

**1L & R/R CLL/SLL****A GUIDE FOR HEALTHCARE PROFESSIONALS****INITIATING CLL/SLL PATIENTS
ON VENCLEXTA¹**

- CLL14 was a randomized (1:1), multicenter, open-label, actively controlled phase 3 trial that evaluated the efficacy and safety of VEN+G versus GClb for previously untreated CLL in 432 patients with coexisting medical conditions (total CIRS score >6 or creatinine clearance <70 mL/min). The primary endpoint was IRC-assessed PFS
- MURANO was a randomized (1:1), multicenter, open-label, actively controlled phase 3 trial that evaluated the efficacy and safety of VENCLEXTA in combination with rituximab versus bendamustine in combination with rituximab in 389 patients with CLL who had received at least one line of prior therapy. The primary endpoint was IRC-assessed PFS

1L=first line; CIRS=Cumulative Illness Rating Scale; CLL=chronic lymphocytic leukemia; GClb=GAZYVA + chlorambucil; IRC=independent review committee; PFS=progression-free survival; R/R=relapsed/refractory; SLL=small lymphocytic lymphoma; VEN+G=VENCLEXTA + GAZYVA® (obinutuzumab).

Indication

- VENCLEXTA is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Select Important Safety Information

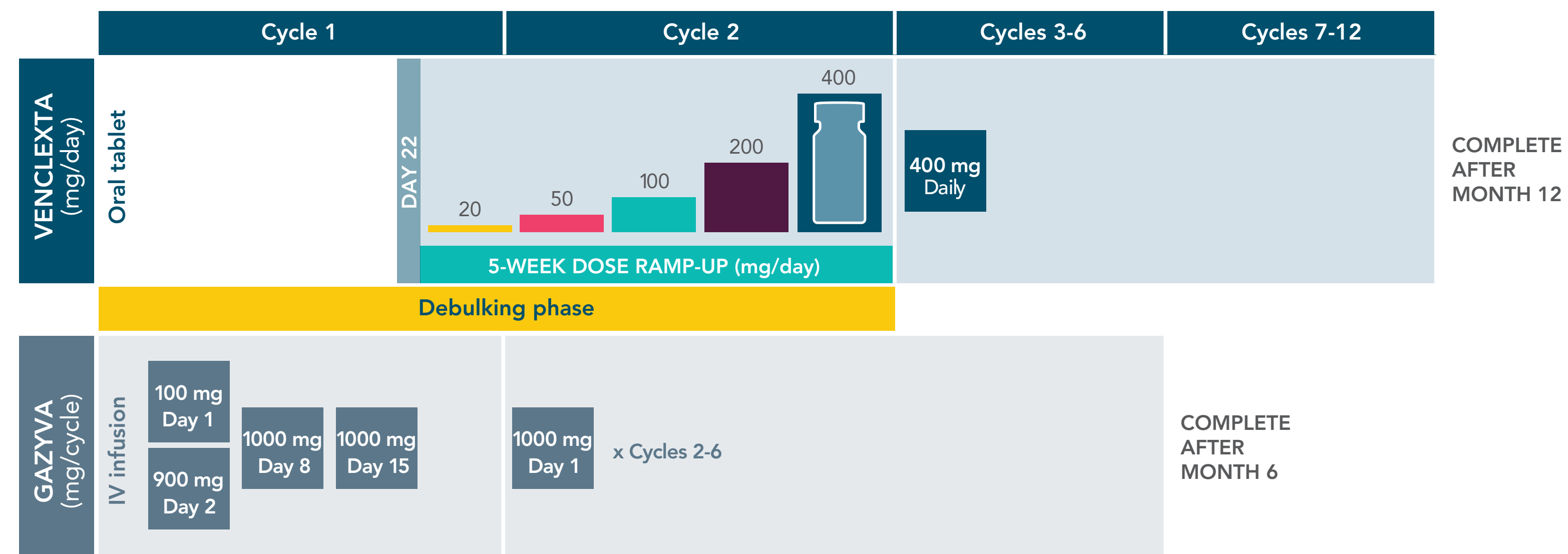
- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).
- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA. Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.
- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor blood counts and for signs of infection; manage as medically appropriate.
- Fatal and serious infections such as pneumonia and sepsis have occurred in patients with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.
- Do not administer live attenuated vaccines prior to, during, or after treatment until B-cell recovery occurs.
- VENCLEXTA may cause embryo-fetal harm. Advise females of reproductive potential to avoid pregnancy during treatment.



