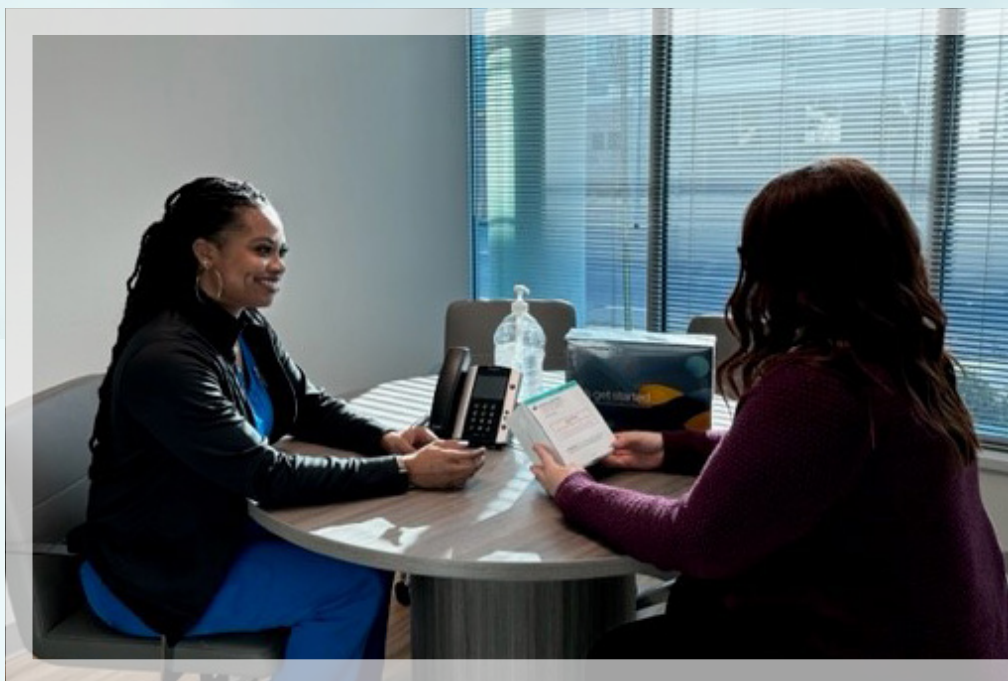


PQI IN ACTION



VENETOCLAX (VENCLEXTA®)
USE IN CHRONIC LYMPHOCYTIC LEUKEMIA



**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 the oncology healthcare team. 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 will cover the use of venetoclax (VENCLEXTA®) treatment in patients with Acute Myeloid Leukemia (AML) and Chronic Lymphocytic Leukemia (CLL), primarily with a focus on the **Venetoclax (VENCLEXTA®) Use in Chronic Lymphocytic Leukemia PQI**. This article will discuss how utilizing the **Venetoclax Use in Chronic Lymphocytic Leukemia PQI** within medically integrated centers Tennessee Oncology (TNONC) and Cancer Specialists of North Florida (CSNF) elevates patient care.

Tennessee Oncology (TNONC), a partner of One Oncology, provides high-quality cancer care, including cutting edge research trials, to patients at over 30 clinics in and around the Nashville, TN area. Park Pharmacy is the medically integrated pharmacy piece of this leading oncology practice. Dual accredited with URAC and ACHC accreditation, Park Pharmacy's mission, which aligns closely with NCODA's mission, is to provide patient-centered care through comprehensive services designed to aid patients in obtaining specialty medications. Park Pharmacy assists with the management of, and education on, complex therapies and their side effects, accurate prescription processing, and logistics for medication orders; all while helping patients achieve the best treatment outcomes by maintaining the highest levels of customer service, responsiveness, and accountability.

Cancer Specialists of North Florida (CSNF) is a physician-owned practice consisting of 34 physicians and offers 13 convenient locations throughout northeast Florida to treat cancer patients. Florida Specialty Pharmacy (FSP) serves as the medically integrated dispensing pharmacy of CSNF and is dual accredited with URAC and ACHC accreditations to provide the highest quality care to patients within the practice. Florida Specialty Pharmacy's mission includes delivering the highest quality of pharmaceutical care to their patients by combining the efforts of oncology pharmacists, experienced physicians, social workers, and financial counselors to achieve the best overall result for every patient.

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DISPENSING VENETOCLAX (VENCLEXTA®) FOR ACUTE MYELOID LEUKEMIA (AML) AND CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) WITHIN MEDICALLY INTEGRATED CLINICS

Acute myeloid leukemia (AML) is a malignant disorder of bone marrow, characterized by the clonal expansion and differentiation arrest of myeloid progenitor cells. In 2022, an estimated 20,000 people were diagnosed with AML.¹ Diagnosis can occur at any age, but is most common in adults over 45 with a median age of diagnosis of 68 years in the United States.^{1,2} In some cases, prior exposure to therapeutic, occupational or environmental DNA-damaging agents is implicated, but most cases of AML remain without clear etiology.^{1,2} Curative therapies, including intensive chemotherapy and allogeneic stem cell transplantation, are generally applicable to a minority of patients who are younger and fit, while older patients exhibit poor prognosis and survival.² Therapeutic advances with targeted therapies, including venetoclax regimens discussed here, are providing patients with additional treatment options, even in refractory disease.²

Chronic Lymphocytic Leukemia (CLL), also a malignant disorder of bone marrow, is characterized by a progressive proliferation and accumulation of mature yet functionally incompetent bone lymphocytes. 2022 statistics almost mirrored that of AML diagnoses, with 20,160 cases.³ CLL is the most common leukemia among adults (very rarely occurs in children), with more than 90% of newly diagnosed cases occurring in adult patients 64 years of age or older.³ The progression of CLL can happen very slowly, with uncontrolled buildup and enlargement of lymphoid tissue occurring in various sites of the body such as lymph nodes, spleen, bone marrow, and lungs.^{2,3} Treatment of CLL is based on symptoms or worsening blood counts and most often will follow Rai staging 0-IV.⁴ “In the absence of disease symptoms, a “watch and wait” approach is often appropriate with low-risk CLL (Rai stage 0 or Binet A) or intermediate-risk CLL (Rai stage I-II or Binet B) and treatment will be beneficial if they become symptomatic or show evidence of progressive disease.⁵ Venetoclax can be offered as a preferred treatment option, monotherapy or in combination with a monoclonal antibody, for CLL patients, based on age, comorbidities and overall fitness level of the patient.⁴

