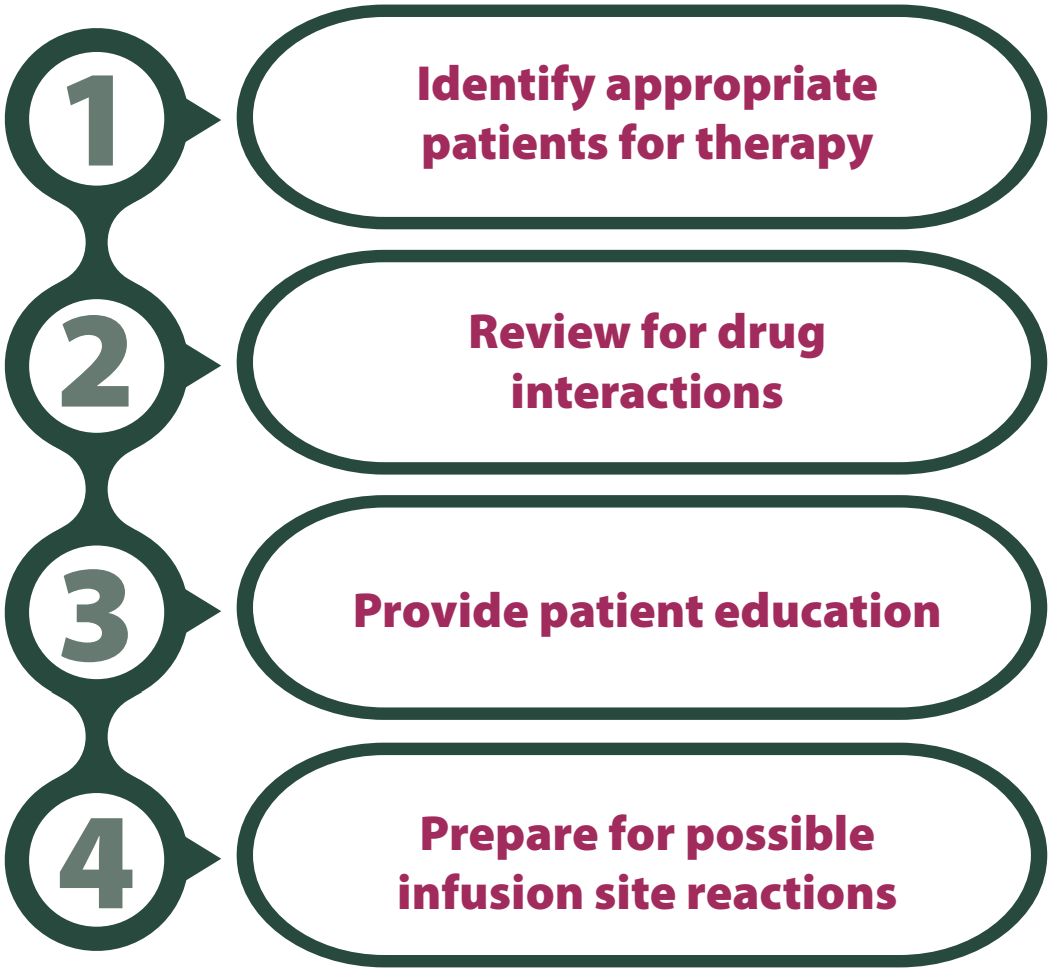
REFERENCES

1. COSELA™ (trilaciclib) [package insert]. Durham, NC: G1 Therapeutics, Inc.; 2021.
2. National Comprehensive Cancer Network. Small Cell Lung Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf . Accessed September 10, 2022.
3. Maxwell MB, Maher KE. Chemotherapy-induced myelosuppression. Semin Oncol Nurs. 1992. 8(2):113-23. doi: 10.1016/0749-2081(92)90027-z.
4. Epstein RS, Weerasinghe RK, Parrish AS, Krenitsky J, Sanborn RE, Salimi T. Real-world burden of chemotherapy-induced myelosuppression in patients with small cell lung cancer: a retrospective analysis of electronic medical data from community cancer care providers. J Med Econ. 2022. 25(1):108-118. doi: 10.1080/13696998.2021.2020570.
5. Ferrarotto R, Anderson I, Medgyasszay B, García-Campelo MR, Edenfield W, Feinstein TM, Johnson JM, Kalmadi S, Lammers PE, Sanchez-Hernandez A, Pritchett Y, Morris SR, Malik RK, Csőszi T. Trilaciclib prior to chemotherapy reduces the usage of supportive care interventions for chemotherapy-induced myelosuppression in patients with small cell lung cancer: Pooled analysis of three randomized phase 2 trials. Cancer Med. 2021. 10(17):5748-5756. doi: 10.1002/cam4.4089.

REFERENCES

6. Hussein M, Maglakelidze M, Richards DA, Sabatini M, Gersten TA, Lerro K, Sinielnikov I, Spira A, Pritchett Y, Antal JM, Malik R, Beck JT. Myelo-protective Effects of Trilaciclib Among Patients with Small Cell Lung Cancer at Increased Risk of Chemotherapy-Induced Myelosuppression: Pooled Results from Three Phase 2, Randomized, Double-Blind, Placebo-Controlled Studies. Cancer Manag Res. 2021. 13:6207-6218. doi: 10.2147/CMAR.S313045.
7. NCODA. NCODA Announces the defining of the Medically Integrated Dispensing Pharmacy. https://www.ncoda.org/medically-integrated-dispensing-pharmacy/. Accessed September 10, 2022.
8. Wimbiscus, B. Medically Integrated Dispensing: An Alternative to How Oral Drugs Get Dispensed. Am J Manag Care. 2019. https://www.ajmc.com/view/medically-integrated-dispensing-an-alternative-to-how-oral-drugs-get-dispensed.
9. Alvarez A. PQI: Trilaciclib (Cosela) Management. 2022. https://www.ncoda.org/wp-content/uploads/pqis/PQI-Trilaciclib-Cosela-Management_PQI_NCODA.pdf.
10. Dillmon MS, Kennedy EB, Reff M. Patient-Centered Medically Integrated Dispensing: ASCO/NCODA Standards Summary. JCO Oncology Practice. 2022. 16(6):344-348. https://ascopubs.org/doi/full/10.1200/OP.19.00668.
11. Cosela™ (trilaciclib) for chemotherapy induced myelosuppression in Adult patients with Extensive-Stage Small cell lung cancer. AMCP DOSSIER 2/18/2021.

PQI PRINCIPLES:



NOTES:

ON THE COVER:

- Nurses at Cone Health review a patient profile before chemotherapy administration.

Helpful Online Resources

- Trilaciclib (COSELATM) Management PQI
- Positive Quality Interventions
- Intravenous Cancer Treatment Education Handouts
- NCODA Website
- NCODA Financial Assistance Tool

Practice panelist's comments reflect their experiences and opinions and should not be used as a substitute for medical judgement.

Important notice: NCODA has developed this Positive Quality Intervention in Action platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.

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