

PQI IN ACTION



**BRENTUXIMAB VEDOTIN
(ADCETRIS®): NEUROPATHY AND
NEUTROPENIA MANAGEMENT PQI**



**NCODA'S POSITIVE QUALITY
INTERVENTION IN ACTION**

INTRODUCTION

In an effort to promote higher quality patient care NCODA created the NCODA Positive Quality Intervention (PQI) as a peer-reviewed clinical guidance resource for healthcare providers. By providing Quality Standards and effective practices around a specific aspect of cancer care, PQIs equip the entire multidisciplinary care team with a sophisticated yet concise resource for managing patients receiving oral or IV oncolytics. This PQI in Action is a follow up to the **Brentuximab Vedotin (ADCETRIS®): Neuropathy and Neutropenia Management PQI** and explores how the Medically Integrated Teams at Smilow Cancer Center at Yale New Haven Health and Cancer Specialists of North Florida incorporate PQIs as part of their daily workflow. This article will discuss how utilizing the **Brentuximab Vedotin (ADCETRIS®): Neuropathy and Neutropenia Management PQI** elevates patient care.

Smilow Cancer Center at Yale New Haven Health includes a main campus center, Smilow Cancer Hospital, and ambulatory centers across the state of Connecticut and Rhode Island. Smilow Cancer Hospital is recognized by the American Society of Clinical Oncology with QOPI certification. Smilow Cancer Hospital has more than a dozen multidisciplinary cancer teams to serve patients.

Cancer Specialists of North Florida (CSNF) has provided cancer treatment to their community for over three decades. They are a physician-owned practice with 12 locations and 31 physicians. CSNF owns Florida Specialty Pharmacy, which serves as their central hub for prescriptions. Their pharmacists work as a team with CSNF physicians to ensure complicated medications are taken in the most effective way.

THE PARTICIPANTS

Smilow Cancer Center at Yale New Haven Health New Haven, CT



Shalin Kothari, MD
Hematologist / Oncologist



Ashley Vitale, RN
Nurse



Kejal Amin, PharmD, MBA, BCOP
Clinical Oncology Pharmacist



Andrea Goodhue, CPhT
Oncology Pharmacy Technician II

Cancer Specialists of North Florida Jacksonville, FL



Bijoy Telivala, MD
Hematologist / Oncologist



Rita Lyles, RN, ASN
Practice Manager



Kristie Fox, PharmD
Clinical Pharmacist



Alexander Stanley, RPhT, CPhT
Lead IV Pharmacy Technician

DEFINING MEDICALLY INTEGRATED PHARMACY AND THE POSITIVE QUALITY INTERVENTION

Medically Integrated Pharmacies (MIP) are a type of service model in which patients receive oral and IV therapies at the site of care with their doctor and are managed by one staff; state-of-the-art pharmacy services are built within the oncologist's office that help to deliver timely and ongoing care as part of a single, multidisciplinary team. Complexity of cancer treatment has recently increased with a growing number of both oral and IV therapies which are delivered across an often-confusing, payer-driven healthcare system. Various treatment settings including community, institutional, and academic centers have made successful efforts to transition to this integrated service model to maintain continuous care of the patient and achieve the best possible clinical outcomes.

Empowered with innovative tools like the PQI, the Medically Integrated Teams have improved the quality of care delivered at their institutions through adoption of NCODA resources. These leading oncology organizations value the PQI which provides concise, clinical guidance information to raise the standard of care across all the professional disciplines. In general, PQIs afford attention to any critical aspect of drug ther-



Sunshine Sousa, RN and Kejal Amin, PharmD, MBA, BCOP discuss a patient case.

apy that may be easily overlooked (“if you see ‘x’, remember to do ‘y’”). In a world where new and novel treatments arise almost daily, healthcare professionals need an easy-to-use reference to enact the key clinical principles for each therapy. The PQI serves that need.