The only chemo-free regimen designed to stop treatment at 12 months in 1L CLL...¹

1L CLL

VENCLEXTA + GAZYVA® (obinutuzumab) for 1L CLL/SLL



Graphic not to scale. Each cycle is 28 days.

- The trial started with an initial cycle of GAZYVA followed by the 5-week VENCLEXTA dose ramp-up to help reduce tumor burden (debulk) and decrease the risk of TLS
- After the first treatment cycle of GAZYVA and before the VENCLEXTA dose ramp-up, patients' ALC was reduced by 98% in the CLL14 trial^{1,2*}
- Per the trial protocol, tumor burden was assessed based on ALC and lymph node size. The effect of the first GAZYVA treatment cycle on lymph node size was not evaluated^{1,3}
- Tumor burden assessments, including radiographic evaluation, and blood chemistry assessments are recommended prior to VENCLEXTA initiation to assess the risk of TLS

GAZYVA

- On Cycle 1, Days 1 and 2, administer GAZYVA 100 mg and 900 mg, respectively
- Administer GAZYVA 1000 mg on Days 8 and 15 of Cycle 1 and on Day 1 of each subsequent 28-day cycle, for a total of 6 cycles
- See pages 4-6 for an overview of GAZYVA dosing and administration

VENCLEXTA

- On Cycle 1, Day 22, start VENCLEXTA according to the dose ramp-up schedule
- The VENCLEXTA starting dose is 20 mg once daily for 7 days, ramping up weekly to 50 mg, 100 mg, 200 mg, and finally 400 mg once daily
- After completing the ramp-up schedule on Cycle 2, Day 28, patients should continue VENCLEXTA 400 mg once daily from Cycle 3, Day 1 until the last day of Cycle 12

*From a median count of 55×10^9 cells/L at baseline to a median count of 1.27×10^9 cells/L at Day 15.² Median lymphocyte counts are descriptive in nature and not powered for any type of comparison. Changes in TLS risk status based on ALC reduction were at the discretion of the trial investigators. ALC=absolute lymphocyte count; IV=intravenous; TLS=tumor lysis syndrome.

Select Important Safety Information

Contraindication

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).

Tumor Lysis Syndrome

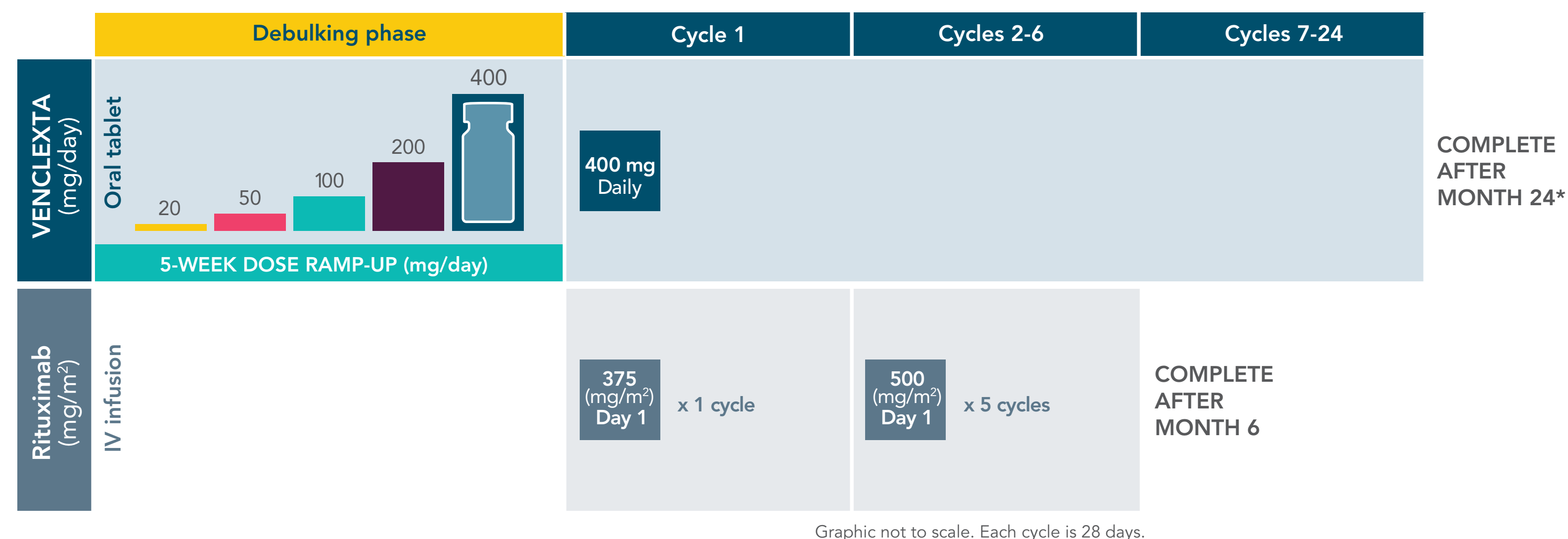
- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.