Venetoclax (VENCLEXTA®), an oral oncolytic agent used to treat AML and CLL patients, is a drug with specific dosing, based on different treatment regimens, and can often



Bethany Mason, RN, Ayed Ayed, MD and Joshua Weeks, CPhT discuss a treatment plan for a patient initiating treatment at the Northside location at Cancer Specialists of North Florida.

seem complicated to the patient. In addition, venetoclax requires a high level of monitoring, including intense hydration, frequent lab work and consistent communication with the patient regarding symptoms and management of side effects. Due to these complexities of treatment, dispensing venetoclax within a medically integrated oncology model, sets the patient up for successful treatment and better patient outcomes. Medically integrated dispensing (MID) clinics have been shown to achieve higher adherence rates in patients on oral medications by providing more personalized individual follow-ups.⁶ NCODA defines Medically Integrated Dispensing (MID) as a dispensing pharmacy within an oncology center of excellence that promotes a patient-centered, multidisciplinary team approach.⁷

The pharmacy team at Park Pharmacy, the dispensing pharmacy within the MID team at TNONC, follows a specific workflow to maximize efficiency and quickly deliver prescriptions to their patients. Working within this medically integrated model, it is easy to recognize the benefits that patients receive by filling prescriptions at Park Pharmacy. Nikole Roesler, PharmD raves about the MID team at Park Pharmacy, “I am always amazed at how quickly our integra-

ted team works to get everything processed and ready for the patient so there is no delay in treatment.” Jennifer Barber, CPhT discusses “Sometimes when we have a patient waiting on a prescription from an outside pharmacy, they state it can take 24-48 hours just to show up in their system. This leads to unnecessary treatment delays, which is unacceptable in cancer patients.” Sarah Paige, CPhT, whose primary job is to process prior authorizations, praises the workflow process at TNONC, “Having all of the departments connected with the same EMR system, with a workflow like ours, ensures that the prescription moves through the process efficiently and allows the prescription to get into the patient’s hands much quicker than if an outside pharmacy fills it (which can sometimes take 1-2 weeks).” Kim Alexander, CPhT, holds a unique role working as a medication therapy management technician, following a step-by-step guide to assess compliance, ask about patient tolerance to medication and report any pertinent issues to the pharmacists for immediate follow up. Alexander states “My role provides a layer of customized care to our patients. When they are forced to fill at outside pharmacies, they miss out on a key piece of personalized care.”

“SOMETIMES WHEN WE HAVE A PATIENT WAITING ON A PRESCRIPTION FROM AN OUTSIDE PHARMACY, THEY STATE IT CAN TAKE 24-48 HOURS JUST TO SHOW UP IN THEIR SYSTEM. THIS LEADS TO UNNECESSARY TREATMENT DELAYS, WHICH IS UNACCEPTABLE IN CANCER PATIENTS.”

Jennifer Barber, CPhT

Florida Specialty Pharmacy provides a similar workflow within their medically integrated team at CSNF. Amit Ranchhod, PharmD, lead retail pharmacist at FSP, notes that the direct access to the patient’s EMR remains one of the biggest benefits to his job. “Having access to the EMR system allows us to see the full picture of the patient. Add in the direct access we have to the offices via phone, email, direct messaging, etc, all of this allows for direct turn around and faster

response rates, which gets the prescription immediately to the patient.” Dr. Ayed Ayed at the Northside CSNF clinic states “I feel very fortunate and privileged to have our specialty pharmacy. The team we have is extremely beneficial in optimizing patient care with quick delivery of medications to patients. Our patients have enough on their plate dealing with cancer, so having the trust in their cancer center to deliver not only the recommendations for treatment, but the treatment itself, is a huge plus.” Joshua Weeks, CPhT at CSNF adds “The response time for anything related to the prescription is so much faster when we can fill the prescription here. I think it also adds an additional layer of personalized care to the patient, as they know who we are and are familiar with how we handle things.” Bethany Mason, RN at CSNF’s Northside Clinic adds “We often have patients come in and tells us that the outside pharmacy that is filling their medication (which they were forced to do and not happy about) requires additional information for filling the prescription. The patients, many of them dealing with a new cancer diagnosis or switching to a new treatment, have no idea what is needed and it causes so much confusion. When we are able to fill the prescription here, much of this is eliminated and it provides timely delivery of the drug to the patient without unnecessary delays.”

“THE RESPONSE TIME FOR ANYTHING RELATED TO THE PRESCRIPTION IS SO MUCH FASTER WHEN WE CAN FILL THE PRESCRIPTION HERE. I THINK IT ALSO ADDS AN ADDITIONAL LAYER OF PERSONALIZED CARE TO THE PATIENT, AS THEY KNOW WHO WE ARE AND ARE FAMILIAR WITH HOW WE HANDLE THINGS.”