THE BRENTUXIMAB VEDOTIN (ADCETRIS®): NEUROPATHY AND NEUTROPENIA MANAGEMENT PQI

Brentuximab vedotin (ADCETRIS®) is a CD30-directed antibody drug conjugate (ADC) with multiple indications in various lymphomas, including front-line treatment for patients with classical stage III/IV Hodgkin's Lymphoma (cHL) or CD30-expressing peripheral T-cell lymphomas (PTCL) in combination with multiagent chemotherapy.¹ ADCs offer a unique modality of drug delivery to cancer cells expressing specific targets.²

The **Brentuximab Vedotin (ADCETRIS®): Neuropathy And Neutropenia Management PQI** gives the multi-disciplinary team a concise resource for safely managing select toxicities associated with brentuximab vedotin. The PQI is laid out in sections and begins with a Description followed by the Background, PQI process, and Patient-Centered Activities sections. Smilow Cancer Center pharmacy technician Andrea Goodhue, CPhT shares, “it is wonderful to have the PQI available. You can see what you need right away.” CSNF

pharmacy technician Alexander Stanley, RPhT, CPhT also finds value in the PQI and adds “there is a lot of information out there for every single drug so it is definitely beneficial to have the information in a consolidated format that anyone on the team can use.”

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Alexander Stanley, RPhT, CPhT

THE MEDICALLY INTEGRATED TEAM: A WINNING APPROACH FOR PATIENTS

Healthcare has not always been approached as the “team sport” we currently know and love.³ The healthcare landscape has changed dramatically in the last 20 years and the clinician operating in isolation is now seen as undesirable.⁴ Incorporating multiple perspectives in healthcare offers the benefit of diverse knowledge and experience, and a high-functioning team is an essential tool for building a more patient-centered, coordinated, and effective healthcare delivery system.⁴ Teams are defined as two or more people who interact dynamically, interdependently, and adaptively to achieve a common, valued goal.³ The oncology team plays a vital role in providing high quality patient care with positive outcomes. Pharmacy plays an important part of the team in both of our participating practices.

shares, “the goal of our practice is to improve patient care by using the appropriate drugs at the right time.” He says that at CSNF the pharmacist plays a very important role in meeting this goal. “They are one of the cornerstones of any oncology practice. They are a check and balance.” He adds, “gone are the days when medicine was a one man, or one woman show. It is a team effort. If you do not have a good team, everyone will suffer in different degrees.”

“WITHOUT PHARMACY, I COULD NOT FUNCTION. I THINK IT IS AN INTEGRAL PART OF OUR TEAM.”

SHALIN KOTHARI, MD

Dr. Shalin Kothari has a clinical focus on aggressive B cell lymphomas at Smilow Cancer Center and also participates in a research lab on mantle cell lymphoma. When asked about the role of pharmacy and the Medically Integrated Team at Smilow he comments, “without pharmacy, I could not function. I think it is an integral part of our team.” He adds that “a very tightly integrated provider and pharmacy team” really plays a role in medication safety and making sure all aspects of drug management and care are correct for patients.

“GONE ARE THE DAYS WHEN MEDICINE WAS A ONE MAN, OR ONE WOMAN SHOW. IT IS A TEAM EFFORT.”

Bijoy Telivala, MD

Bijoy Telivala, MD is a board member at CSNF that actively participates in GPO negotiations, the Clinical Excellence Committee, and the Oncology Care Model Committee. He

THE PQI DESCRIPTION AND BACKGROUND

The first two sections of the Brentuximab Vedotin (ADCETRIS®) PQI are the Description and Background. The Description gives the FDA approved indication and purpose of the PQI. The Background lists study information and other information on brentuximab vedotin. It gives the mechanism of the drug and explains that a monomethyl auristatin E (MMAE) is attached via a linker to a mAb directed against CD30. Upon

binding to CD30 on the cell surface, brentuximab vedotin is internalized, and the linker is cleaved to release MMAE, which then exerts its cytotoxic effect.^{1,2} Dr. Telivala shares, “it is a very good drug made by Seagen. It is a conjugate with the cytotoxic loaded to a linker which helps pinpoint therapy. The important thing to remember is that it is not a benign drug. For a matter of fact, there is no drug which is benign.”