...and 24 months* in R/R CLL¹

R/R CLL

VENCLEXTA + rituximab (VEN+R) for R/R CLL/SLL



- To gradually reduce tumor burden (debulk) and decrease the risk of TLS, start with the 5-week VENCLEXTA dose ramp-up

*24 months from Cycle 1, Day 1 of rituximab.

VENCLEXTA

- The VENCLEXTA starting dose is 20 mg once daily for 7 days, ramping up weekly to 50 mg, 100 mg, 200 mg, and finally 400 mg once daily
- After ramp-up, VENCLEXTA should be taken at the recommended daily dose for 24 months

Rituximab

- Start rituximab 375 mg/m² after the patient has received the 400-mg dose of VENCLEXTA for 7 days
- Administer rituximab 500 mg/m² on Day 1 of each subsequent cycle, for a total of 6 cycles

Note: VENCLEXTA may also be given as monotherapy until disease progression or unacceptable toxicity. Please see the full Prescribing Information for more information.

Select Important Safety Information

Tumor Lysis Syndrome (cont'd)

- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.



GAZYVA® (obinutuzumab) dosing and administration overview⁴

6-cycle dosing schedule

Each dose of GAZYVA is 1000 mg administered intravenously with the exception of the first infusions in Cycle 1, which are administered on Day 1 (100 mg) and Day 2 (900 mg).

GAZYVA dosing schedule			
Day of treatment cycle		Dose	Rate of infusion
Cycle 1 (loading doses)	Day 1	100 mg	<ul style="list-style-type: none"> Administer at 25 mg/hr over 4 hours Do not increase the infusion rate
	Day 2	900 mg	<ul style="list-style-type: none"> If no infusion-related reaction occurred during the previous infusion, administer at 50 mg/hr. The rate of the infusion can be escalated in increments of 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr If an infusion-related reaction occurred during the previous infusion, administer at 25 mg/hr. The rate of infusion can be escalated in increments of up to 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr
	Day 8	1000 mg	<ul style="list-style-type: none"> If no infusion-related reaction occurred during the previous infusion and the final infusion rate was 100 mg/hr or faster, infusions can be started at a rate of 100 mg/hr and increased by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr If an infusion-related reaction occurred during the previous infusion, administer at 50 mg/hr. The rate of infusion can be escalated in increments of 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr
Day 15	1000 mg		
Cycles 2–6	Day 1	1000 mg	<ul style="list-style-type: none"> If no infusion-related reaction occurred during the previous infusion and the final infusion rate was 100 mg/hr or faster, infusions can be started at a rate of 100 mg/hr and increased by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr If an infusion-related reaction occurred during the previous infusion, administer at 50 mg/hr. The rate of infusion can be escalated in increments of 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr

If a planned dose of GAZYVA is missed, administer the missed dose as soon as possible and adjust dosing schedule to maintain the time interval between doses. If appropriate, patients who do not complete the Day 1 Cycle 1 dose may proceed to the Day 2 Cycle 1 dose.

Premedication and administration

- Premedicate before each infusion
- Provide prophylactic hydration and antihyperuricemics to patients at high risk of TLS

- Administer only as an intravenous infusion through a dedicated line
- Do not administer as an intravenous push or bolus
- Monitor blood counts at regular intervals
- GAZYVA should only be administered by a healthcare professional with appropriate medical support to manage severe IRRs that can be fatal if they occur

IRR=infusion-related reaction.

Please see additional Important Safety Information for GAZYVA on page 7. Please see accompanying full Prescribing Information for GAZYVA or visit https://www.gene.com/download/pdf/gazyva_prescribing.pdf.