Joshua Weeks, CPhT

VENETOCLAX (VENCLEXTA®) MECHANISM OF ACTION, DRUG MONITORING AND PATIENT TOLERABILITY WHEN TREATING AML AND CLL PATIENTS

Venetoclax is a potent, selective, and orally bioavailable small-molecule inhibitor of B-cell lymphoma 2 (BCL-2). BCL-2 is a protein that is overexpressed in chronic lymphocytic leukemia (CLL)/small lymphocytic leukemia (SLL) and acute myeloid leukemia (AML), independent of functional TP53 mutation.⁸⁻¹¹ BCL-2 mediates tumor cell survival and has been associated with chemotherapy resistance.⁴ Venetoclax binds directly to the BCL-2 protein, displacing pro-apoptotic proteins and restoring the apoptotic process.⁴

Tumor lysis syndrome (TLS) is a potential risk associated with venetoclax treatment with severity of risk based on tumor burden and comorbidities. TLS occurs as a direct result of tumor cell death, which causes massive release of intracellular contents into the systemic circulation.¹² Characteristic findings include hyperuricemia, hyperphosphotemia, hyperkalemia, hypocalcemia, and uremia, all of which can lead to cardiac arrhythmia, seizures, renal failure, and sudden death.¹² Risk assessment and prevention are key to the management of TLS and rely on clinician awareness, prophylactic measures, and vigilant laboratory monitoring. Baseline labs, adequate hydration prior to beginning therapy and the use of anti-hyperuricemic agents are recommended to help prevent TLS.¹²

Risk stratification of tumor lysis syndrome should be assessed for all AML and CLL patients prior to initiating treatment with venetoclax. Patients at increased risk for TLS include those with renal impairment, high disease burden, dehydration, and baseline hyperuricemia. Preventative measures such as hydration and anti-hyperuricemic agents are recommended. Specifics on risk assessment and treatment based on tumor burden in CLL patients will be discussed further in the PQI Process section below. In AML patients, WBC should be $< 25 \times 10^9/L$ prior to starting venetoclax treatment. If WBC $> 25 \times 10^9/L$, cytoreduction is recommended prior to treatment initiation.¹³ The ramp up cycle used for venetoclax patients with AML has greatly reduced TLS in these patients. The dose escalation for venetoclax treatment given with a hypomethylating agent (HMA) is 100mg, 200mg, and 400mg given on days 1 to 3 and the dose escalation for venetoclax with low dose cytarabine (LDAC) is 100mg, 200mg, 400mg and 600mg given on days 1 to 4.¹³ To minimize and avert further risk of tumor lysis syndrome, it is recommended to aggressively monitor blood chemistries, monitor and manage electrolyte imbalances and treat with anti-hyperuricemic agents as indicated.¹³ Knowing

that hydration plays a key factor in the successful initiation and maintenance of venetoclax therapy, Mason at CSNF is sure to counsel all patients on this point. “In addition to stressing the importance of hydration and guiding patients on how to achieve this, I also stress to them that without hydrating appropriately, they could become very sick, which could ultimately lead to a hospital stay for fluids and monitoring. I find that by stating this up front, it encourages them to listen and push oral hydration.”

Neutropenia at varying grade levels is common and must also be a monitoring consideration when treating AML and CLL patients with venetoclax. It is likely that the potent and selective BCL-2 inhibition displayed by venetoclax, in particular its on-target inhibition of BCL-2 in neutrophil precursors, drives the incidence of neutropenia that is observed in these patients.¹⁴ In pooled single-arm trials of venetoclax therapy in patients with CLL or SLL, 45% of patients experienced grade anti-hyperuricemic 3 neutropenia.¹⁵⁻¹⁸ With venetoclax-rituximab or venetoclax-obinutuzumab regimens, the rates of neutropenia were 57.7% and 52.8% respectively.¹⁹ In patients with AML who received venetoclax-azacitidine and venetoclax-low dose cytarabine regimen combinations, the incidence of grade ≥ 3 neutropenia was 42% and 46% respectively.^{21,22} Management of neutropenia in these patients depends on several factors including the grade of neutropenia, the risk of febrile neutropenia, and the patient’s remission status at the time of neutropenia (determined by bone marrow biopsy). NCODA provides a tool to aid the clinician in determining dose reductions and/or interruptions based on these neutropenic factors.

Despite the initial complexity that may sometimes overwhelm a new patient or a clinician treating a patient with venetoclax, once patients are stabilized on a steady-state treatment dose, tolerability of venetoclax is often achieved. Camille Ballance, MSN, FNP-BC of TNONC comments “When counseling venetoclax patients, I do mention the TLS risk. I also point out that we do the ramp up dosing and this is what helps to prevent TLS. The neutropenia, especially in AML patients, is what I tend to see most often and will require dose reductions.” Alexander adds “I find that most patients on venetoclax tolerate it well. Fatigue and diarrhea come to mind as side effects these patients experience most when I speak to them on MTM calls.”

[CLICK HERE TO VIEW
DOSE MODIFICATION
CHARTS](#)

THE POSITIVE QUALITY INTERVENTION: A VALUABLE CLINICAL RESOURCE

This Positive Quality Intervention titled “**Venetoclax Use in Chronic Lymphocytic Leukemia**”, offers providers valuable information on a BCL-2 targeted oral therapy option in CLL patients. Both medically integrated centers find clear benefit in using the PQI within their practices. Matthew Hoak, PharmD at Park Pharmacy states, “I love the clear and concise format of the PQIs. Providing links to other educational pieces is very helpful and saves time by not having to look in several places for the information. The PQI has become a part of everyday practice for me.” Ayed of CSNF comments on the PQI, “The PQIs for both AML and CLL are helpful resources. The inclusion of the landmark studies that led to the approvals and the information on drug-drug interactions are the key components for me. I love that both are clean and succinct.” Golden adds “The PQI is a very informative document that helps us as pharmacists to ensure we are dispensing the drug properly.”

The processes within an oncology pharmacy can be overwhelming to anyone with all the new drugs and new indications consistently entering our space. Venetoclax is often combi-

[CLICK HERE
TO VIEW
THIS PQI](#)

ned with other intravenous or subcutaneous therapies, with different dosing schedules and potential for adverse events, which requires highly consistent monitoring and coordination of care to ensure a successful treatment course for the patient. The **Venetoclax Use in Chronic Lymphocytic Leukemia** PQI provides the user with specific guidance on dosing (monotherapy or in a combination regimen), assessing risk category, prevention and monitoring parameters for TLS and drug-drug interactions, and key takeaways for the patient within the patient-centered activities.