The PQI Background goes on to discuss the Echelon-1 and Echelon-2 trials. In both trials outcomes favored brentuximab vedotin and chemotherapy combination over standard of care chemotherapy.² It was concluded that the brentuximab vedotin and chemotherapy regimen was associated with more myelotoxicity and neurotoxicity (which is largely reversible) than standard of care but substantially less pulmonary toxicity.⁵ It also appeared to be more effective for the frontline treatment of advanced-stage classic Hodgkin's lymphoma.⁵ The PQI discusses the need for the clinician to be aware of the potential adverse events of neuropathy and hematologic toxicities and how to optimally manage these events.² Patients with cHL can be treated with the intent to cure, so these measures may be particularly important in this group.² Dr. Kothari agrees with the importance of managing toxicities in the upfront HL population. He shares “we want to stick to the schedule because there is a lot to lose since 95% of patients will go into remission. We don't want to hamper that chance of remission.”



Kristie Fox, PharmD, works with CSNF pharmacy technicians to ensure proper drug delivery.

THE PQI PROCESS

The Brentuximab PQI Process section consists of two parts. The first part is on Neutropenia Prevention and Management. It covers five points for the multidisciplinary team.

- ▶ Patients initiating front-line therapy with brentuximab vedotin for HL or PTCL should receive granulocyte colony-stimulating factor (G-CSF) beginning with Cycle 1, Day 1.
- ▶ The choice of G-CSF therapy should follow institutional standard and formulary. The use of long acting G-CSF agents is appropriate when indicated as both treatment regimens are administered every 14 or 21 days.
- ▶ Brentuximab vedotin for HL offers a bleomycin-free treatment option for patients.
- ▶ All patients who experience Grade ≥ 3 neutropenia who did not receive primary G-CSF prophylaxis should receive it with subsequent cycles.
- ▶ CBC with differential should be assessed prior to each dose of brentuximab vedotin.

CSNF Clinical Pharmacist, Kristie Fox, PharmD, shares G-CSF prophylaxis is built into the brentuximab care plans in the EMR at her practice. She says it varies depending on indication and regimen, but the prophylaxis is set up and “the providers can alter and change that if they see fit.” Smilow Cancer Center Clinical Oncology Pharmacist, Kejal Amin, PharmD, MBA, BCOP, describes the pharmacist clinical evaluation process at her center, “we check for supportive care.” She adds the pharmacist checks to ensure the patient is “on the right antiemetics and has a growth factor prescribed to them.” Her clinical pharmacy team checks labs so they can identify if a patient has any neutropenia. Smilow oncology nurse Ashley Vitale, RN says nursing also verifies labs prior to each treatment and alerts the provider at a certain level ANC or of any new problems that arise. Dr. Kothari comments, “we just assume that myelotoxicity is going to be quite high, more than the traditional AVBD regimen and hence we always follow AVD plus brentuximab with G-CSF support. It has become kind of a standard as per the Echelon-1 trial.”

One newer challenge both practices are facing is the emergence of biosimilars for the growth factors. Biosimilars were first introduced in the United States in 2015 and their approval and utilization continues to grow each year.⁶ The goal

of a biosimilar form is to offer the same high-quality biologic product at a fraction of the cost.⁶ NCODA has offered multiple international meeting presentations on the subject as well as an article in the Fall 2020 edition of *Oncolytics Today*. The use of biosimilars as well as specific product selection is heavily influenced by a patient's medical insurance, and the need to stock and utilize multiple biosimilars for the same biologic agent requires extra care and coordination from oncology practices. CSNF practice manager Rita Lyles, RN, ASN discusses biosimilar utilization for growth factors in her practice. She shares, "we are very fortunate at CSNF to have our own authorization team. We also have hard stops in care plans so the G-CSF product must be authorized, or it will not allow you to print the order or pull the medication from the dispensing cabinet."

The next part of the Brentuximab PQI section covers Neuropathy Prevention and Management.

Neuropathy Prevention and Management

- ▶ Neuropathies, primarily sensory rather than motor, may be seen in approximately >50% of patients. In clinical trials, most patients experienced only Grade 1 or 2 neuropathy and majority improved with intervention.
- ▶ Symptoms of hypo- or hyperesthesia, paresthesia, discomfort, burning sensation, weakness, tingling and neuropathic pain should be assessed with each cycle.
- ▶ Counsel patients to report any numbness or tingling in their hands or feet or muscle weakness.