Select Important Safety Information

BOXED WARNINGS: HEPATITIS B VIRUS REACTIVATION AND PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- Hepatitis B Virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients receiving CD20-directed cytolytic antibodies, including GAZYVA. Screen all patients for HBV infection before treatment initiation. Monitor HBV-positive patients during and after treatment with GAZYVA. Discontinue GAZYVA and concomitant medications in the event of HBV reactivation
- Progressive Multifocal Leukoencephalopathy (PML) including fatal PML, can occur in patients receiving GAZYVA



GAZYVA® (obinutuzumab) dosing and administration overview (cont'd)⁴

Recommended premedications

The following premedications are recommended before GAZYVA infusion begins to reduce the risk of IRRs:

	Cycle 1, Days 1 and 2	All subsequent infusions		
Complete before infusion	All patients	All patients	Patients with an IRR (grade 1–2) with the previous infusion	Patients with a grade 3 IRR with the previous infusion OR with a lymphocyte count >25 x 10 ⁹ /L prior to next treatment
60 minutes prior Intravenous glucocorticoid*†	✓			✓
30 minutes prior Antihistamine‡	✓		✓	✓
30 minutes prior Acetaminophen§	✓	✓	✓	✓

*20 mg dexamethasone or 80 mg methylprednisolone. Hydrocortisone is not recommended as it has not been effective in reducing the rate of IRRs.

†If a glucocorticoid-containing chemotherapy regimen is administered on the same day as GAZYVA, the glucocorticoid can be administered as an oral medication if given at least 1 hour prior to GAZYVA, in which case additional intravenous glucocorticoid as premedication is not required.

‡E.g., 50 mg diphenhydramine.

§650–1000 mg.

Premedication and close monitoring are recommended for all patients

- Patients with preexisting cardiac or pulmonary conditions may be at greater risk of experiencing more severe IRRs
- Hypotension may occur during GAZYVA intravenous infusions. Consider withholding antihypertensive treatments for 12 hours prior to and throughout each GAZYVA infusion and for the first hour after administration
- Patients with high tumor burden, high circulating absolute lymphocyte counts (greater than 25 x 10⁹/L), or renal

impairment are considered at risk of TLS and should receive prophylaxis. Premedicate with antihyperuricemics (eg, allopurinol or rasburicase) and ensure adequate hydration prior to start of GAZYVA therapy. Continue prophylaxis prior to each subsequent GAZYVA infusion, as needed

- Patients with grade 3 to 4 neutropenia lasting more than 1 week are strongly recommended to receive antimicrobial prophylaxis until resolution of neutropenia to grade 1 or 2. Antiviral and antifungal prophylaxis should be considered

Please see additional Important Safety Information for GAZYVA on page 7. Please see accompanying full Prescribing Information for GAZYVA or visit https://www.gene.com/download/pdf/gazyva_prescribing.pdf.



GAZYVA® (obinutuzumab) dosing and administration overview (cont'd)⁴

Adjusting infusions in case of IRRs

If a patient experiences an IRR of any grade during infusion, adjust the infusion as follows:

IRRs	Recommendations per prescribing information
Grade 4 (life-threatening)	Stop infusion immediately and permanently discontinue GAZYVA therapy
Grade 3 (severe)	<p>Interrupt infusion and manage symptoms</p> <ul style="list-style-type: none"> • Upon resolution of symptoms, consider restarting GAZYVA infusion at no more than half the previous rate (the rate being used at the time that the IRR occurred) and, if patient does not experience any further IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment cycle dose • Permanently discontinue treatment if patients experience a grade 3 IRR at rechallenge <ul style="list-style-type: none"> – The Day 1 infusion rate may be increased back up to 25 mg/hr after 1 hour but not increased further
Grades 1–2 (mild to moderate)	<p>Reduce infusion rate or interrupt infusion and manage symptoms</p> <ul style="list-style-type: none"> • Upon resolution of symptoms, continue or resume infusion and, if patient does not experience any further IRR symptoms, infusion rate escalation may resume at the increments and intervals as appropriate for the treatment cycle dose <ul style="list-style-type: none"> – The Day 1 infusion rate may be increased back up to 25 mg/hr after 1 hour but not increased further

- Closely monitor patients during the entire infusion. IRRs within 24 hours of receiving GAZYVA have occurred
- Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, and/or oxygen) for IRRs as needed

Incidence of IRRs

- In the VEN+G clinical trial, IRRs (any grade) occurred in 48% (205/426) of patients. Grade 3 or 4 IRRs occurred in 9% (40/426) of patients²

Please see additional Important Safety Information for GAZYVA on page 7. Please see accompanying full Prescribing Information for GAZYVA or visit https://www.gene.com/download/pdf/gazyva_prescribing.pdf.