“THE PQIS FOR BOTH AML AND CLL ARE HELPFUL RESOURCES. THE INCLUSION OF THE LANDMARK STUDIES THAT LED TO THE APPROVALS AND THE INFORMATION ON DRUG-DRUG INTERACTIONS ARE THE KEY COMPONENTS FOR ME. I LOVE THAT BOTH ARE CLEAN AND SUCCINCT.”

Ayed Ayed, MD

PUTTING THE VENETOCLAX (VENCLEXTA®) USE IN CHRONIC LYMPHOCYTIC LEUKEMIA PQI INTO ACTION: THE MURANO AND CLL14 TRIAL DATA

The PQI is a precise and concise peer-reviewed clinical guidance resource that provides Quality Standards and effective practices around a specific aspect of cancer care. The Medically Integrated Pharmacy team is in a unique position to ensure appropriate treatment, increase compliance, and maximize clinical outcomes. Positive Quality Interventions (PQIs), an NCODA Quality Standard, are designed to operationalize and standardize those practices to achieve these positive clinical outcomes. The **Venetoclax Use in Chronic Lymphocytic Leukemia** PQI is written in sections beginning with a Description

and ending with Patient-Centered Activities and References. Also included is a Supplemental Information Table “Recommended TLS Prophylaxis Based on Tumor Burden in Patients with CLL”, which is included in the next section of this article. In this section, we will focus on the trials that led to venetoclax approvals in the CLL landscape.

The Description and Background sections provide information on the use of venetoclax in chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL), monitoring considerations with combination regimens including IV monoclonal antibody therapies, specific mechanism of action

directed at CLL/SLL cells, and the important clinical trial information surrounding venetoclax and its labeled uses for CLL treatment. Regarding venetoclax, the drug has been approved for the treatment of adult patients with CLL or SLL as monotherapy or in combination with rituximab or obinutuzumab. It was initially granted accelerated approval in the United States for the treatment of adult patients with CLL with 17p deletion and who received at least one prior line treatment.²² This approval was expanded to all patients with relapsed/refractory CLL based on the results of the MURANO trial, a phase III study evaluating the efficacy of venetoclax in combination with rituximab for a 2-year fixed duration vs. that of bendamustine-rituximab for 6 cycles.¹⁹ The MURANO trial results showed a higher rate of 2-year PFS in relapsed/refractory CLL patients treated with venetoclax-rituximab vs. bendamustine-rituximab 83% vs 39% (HR=0.19, 95% CI, P<0.0001), including patients with del(17p) or TP53 mutation status.¹⁹ The CLL14 trial followed which was a multinational, open-label, phase III trial of venetoclax/obinutuzumab vs. chlorambucil/obinutuzumab in patients with previously untreated CLL and coexisting medical conditions.²³ After a median follow-up of 28.1 months, 30 primary end-point events (disease progression or death)

had occurred in the venetoclax-obinutuzumab group and 77 had occurred in the chlorambucil-obinutuzumab group (HR=0.35, 95%CI, P<0.001).²³ The Kaplan-Meier estimate of the percentage of patients with PFS at 24 months was significantly higher in the venetoclax-obinutuzumab group than in the chlorambucil-obinutuzumab group: 88.2% vs. 64.1% respectively, and was observed in patients with TP53 deletion, mutation, or both and in patients with unmutated immunoglobulin heavy-chain genes.²³

The above trial data and real-world treatment of these patients in clinical practice continue to show that venetoclax treatment regimens are effective in treating disease burden in CLL and allowing patients to achieve periods of remission. Jonathan Abbas, MD at TNONC is an advocate of venetoclax treatment in CLL. “Venetoclax has become one of my favorite therapies in the CLL space, both frontline and relapsed/refractory, largely due to the treatment-free remission that is achieved.” Paige states “The background section of the PQI that contains all of the approval and trial information with exact indications listed is helpful in my role. This information is exactly what is needed from the insurance company as proof that the patient requires the medication.”

THE VENETOCLAX PQI PROCESS: REGIMEN SELECTION, DOSING STRATEGIES AND EXTENSIVE MONITORING FOR ENHANCING TREATMENT SUCCESS

The next section of the **Venetoclax Use in Chronic Lymphocytic Leukemia PQI** is the PQI Process and Dosing Guideline. This section lays out the intervention in step by step points and guides the clinician on CLL regimen selection, dosing based on TLS risk category, how to monitor patients and when to draw labs, and how to approach drug-drug interactions when initiating therapy. This section also contains a link to an NCODA Resource Tool titled “Venetoclax TLS Risk Assessment Tool”, which helps identify patients at risk for TLS, while also containing helpful dosing charts based on treatment regimens. In addition, there is helpful guidance on dosing venetoclax in patients who are currently taking drugs that may interact with the cancer treatment.

The first step in the PQI Process is to determine the risk category for the patient. TLS risk in CLL patients is based on tumor burden and should be managed according to low

risk, medium risk and high risk depending on this factor.⁴ The prescribing clinician should consider all patient comorbidities before final determination of prophylaxis and monitoring schedule.⁴ The gradual stepwise ramp-up dosing of venetoclax over a 5 week period along with TLS prophylaxis is recommended to mitigate the risk and frequency of TLS.¹⁵ The chart below provides recommendations for prophylactic treatment and monitoring in CLL patients, based on tumor burden. Ballance comments on the TLS prophylaxis chart within the PQI, “I refer to this chart almost on a daily basis to ensure I am assigning the appropriate risk and treatment for my patients based on their tumor burden.” Charity Golden, PharmD expresses that the tumor burden chart is her favorite piece of the PQI, “I love the TLS tumor burden chart. It is helpful for me to refer to this and determine that the patients are getting what they need.” The next step in the PQI Process reviews the steps to follow if a patient is assigned to “high-