Dr. Kothari shares, "neuropathy is not an easily reversible side effect, if it does reverse it takes many months before patients feel like they are at their baseline. I feel like the best thing to do is prevent it, so a detailed history of a patient's comorbidities is extremely vital." Dr. Telivala comments, "neuropathy is real, and it is disabling. We may start gabapentin, pregabalin or duloxetine in patients and it sometimes works but is usually not a home run." He discusses that management is important to the patient who is having to deal with this day in and day out and when necessary he does drop the brentuximab vedotin dose. He says it is important to remember that "the trial population is the best population. It has the most fit patients, multiple pharmacists and multiple coordinators. If the trial required dose adjustments, real life is likely to require them even more."

Lyles has over 30 years of nursing experience and shares that many times nurses pick up on neuropathy when a patient is in the chair for their IV infusion. "While in the infusion chair, patients will tell the nurses things they do not think about with the physician. When they are with the doctor, they want to discuss the state of their cancer and they forget about things like neuropathy and diarrhea. When they get in the chair they are more relaxed. We complete our full assessment and ask about side effects and that is when they may remember the tingling in their legs, feet, or fingers. The nurses then have the ability to go back to the physician with an updated assessment so the provider can determine what needs to be done." According to Vitale, the nurses at Smilow Cancer Center are also completing a nursing assessment prior to each treatment including a neuropathy assessment. The assessment is part of their EMR workflow and asks patients about numbness, tingling, loss of sensation, and various activities of daily living. After completing the assessment, the nurse alerts the provider of any problems.

"WHILE IN THE INFUSION CHAIR, PATIENTS WILL TELL THE NURSES THINGS THEY DO NOT THINK ABOUT WITH THE PHYSICIAN. WHEN THEY ARE WITH THE DOCTOR, THEY WANT TO DISCUSS THE STATE OF THEIR CANCER AND THEY FORGET ABOUT THINGS LIKE NEUROPATHY AND DIARRHEA. WHEN THEY GET IN THE CHAIR THEY ARE MORE RELAXED."

RITA LYLES, RN, ASN

The PQI Process section includes a table on potential dose adjustments for neuropathy. Amin feels this table is the most important part of the Brentuximab PQI. Dr. Kothari agrees and says he would say the most beneficial part of the PQI

is the table. He explains, “I think this is probably the most important thing. If there is sensory neuropathy we typically continue because it is usually short-lived, especially in the early grades. For motor neuropathy, there is a lot to lose, so we would reduce it at grade 2 or even discontinue at grade 3.” He does mention that the dose adjusting is very nuanced based

on the physician and patient. Dr. Telivala also discusses the difficulty that can present in grading neuropathies and distinguishing between grades 2 and 3. In the event a dose does have to be reduced, both practices can make the adjustments real-time. Stanley comments, “since we are all connected, it is very easy to readjust for immediate changes.”

DOSE ADJUSTMENTS FOR NEUROPATHY		
Brentuximab vedotin (ADCETRIS®) Dose ¹	Grade	Intervention
1.8 mg/kg (max 180mg) every 3 weeks + CHP*	2	Sensory: Continue Motor: Reduce to 1.2 mg/kg
	3	Sensory: Reduce to 1.2 mg/kg Motor: Discontinue
	4	Discontinue
1.2 mg/kg (max 120mg) every 2 weeks + AVD**	2	Reduce to 0.9 mg/kg
	3	Hold until recovers to ≤ grade 2 and restart at 0.9 mg/kg Consider modifying other neurotoxic chemo
	4	Discontinue

PATIENT-CENTERED ACTIVITIES: KEEPING THE FOCUS ON PATIENTS

The Patient-Centered Activities section follows the PQI Process and gives patient-centered guidance for the team. The Brentuximab PQI Patient-Centered Activities reviews patient education and symptom reporting. Fox comments, “I really like the Patient-Centered Activities. I think everything on here is very helpful and I can tell you that when our interns and oral chemotherapy pharmacists make patient phone calls I have highly encouraged them to use the PQIs. They often receive questions about the IV infusions while they are on the phone with patients discussing oral therapies, so to be able to pull one of these quickly is very helpful to answer any questions the patients might have.”