Important Safety Information for GAZYVA[®] (obinutuzumab)

Important Safety Information

BOXED WARNINGS: HEPATITIS B VIRUS REACTIVATION AND PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- **Hepatitis B Virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients receiving CD20-directed cytolytic antibodies, including GAZYVA. Screen all patients for HBV infection before treatment initiation. Monitor HBV-positive patients during and after treatment with GAZYVA. Discontinue GAZYVA and concomitant medications in the event of HBV reactivation**
- **Progressive Multifocal Leukoencephalopathy (PML) including fatal PML, can occur in patients receiving GAZYVA**

Contraindications

- GAZYVA is contraindicated in patients with known hypersensitivity reactions (e.g. anaphylaxis) to obinutuzumab or to any of the excipients, or serum sickness with prior obinutuzumab use

Additional Warnings and Precautions

- **Infusion-Related Reactions:** Premedicate patients with glucocorticoid, acetaminophen, and antihistamine. Monitor patients closely during infusions. Interrupt, reduce rate, or discontinue for infusion-related reactions based on severity
- **Hypersensitivity Reactions Including Serum Sickness:** Discontinue GAZYVA permanently

- **Tumor Lysis Syndrome (TLS):** Premedicate with antihyperuricemics and adequate hydration, especially for patients with high tumor burden, high circulating lymphocyte count or renal impairment. Correct electrolyte abnormalities, provide supportive care, and monitor renal function and fluid balance
- **Infections:** Do not administer GAZYVA to patients with an active infection. Patients with a history of recurring or chronic infections may be at increased risk of infection
- **Neutropenia:** In patients with Grade 3 to 4 neutropenia, monitor laboratory tests until resolution and for infection. Consider dose delays and infection prophylaxis, as appropriate
- **Thrombocytopenia:** Monitor platelet counts and for bleeding. Transfusion may be necessary
- **Immunization:** Avoid administration of live virus vaccines during GAZYVA treatment and until B-cell recovery
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception

Additional Important Safety Information

- The most common adverse reactions (incidence $\geq 20\%$ and $\geq 2\%$ greater in the GAZYVA treated arm) observed in patients with CLL were infusion-related reactions (66%), and neutropenia (38%)

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

Please see accompanying full Prescribing Information for additional Important Safety Information, including BOXED WARNINGS.

Please see accompanying full Prescribing Information for GAZYVA or visit https://www.gene.com/download/pdf/gazyva_prescribing.pdf.



Initiating VENCLEXTA¹

3 STEPS: ASSESS, PREPARE, INITIATE

	LOW TUMOR BURDEN	MEDIUM TUMOR BURDEN	HIGH TUMOR BURDEN																																																																																					
STEP 1: ASSESS Prior to initiation	All lymph nodes (LN) <5 cm AND Absolute lymphocyte count (ALC) <25 x 10 ⁹ /L	Any LN 5 cm to <10 cm OR ALC ≥25 x 10 ⁹ /L	Any LN ≥10 cm OR Any LN ≥5 cm and ALC ≥25 x 10 ⁹ /L																																																																																					
STEP 2: PREPARE At least 2 days prior to first dose	Oral hydration*: 1.5–2 L Allopurinol [†]	Oral hydration*: 1.5–2 L Allopurinol [†] IV hydration^{1,3}: Consider for patients with medium tumor burden, occurring during outpatient stay	Oral hydration*: 1.5–2 L IV hydration: 150–200 mL/h as tolerated prior to first dose Allopurinol [§] Rasburicase^{1,3}: Consider for elevated uric acid (>8 mg/dL)																																																																																					
STEP 3: INITIATE And monitor blood chemistry [‡] for first dose of each ramp-up week	OUTPATIENT <table border="1"> <thead> <tr> <th>Day 1, Week:</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> </tr> </thead> <tbody> <tr> <td>Dosage</td> <td>20 mg</td> <td>50 mg</td> <td>100 mg</td> <td>200 mg</td> <td>400 mg</td> </tr> <tr> <td>Blood chemistry labs</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Pre-Dose</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6-8 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>—</td> <td>—</td> <td>—</td> </tr> <tr> <td>24 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>—</td> <td>—</td> <td>—</td> </tr> </tbody> </table>		Day 1, Week:	1	2	3	4	5	Dosage	20 mg	50 mg	100 mg	200 mg	400 mg	Blood chemistry labs						Pre-Dose	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6-8 Hours	<input type="checkbox"/>	<input type="checkbox"/>	—	—	—	24 Hours	<input type="checkbox"/>	<input type="checkbox"/>	—	—	—	HOSPITAL OUTPATIENT <table border="1"> <thead> <tr> <th>Day 1, Week:</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> </tr> </thead> <tbody> <tr> <td>Dosage</td> <td>20 mg</td> <td>50 mg</td> <td>100 mg</td> <td>200 mg</td> <td>400 mg</td> </tr> <tr> <td>Blood chemistry labs</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Pre-Dose</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>4 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>—</td> <td>—</td> <td>—</td> </tr> <tr> <td>8 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>12 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>—</td> <td>—</td> <td>—</td> </tr> <tr> <td>24 Hours</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </tbody> </table>		Day 1, Week:	1	2	3	4	5	Dosage	20 mg	50 mg	100 mg	200 mg	400 mg	Blood chemistry labs						Pre-Dose	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	4 Hours	<input type="checkbox"/>	<input type="checkbox"/>	—	—	—	8 Hours	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	12 Hours	<input type="checkbox"/>	<input type="checkbox"/>	—	—	—	24 Hours	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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For the first doses of 20 mg and 50 mg, consider hospitalization for patients with medium tumor burden and CLcr <80 mL/min; for these patients, see table to the right for monitoring in hospital.