RECOMMENDED TLS PROPHYLAXIS BASED ON TUMOR BURDEN IN PATIENTS WITH CLL

Tumor Burden	Anti-hyperuricemics	Hydration	Lab Monitoring
Low Tumor Burden			
All lymph nodes <5 cm and ALC < 25 x 10 ⁹ /L	Allopurinol Start 2-3 days prior to first dose	Oral (1.5-2 L/day) beginning 2-3 days prior to first dose	Outpatient: First dose of 20 mg and 50 mg: Pre-dose, 6-8 hrs and 24 hrs Subsequent ramp up doses: Pre-dose only
Medium Tumor Burden			
Any lymph node 5 cm to <10 cm or ALC ≥ 25 x 10 ⁹ /L	Allopurinol Start 2-3 days prior to first dose	Oral (1.5-2 L/day) beginning 2-3 days prior to first dose Consider additional IV if in hospital	Outpatient: First dose of 20 mg and 50 mg: Pre-dose, 6-8 hrs and 24 hrs Subsequent ramp up doses: Pre-dose only If CrCl<80 ml/min consider hospitalization and follow lab monitoring for inpatient below
High Tumor Burden			
Any lymph node ≥ 10 cm or Any lymph node ≥ 5 cm and ALC ≥ 25 x 10 ⁹ /L	Allopurinol Start 2-3 days prior to first dose Consider rasburicase if elevated baseline uric acid Check with inpatient pharmacy for availability	Oral (1.5-2 L/day) beginning 2-3 days prior to first dose and IV (150- 200 mL/hr as tolerated)	In hospital: For first dose of 20 mg and 50 mg: Pre-dose, 4, 8, 12 and 24 hrs Outpatient: For subsequent ramp-up doses: Pre-dose, 6-8 hrs and 24 hrs

risk". Hospital admission should be considered for patients in the high-risk category, as well as, medium-risk patients with inadequate renal function (CrCl < 80 mL/min). To ensure coordination of care for these patients requiring hospitalization, please follow the steps below.

- Ensure patient will have medication on hand prior to admission
- Coordinate timing of patient labs with the inpatient team to ensure necessary lab work without delays
- Labs will need to be ordered for the first dose of 20mg and 50mg doses and will occur on 2 separate admissions
- Labs need to be drawn pre-dose, 4, 8, 12 and 24 hours after the dose. Recommended labs to be drawn include uric acid, serum potassium, serum phosphorous, corrected calcium and serum creatinine. Ensure inpatient staff are educated on the frequency and importance of these labs and that they are being evaluated in "real time" for early detection of TLS. In select patients, rasburicase may be used for TLS management. NCODA offers a PQI on the

use of rasburicase and can be accessed using the QR code below.

The Dosing Guideline section of the PQI Process lists the dosing regimens and the ramp up dosing chart for venetoclax monotherapy. Helpful charts are also listed within the "Venetoclax TLS Risk Assessment Tool". Barber of TNONC, comments on the dosing charts, "The dosing charts provided in the PQIs are helpful to me. I use these charts to compare what we are entering into the pharmacy software as technicians and use it as a double-check on my end."

For patients assigned to low or medium risk categories, determine the treatment regimen and follow the dosing charts listed here.

The final piece of the PQI Process section covers reviewing medication lists for possible drug interactions, specifically drugs that inhibit the CYP3A system. It is common for patients treated with venetoclax to also require treatment

[CLICK HERE TO
VIEW VENETOCLAX
TLS RISK
ASSESSMENT TOOL](#)

RECOMMENDED TLS PROPHYLAXIS BASED ON TUMOR BURDEN IN PATIENTS WITH CLL

VENETOCLAX Monotherapy	
Week 1	20mg QD
Week 2	50mg QD
Week 3	100mg QD
Week 4	200mg QD
Week 5	400mg QD
After week 5, continue with 400mg QD until disease progression or unacceptable toxicity	

CLL VENETOCLAX PLUS OBINUTUZUMAB DOSING

VENETOCLAX + OBINUTUZUMAB 1st line	
Week 1 (Cycle 1, Day 22)	20mg QD
Week 2	50mg QD
Week 3	100mg QD
Week 4	200mg QD
Week 5 (Cycle 3, Day 1)	400mg QD (Continue through Cycle 12)
Obinutuzumab Cycle 1, Day 1 for a total of 6 cycles - refer to package insert for additional information	

CLL VENETOCLAX PLUS RITUXIMAB DOSING

VENETOCLAX + RITUXIMAB R/R	
Week 1	20mg QD
Week 2	50mg QD
Week 3	100mg QD
Week 4	200mg QD
Week 5	400mg QD
Begin Rituximab after patient has completed the 5 week ramp up schedule above - refer to package insert for additional information. 400mg QD Ven dose continues for 24 months from Cycle 1 Day 1 of Rituximab	

with azole antifungals or antimicrobial agents for infection prophylaxis or in some cases, active infections. In addition, patients may also be on other medications that inhibit the metabolism of venetoclax via the CYP3A metabolic system, thus requiring adjustments to their venetoclax dosing. The chart below is included in the “Venetoclax TLS Risk Assessment Tool” and serves to help guide clinicians when treatment with both agents is warranted. Golden comments on dose modifications, “I will see dose reductions when patients are taking other drugs that interact with venetoclax. When the interacting therapy has been completed or is removed

from the treatment plan, we ensure that the venetoclax dose is titrated back to maintenance dosing. The pharmacists act as a double-check to ensure that these dose modifications are performed correctly.”

CLL DOSE MODIFICATION DURING RAMP UP WITH MODERATE CYP3A INHIBITORS

Moderate CYP3A Inhibitors include but are not limited to the following: Ciprofloxacin Erythromycin Diltiazem Fluconazole Dronedarone Verapamil	Week 1	10mg
	Week 2	20mg
	Week 3	50mg
	Week 4	100mg
	Week 5	200mg

If initiating **Moderate CYP3A Inhibitor** treatment during Venetoclax treatment, dose reduce Venetoclax by at least 50%, with steady state dosing at 200mg or less.