Both the Smilow Cancer Center and CSNF teams place an emphasis on patient education and consider it extremely important. In 2020 Smilow Cancer Center implemented phar-

“WE GO IN TOGETHER AND WE TAG-TEAM. IT HAS BEEN REALLY GREAT FOR BOTH OF US. I HAVE LEARNED A LOT FROM NURSING.”
Kejal Amin, PharmD, MBA, BCOP

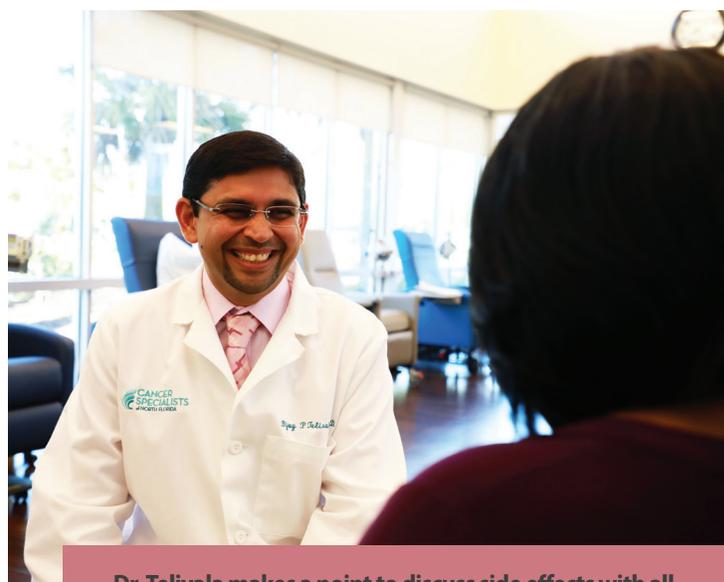
macy and nursing co-counseling. Anytime a patient is started on a new therapy, a pharmacist and nurse provide education together. The pharmacist discusses the drug, and the nurse discusses things like line care, what to expect at each appointment, labs and how often patients will return to the clinic.

Amin shares “we go in together and we tag-team. It has been really great for both of us. I have learned a lot from nursing.” Nurses at CSNF provide an initial chemotherapy teach. Lyles explains “all new patients are scheduled for a completely independent teaching. We pull the patient and the family into our teaching room and we are able to sit down in a relaxed environment to help them understand drug information, potential side effects and how to manage these effects. We explain what they should be looking for and when to let us know. We tell them to call first and call early.”

The PQI reminds the team to educate patients to report fevers and signs of infection to the provider immediately. The team can also educate the patient on the G-CSF therapy they may be receiving. The PQI also discusses the potential for patients (especially those with HL) to under report symptoms due to a concern of diminished efficacy with interventions.² Helping patients understand the balance between safety and efficacy is important, and this is one more way that having access to the Medically Integrated Team and total care in-house can improve patient outcomes. Dr. Telivala is a proponent of having the infusion center right there with his office and the unparalleled access it gives his patients. He says, “it is very easy for us to walk the twenty steps and talk to them and answer a question they may have forgotten earlier.”

Dr. Telivala also feels that toxicity checks are an important part of the care his team provides. He says these visits are important whether in-person or via telemedicine. “Do not just give the medication and not see the patient again. If you are worried about neuropathy, you can have the patient walk down the hallway. If you see that the gait is changing, you

know that something is happening. Talk to the family. Two or three simple questions can provide you with a lot of information and then you as the physician or healthcare provider can decide. There is no one size fits all but not talking to and discussing with the patient is where the majority of trouble happens.” The PQI Patient Activities acknowledges the importance of building this rapport with patients. It lists other tests that can help assess for neuropathy including buttoning a shirt or picking up a coin off a flat surface. The PQI also reminds the team that colder temperatures may exacerbate the neuropathies and that patients who initially do not report symptoms with a caregiver and later do could be underreporting symptoms.²



Dr. Telivala makes a point to discuss side effects with all patients and their families.