*1.5–2 L of water (~56 ounces) should be consumed every day starting at least 2 days before the first dose and throughout the ramp-up phase, especially the first day of each dose increase. Administer intravenous hydration for any patient who cannot tolerate oral hydration.^{1,3}

[†]For patients with low tumor burden, start allopurinol or xanthine oxidase inhibitor 2 to 3 days prior to initiation of VENCLEXTA. For patients with medium tumor burden, allopurinol or other uric acid reducers should be taken at least 3 days prior to initiation.^{1,3}

[‡]Review in real time.

[§]Or other uric acid reducers should be taken at least 3 days prior to first dose.³

CLcr=creatinine clearance.

Considerations for TLS with VENCLEXTA

- The risk of TLS may decrease as tumor burden decreases
- The risk of TLS is a continuum based on multiple factors, including tumor burden and comorbidities
- Reduced renal function (CLcr <80 mL/min) further increases the risk
- Consider all patient comorbidities before final determination of prophylaxis and monitoring schedule
- Correct pre-existing abnormalities prior to initiation of treatment with VENCLEXTA

Appropriate prophylaxis can help lower the risk of TLS.

Assess blood chemistry prior to initiation of treatment and continue to monitor during ramp-up period:

- Potassium
- Uric acid
- Phosphorus
- Calcium
- Creatinine

Review in real time.

Select Important Safety Information

Tumor Lysis Syndrome

- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.

Hepatic Impairment

- Reduce the dose of VENCLEXTA for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more closely for signs of toxicity. No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

Please see additional Important Safety Information on pages 18 and 19. Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.



Confidently start treatment with VENCLEXTA regimens¹

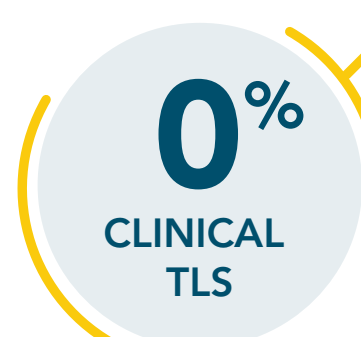
Patients with low or medium tumor burden may be initiated in the outpatient setting



- Consider all patient comorbidities before final determination of prophylaxis and monitoring schedule
- Follow the risk assessment tool on page 8 for recommended TLS prophylaxis based on tumor burden
- Patients who may be initiated in the outpatient setting:
 - **Low tumor burden:** those with all lymph nodes (LN) <5 cm and an absolute lymphocyte count (ALC) <25 x 10⁹/L
 - **Medium tumor burden:** those with any LN from 5 cm to <10 cm or an ALC ≥25 x 10⁹/L
- For the first doses of 20 mg and 50 mg, consider hospitalization for patients with medium tumor burden and CLcr<80 mL/min
- Patients with high tumor burden—those with any LN ≥10 cm, or those with ALC ≥25 x10⁹/L and any LN ≥5 cm—should be initiated in the hospital
- In the CLL14 and MURANO clinical trials, TLS risk category was chosen based on investigator discretion, LN size, and ALC
 - Baseline characteristics in the CLL14 trial: 13% (29/216) of VEN+G patients had low, 64% (139/216) had medium, and 22% (48/216) had high TLS risk²
 - Baseline characteristics in the MURANO trial: 18% (34/194) of VEN+R patients had low, 55% (106/194) had medium, and 28% (54/194) had high TLS risk⁵
- After the first treatment cycle of GAZYVA® (obinutuzumab) and before the VENCLEXTA dose ramp-up, patients' ALC was reduced by 98% in the CLL14 trial^{1,2*}
 - The effect of the first GAZYVA treatment cycle on LN size was not evaluated in the CLL14 trial³

*From a median count of 55 x 10⁹ cells/L at baseline to a median count of 1.27 x 10⁹ cells/L at Day 15.² Median lymphocyte counts are descriptive in nature and not powered for any type of comparison. Changes in TLS risk status based on ALC reduction were at the discretion of the trial investigators.