CLL DOSE MODIFICATION DURING RAMP UP WITH STRONG CYP3A INHIBITORS

Strong CYP3A Inhibitors include but are not limited to the following: Clarithromycin Lopinavir Indinavir Posaconazole Itraconazole Ritonavir Ketoconazole Voriconazole	<p>Contraindicated during ramp up of Venetoclax. If use of both Venetoclax and Strong CYP3A is warranted, consider dose interruption/pause of CYP3A treatment during ramp up phase, with final Venetoclax steady state dose of 100mg (complete ramp up at week 4 and continue dosing at 100mg daily for treatment dose). Restart CYP3A treatment once at steady state Venetoclax dose and monitor.</p> <p>For concomitant Posaconazole, reduce week 4 ramp up Venetoclax dosing from 100mg to 70mg, with 70mg daily as final steady state Venetoclax treatment dose.</p>
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If the use of a Strong CYP3A Inhibitor is warranted during Venetoclax treatment, consider dose interruption/pause of Venetoclax treatment for course of Strong CYP3A Inhibitor, then resume Venetoclax dose 2-3 days after discontinuation of Strong CYP3A Inhibitor.

PATIENT-CENTERED ACTIVITIES: KEEPING PATIENTS FIRST

The Patient-Centered Activities section follows the PQI Process and gives patient-centered guidance for the team. Patient counseling is critical for any patient receiving venetoclax treatment and should be arranged to be delivered upon the dispensing of the medication, preferably with enough time to perform preventative hydration and premedications. Roesler states “We typically wait to educate venetoclax patients until we can place the prescription, along with a treatment kit provided by the manufacturer, in hand. It is much easier to walk them through the patient-centered points when everything is available and in front of us.” She continues to add “The manufacturer provided venetoclax kits come with a huge water bottle, which all the patients seem to love, which stresses the importance of hydration and water intake early on.”

The **Venetoclax Use in Chronic Lymphocytic Leukemia** PQI Patient-Centered Activities suggests providing the patient with an Oral Chemotherapy Education (OCE) sheet. OCE sheets are an NCO-DA-led initiative and provide information about oral chemo-

[CLICK HERE TO
VIEW OCE SHEET](#)

“WE TYPICALLY WAIT TO EDUCATE VENETOCLAX PATIENTS UNTIL WE CAN PLACE THE PRESCRIPTION, ALONG WITH A TREATMENT KIT PROVIDED BY THE MANUFACTURER, IN HAND. IT IS MUCH EASIER TO WALK THEM THROUGH THE PATIENT-CENTERED POINTS WHEN EVERYTHING IS AVAILABLE AND IN FRONT OF US.”

Nikole Roesler, PharmD

therapy drugs and their side effects to both cancer patients and caregivers. In 2019 the Patient-Centered Standards for Medically Integrated Dispensing: ASCO/NCODA Standards were published to provide standards for medically

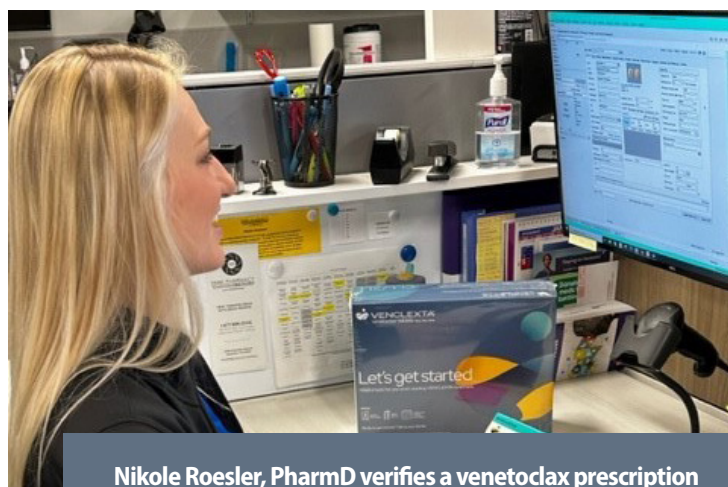
integrated dispensing of oral anticancer drugs and supportive care medications.²⁵ Standard 1.2 of the ASCO/NCODA Standards reads: Prior to initiation of an oral anticancer drug, a formalized patient education session should occur with an experienced clinical educator such as a nurse, physician, pharmacist, nurse practitioner, or physician assistant. The discussion should include drug name (generic and brand), drug dose, schedule, potential adverse effects and how to properly manage them, fertility (where applicable), treatment goal, duration of therapy, and financial and affordability considerations.²⁵

After preparing an OCE sheet on venetoclax, the clinician should review the titration schedule of venetoclax with the patient and provide any helpful calendars or tools to aid in care coordination of oral/IV regimen dosing and clinic appointments. Mason is an advocate of the calendars provided in the VENCLEXTA[®] manufacturer kits stating, “To help with coordination of care, I really like to provide the patient a detailed, color-coded calendar. The manufacturer supplied kits now come with printed calendars and they are amazing. They come with stickers to personalize each patient’s treatment plan. The calendars have been a tremendous help in assisting coordination of care with the IV/PO regimens.”

“TO HELP WITH COORDINATION OF CARE, I REALLY LIKE TO PROVIDE THE PATIENT A DETAILED, COLOR-CODED CALENDAR. THE MANUFACTURER SUPPLIED KITS NOW COME WITH PRINTED CALENDARS AND THEY ARE AMAZING. THEY COME WITH STICKERS TO PERSONALIZE EACH PATIENT’S TREATMENT PLAN. THE CALENDARS HAVE BEEN A TREMENDOUS HELP IN ASSISTING COORDINATION OF CARE WITH THE IV/PO REGIMENS.”