THE MEDICALLY INTEGRATED TEAM: PROVIDING SAFE AND INNOVATIVE TREATMENT

NCODA member practices vary in size, type and geographical area. Something can be learned from each practice, and we find unique ways of providing top-notch patient-centered care across multiple practice settings. Pharmacy team members often take on tasks that directly impact the safety and quality of care. Amin enjoys working at Smilow Cancer Center and comments, “I’ve never felt so part of a team. The nurses, doctors, and pharmacy team really collaborates well together. We rely on each other to help answer questions and problem solve together. Everyone is so welcoming, really patient-cen-

tered, and values what everyone can bring to the table from their own specialties.” Smilow Cancer Center has innovative programs like pharmacists sitting in the physician area for consultation and utilizing a pharmacy workflow management system that increases patient safety. Pharmacists also in-service nursing and other staff on new medications.

Fox is overseeing the construction of all new USP 797 and 800 clean rooms at CSNF as well as management of the rooms following construction. She provides education for all IV pharmacy technicians on new medications and fields

clinical questions that come in from various team members. Stanley is her lead IV pharmacy technician and fills in for absences, oversees inventory management and some purchasing and trains new IV technicians that come on board. He says the pharmacy department plays an important role on the team “to focus on sterility issues and making sure the medications are being properly mixed as well as hung at the appropriate times. Pharmacy also provides education on drug interactions and extravasation management. The pharmacy department is an important reference for all employees.” Pharmacy staff members along with their counterparts in nursing, social work, and financial counseling are making a difference for patients each day.

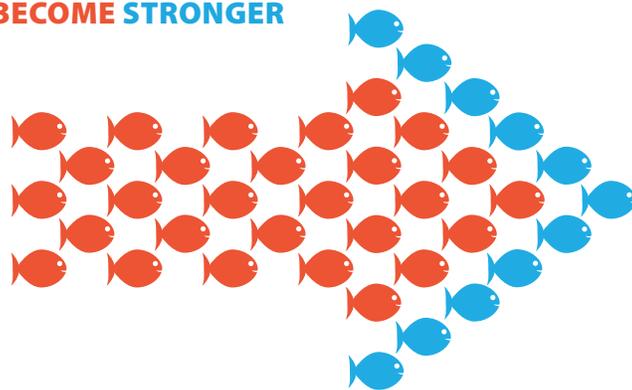
“I’VE NEVER FELT SO PART OF A TEAM. THE NURSES, DOCTORS, AND PHARMACY TEAM REALLY COLLABORATES WELL TOGETHER. WE RELY ON EACH OTHER TO HELP ANSWER QUESTIONS AND PROBLEM SOLVE TOGETHER. EVERYONE IS SO WELCOMING, REALLY PATIENT-CENTERED AND VALUES WHAT EVERYONE CAN BRING TO THE TABLE FROM THEIR OWN SPECIALTIES.”

Kejal Amin, PharmD, MBA, BCOP

CONCLUSION: NCODA, THE MEDICALLY INTEGRATED TEAM AND BRENTUXIMAB VEDOTIN PQI: OPTIMIZING PATIENT OUTCOMES

The Medically Integrated Team provides value to patients. Goodhue sums up the team and says “we all work like a family together. We get the medications to patients safely and quickly as we work together as a team.” The **Brentuximab Vedotin (ADCETRIS®): Neuropathy and Neutropenia Management PQI** provides the Medically Integrated Team with an easy to use, compact clinical resource guide when treating patients on brentuximab vedotin. It helps the team ensure they are managing side effects properly and providing patients with the tools and education to improve clinical outcomes. Pairing the Medically Integrated Team with the **Brentuximab Vedotin (ADCETRIS®): Neuropathy and Neutropenia Management PQI** meets NCODA’s Guiding Values of being Patient-Centered and Always Collaborative.

WORKING TOGETHER,
WE BECOME STRONGER



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ON THE COVER:

- Alex Stanley, RPhT, CPhT prepares IV medications for patients at Cancer Specialists of North Florida.



Helpful Online Resources



NCODA Website



Positive Quality Interventions



Oral Chemotherapy Education Sheets



Brentuximab PQI

PQI PRINCIPLES:

- 1** **Neutropenia prevention and management strategies**
- 2** **Neuropathy prevention and management strategies**
- 3** **Patient education and assessment**

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.



NCODA'S POSITIVE QUALITY INTERVENTION IN ACTION