0% clinical TLS^{1,2}



- The dose ramp-up is designed to gradually reduce tumor burden (debulk) and decrease the risk of TLS¹
- With TLS prophylaxis and monitoring protocols, 0% incidence of clinical TLS was observed in the CLL14 trial^{1,2,6}
 - Laboratory TLS occurred in 1% (3/212) of patients treated with VEN+G. All 3 TLS events resolved and did not lead to withdrawal from the study. GAZYVA administration was delayed in 2 cases in response to the TLS events¹
- After the MURANO trial protocol was amended to implement TLS prophylaxis and monitoring, 0% incidence of clinical TLS was observed in the R/R CLL trial. Incidence of TLS occurred in 3% (6/194) of patients treated with VEN+R overall¹
 - All TLS events occurred during the ramp-up period and were resolved within 2 days. All 6 patients completed the ramp-up and reached the recommended daily dose of 400 mg of VENCLEXTA¹

Select Important Safety Information

Tumor Lysis Syndrome

- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.
- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.



Instructions for taking VENCLEXTA¹

Advise patients to:

- ✓ Take VENCLEXTA tablets exactly as they are prescribed and not to change or interrupt their dose unless they are told to do so by their doctor.
- ✓ Take their prescribed VENCLEXTA tablet orally once daily, whole with a meal and water at approximately the same time each day.
- ✓ Be adequately hydrated every day they take VENCLEXTA to reduce the risk of TLS. The recommended volume is 6-8 glasses (~56 ounces) of water every day starting 2 days before the first dose and throughout the ramp-up phase, especially the first day of each dose increase.
- ✓ Attend every scheduled appointment for blood work or other laboratory tests.

Advise patients NOT to:

- ✗ Crush, chew, or break their VENCLEXTA tablets. Tablets should be swallowed whole.
- ✗ Remove their VENCLEXTA tablets from the original packaging during the first 4 weeks of treatment, and do not transfer them to a different container.
- ✗ Take an additional dose if vomiting occurs after taking VENCLEXTA. They should take the next dose at the usual time the following day.
- ✗ Consume grapefruit products, Seville oranges, or starfruit during treatment with VENCLEXTA.

If a patient misses a dose:

Within 8 hours of the time it is usually taken, the patient should take the missed dose right away and take the next dose as usual.

By more than 8 hours, the patient should not take the missed dose and should take the next dose at the usual time.

Select Important Safety Information

Neutropenia

- In patients with CLL, Grade 3 or 4 neutropenia developed in 63% to 64% of patients and Grade 4 neutropenia developed in 31% to 33% of patients treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients treated with VENCLEXTA in combination and monotherapy studies.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF).

Infections

- Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.



EXAMPLE OF TREATMENT INITIATION CALENDAR FOR VENCLEXTA

LOW OR MEDIUM TUMOR BURDEN¹

This example is provided to help you in using the full Prescribing Information and is for illustrative purposes only. No two patients are the same. Refer to the full Prescribing Information when making treatment decisions.

Order VENCLEXTA Starting Pack: Dosing for Weeks 1–4 ✓
Order bottle of 100-mg tablets: Dosing for Week 5+ ✓

STEP 1: ASSESS

Assess tumor burden, renal function and comorbidities, and blood chemistries. Correct pre-existing abnormalities prior to VENCLEXTA initiation.

STEP 2: PREPARE

2–3 DAYS PRIOR TO VENCLEXTA INITIATION	AT LEAST 2 DAYS PRIOR TO VENCLEXTA INITIATION	BEFORE EACH DOSE INCREASE
Start allopurinol*	Start oral/IV hydration	Pre-dose labs

Blood Chemistry Monitoring: Potassium, calcium, creatinine, phosphorus, uric acid (review in real time). Evaluate and manage any abnormalities promptly.