Bethany Mason, RN

Next, review the oral hydration schedule with the patient. Ensure the patients understand the importance of this hydra-



Nikole Roesler, PharmD verifies a venetoclax prescription for a patient at Park Pharmacy.

tion prior to and during treatment with venetoclax. Water bottles are provided in the manufacturer provided kits and can be helpful for patients who need reminders or help measuring water intake.

- Patient should consume 6-8 (8 oz) glasses of water or as instructed by provider starting 2 days before the first dose throughout the ramp up phase. This is important during the first day of each dose increase.
- Patients admitted to the hospital will receive IV fluids
- Outpatients may be considered for IV hydration if oral hydration is inadequate or patient has problems tolerating fluid intake

After reviewing hydration expectations, review with the patient what to do if they miss a scheduled dose of venetoclax.

- If within 8 hours of the usual time, take as soon as possible and resume normal schedule
- If greater than 8 hour past usual time, skip dose and resume normal schedule the next day

If hospital admission is warranted, confirm that the patient understands details surrounding the admission (date, time, hospital location). Make certain that the patient has contact numbers of who to contact if they have questions regarding this process or run into any issues on admission day.

All patients who begin venetoclax therapy should have follow up calls scheduled with a trained staff member within the clinic or pharmacy. It is essential that communication remains fluid between patient and clinic staff during initiation of therapy and each dose escalation to confirm the patient is taking the medication as instructed.

The last piece of the Patient-Centered Activities section is the NCODA Financial Assistance Tool. In addition to ensuring all of the above counseling points are followed, it is also important to make sure the patient can afford the medication. The impact of cancer treatment on patient financial well-being is a topic of major concern in the oncology community.²⁶ Financial toxicity has been linked to an increased patient risk of medical noncompliance.²⁶ While insurance coverage does sometimes help to cover the cost of these medications, it often is not enough and

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ASSISTANCE TOOL](#)

patients will require additional assistance. Abbas commends his pharmacy team for helping patients achieve affordability. “Our pharmacy team is highly efficient to not only process and fill the prescriptions in a timely manner, but also assuring affordability of the medications by applying patient assistance. We are blessed to have this service for our patients.” Banes, who serves as a co-pay assistance specialist at TNONC, appreciates firsthand what co-pay assistance does for patients. “For venetoclax, the manufacturers have improved their processes to allow more access to free drug and patient assistance. This usually helps to cover the patient from first fill until treatment completion.”

CONCLUSION: PQI, MID AND COORDINATION OF CARE

All team members of TNONC and CSNF agree that the MID model and the PQI Clinical Resources and Venetoclax Tools are valuable to the team and to patients. Communication and teamwork are essential components of what make this model work effectively and efficiently. Hoak advocates this communication, “Communication and the trust we have amongst the team is a huge benefit of having the MID team in place. Sharing this mutual understanding that we are all in this to help the patient allows for a more coordinated effort to get patients what they need, when they need it.”

“COMMUNICATION AND THE TRUST WE HAVE AMONGST THE TEAM IS A HUGE BENEFIT OF HAVING THE MID TEAM IN PLACE. SHARING THIS MUTUAL UNDERSTANDING THAT WE ARE ALL IN THIS TO HELP THE PATIENT ALLOWS FOR A MORE COORDINATED EFFORT TO GET PATIENTS WHAT THEY NEED, WHEN THEY NEED IT.”

Matt Hoak, PharmD

pharmacy, they miss out on having the effective pieces our pharmacy team provides. Our pharmacy staff at CSNF are wonderful advocates for our patients and they function effectively as liaisons communicating concerns and serving as a link between the moment of medication prescribing to having it delivered into the hands of the patient.”

Mason, RN at the Northside clinic at CSNF, is very specific when it comes to the treatment of venetoclax. “Sometimes when mail order fills venetoclax, we must be very diligent to remind the patients not to start it as soon as it arrives. We like to tell them to bring it in when they have their initial start appointment so we can reinforce dosing instructions and provide our calendar to them AND ensure they received the correct medication.”

The essential components of the **Venetoclax Use in Chronic Lymphocytic Leukemia PQI** and the Venetoclax Tools empower clinicians to ensure appropriate medication use per indication, patient risk, selection of dose and appropriate regimens, TLS prevention measures, monitoring, and care coordination across multiple disciplines within the Medically Integrated Teams and beyond. Ballance comments on the PQI, “I think what NCODA is doing with PQIs specifically is great. Anything that can help bridge the gaps between the medical community and patients, especially when treating complex oncology patients, is beyond beneficial.” Mason adds “Anything listed “patient-centered” or “patient-specific” catches my eye as something I know I need to read so I can be sure to inform the patient.”

An important key to care coordination is being able to provide the patients with everything they need when they need it. When the pharmacy within the MID model is forced to send out their patient’s prescription, this can lead to discon-

To provide the best quality care, cancer patients should always have a direct line of communication to their medical team. This personalized care is what the MID model can offer and is the key to distinguishing MID over outside pharmacies. Ayed adds “When patients are forced to fill at an outside

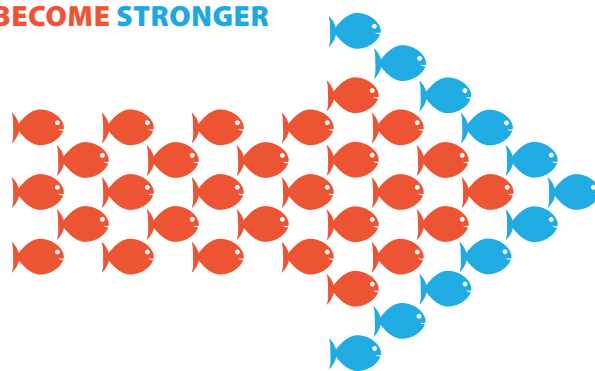
"I THINK WHAT NCODA IS DOING WITH PQIS SPECIFICALLY IS GREAT. ANYTHING THAT CAN HELP BRIDGE THE GAPS BETWEEN THE MEDICAL COMMUNITY AND PATIENTS, ESPECIALLY WHEN TREATING COMPLEX ONCOLOGY PATIENTS, IS BEYOND BENEFICIAL."

Camille Ballance, MSN, FNP-BC

nections in care coordination. Hoak explains, "It can be really confusing to patients when they have to fill with outside pharmacies. At Park Pharmacy, we do all follow-up calls on our patients, even if they do not fill in house. In these follow-up calls, we provide patients with important information regarding when next appointments are. Outside pharmacies, not having the direct EMR connection, would not be able to provide them with this information and this could lead to patients not understanding and missing appointments. It also leads to a very important question which all of us have a hard time understanding, "Why aren't you just filling my prescription?"

Venetoclax serves as an excellent treatment option for AML and CLL/SLL patients. The PQI provides the MID program with an easy to use, concise clinical resource guide when determining regimens, risk factors and initial dosing and dose reductions with Venclexta®. It helps the team ensure they are providing patients with the tools and education to improve clinical outcomes. Pairing Medically Integrated Dispensing with the **Venetoclax Use in Chronic Lymphocytic Leukemia** PQI meets NCODA's Guiding Values of being Patient-Centered and Always Collaborative.

**WORKING TOGETHER,
WE BECOME STRONGER**








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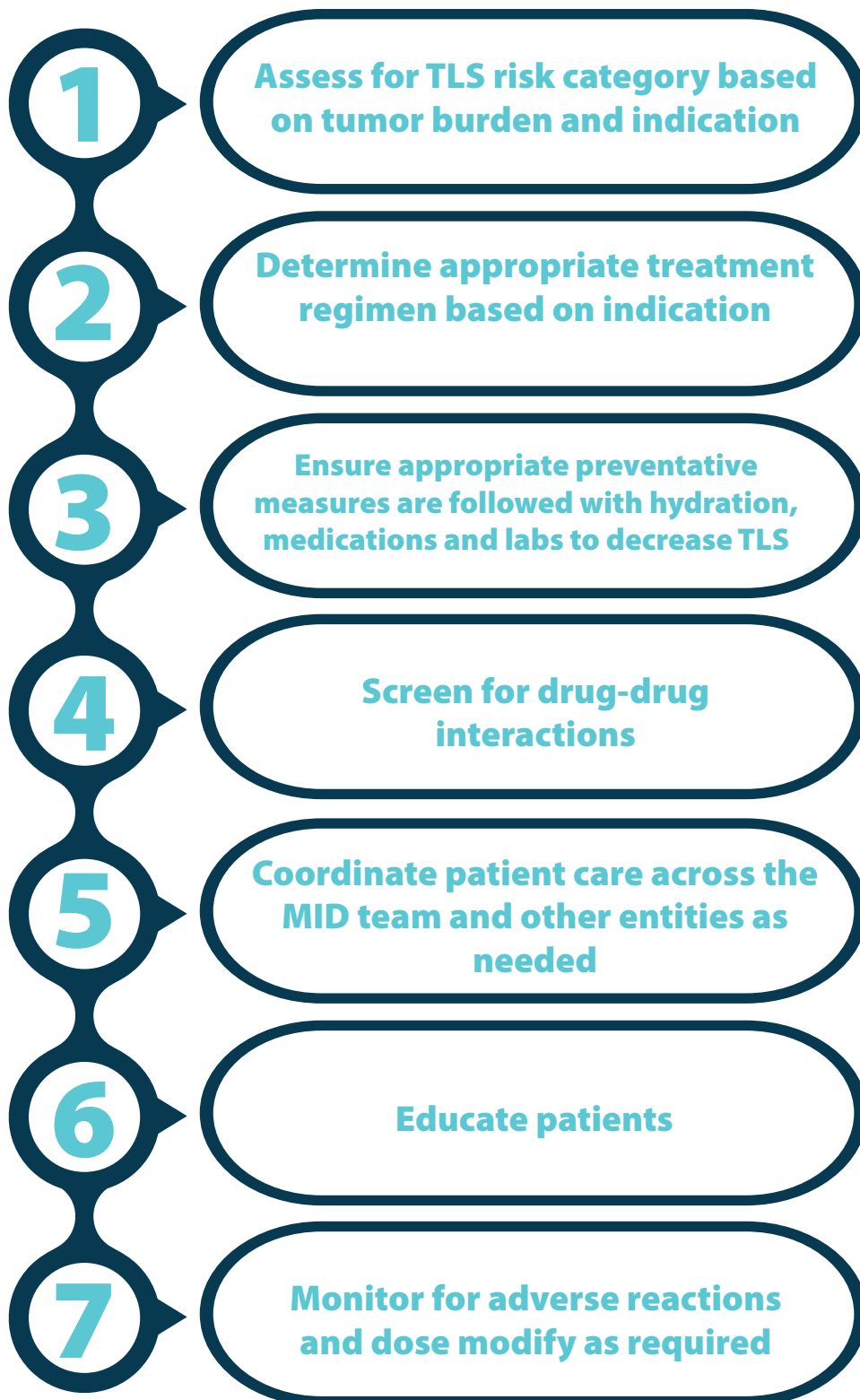
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Helpful Online Resources

-  [Venetoclax \(Venclexta®\) Use in Chronic Lymphocytic Leukemia PQI](#)
-  [Positive Quality Interventions](#)
-  [Venclexta® \(venetoclax\) Oral Chemotherapy Education Sheets](#)
-  [NCODA Website](#)
-  [NCODA Financial Assistance Tool](#)

PQI PRINCIPLES:



ON THE COVER:

- Charity Golden, PharmD counsels a patient receiving oral chemotherapy at Park Pharmacy in Nashville, TN.

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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