STEP 3: INITIATE

	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
WEEK 1 20 mg Take two 10-mg tablets once daily	6-8 HOUR POST-DOSE LABS 10 mg x2	24-HOUR POST-DOSE LABS 10 mg x2	10 mg x2	10 mg x2	10 mg x2	10 mg x2	PRE-DOSE LABS BEFORE NEXT DOSE 10 mg x2
WEEK 2 50 mg Take one 50-mg tablet once daily	6-8 HOUR POST-DOSE LABS 50 mg	24-HOUR POST-DOSE LABS 50 mg	50 mg	50 mg	50 mg	50 mg	PRE-DOSE LABS BEFORE NEXT DOSE 50 mg
WEEK 3 100 mg Take one 100-mg tablet once daily	Reminder: Order bottle of 100-mg tablets—Dosing for Week 5+						PRE-DOSE LABS BEFORE NEXT DOSE 100 mg
WEEK 4 200 mg Take two 100-mg tablets once daily	100 mg x2	100 mg x2	100 mg x2	100 mg x2	100 mg x2	100 mg x2	PRE-DOSE LABS BEFORE NEXT DOSE 100 mg x2
WEEK 5 400 mg Take four 100-mg tablets once daily	100 mg x4	100 mg x4	100 mg x4	100 mg x4	100 mg x4	100 mg x4	100 mg x4

✓ Continue VENCLEXTA 400 mg once daily for the prescribed duration.

Advise patients to drink 1.5–2 L (~56 ounces) of water daily while taking VENCLEXTA.

*For patients with low tumor burden, start allopurinol or xanthine oxidase inhibitor 2 to 3 days prior to initiation of VENCLEXTA. For patients with medium tumor burden, allopurinol or other uric acid reducers should be taken at least 3 days prior to initiation.^{1,3}

Please see Important Safety Information on pages 18 and 19. Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.



Dose modifications¹

Interrupt dosing or reduce dose for toxicities

- For patients who have had a dosing interruption greater than 1 week during the first 5 weeks of ramp-up phase or greater than 2 weeks after completing the ramp-up phase, reassess the risk of TLS to determine if reinitiation with a reduced dose is necessary (e.g., all or some levels of the ramp-up schedule)

Consider discontinuing VENCLEXTA for patients who require dose reductions to less than 100 mg for more than 2 weeks.

Recommended VENCLEXTA dose modifications for toxicities*	
TLS	
Any occurrence: Blood chemistry changes or symptoms suggestive of TLS	Withhold the next day's dose. If resolved within 24–48 hours of last dose, resume at the same dose.
	For any blood chemistry changes requiring more than 48 hours to resolve, resume at a reduced dose. See dose reduction guidelines on page 13.
	For any events of clinical TLS, [†] resume at a reduced dose following resolution. See dose reduction guidelines on page 13.
Nonhematologic toxicities	
1st occurrence: Grade 3 or 4 nonhematologic toxicities	Interrupt VENCLEXTA. Once the toxicity has resolved to grade 1 or baseline level, VENCLEXTA therapy may be resumed at the same dose. No dose modification is required.
2nd and subsequent occurrences: Grade 3 or 4 nonhematologic toxicities	Interrupt VENCLEXTA. Follow dose reduction guidelines on page 13 when resuming VENCLEXTA treatment after resolution. A larger dose reduction may occur at the discretion of the physician.
Hematologic toxicities	
1st occurrence: Grade 3 neutropenia with infection or fever or grade 4 hematologic toxicities (except lymphopenia)	Interrupt VENCLEXTA. To reduce the infection risks associated with neutropenia, granulocyte-colony stimulating factor (G-CSF) may be administered with VENCLEXTA if clinically indicated. Once the toxicity has resolved to grade 1 or baseline level, VENCLEXTA therapy may be resumed at the same dose.
2nd and subsequent occurrences: Grade 3 neutropenia with infection or fever or grade 4 hematologic toxicities (except lymphopenia)	Interrupt VENCLEXTA. Consider using G-CSF as clinically indicated. Follow dose reduction guidelines on page 13 when resuming VENCLEXTA treatment after resolution. A larger dose reduction may occur at the discretion of the physician.

- Monitor complete blood counts throughout the treatment period

*Adverse reactions were graded using NCI CTCAE version 4.0.

[†]Clinical TLS was defined as laboratory TLS with clinical consequences such as acute renal failure, cardiac arrhythmias, or sudden death and/or seizures. CTCAE=Common Terminology Criteria for Adverse Events, NCI=National Cancer Institute.



Dose modifications (cont'd)¹

Dose reduction for toxicity during VENCLEXTA treatment	
Dose at interruption, mg	Restart dose, mg*
400	300
300	200
200	100
100	50
50	20
20	10

*During the ramp-up phase, continue the reduced dose for 1 week before increasing the dose.

Dosage modifications for concomitant use with strong or moderate CYP3A inhibitors or P-gp inhibitors

Concomitant use of VENCLEXTA with strong CYP3A inhibitors at initiation and during the ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of TLS.

Management of potential VENCLEXTA interactions with CYP3A and P-gp inhibitors		
Coadministered drug	Initiation and ramp-up phase	Steady daily dose [†] (after ramp-up phase)
Posaconazole	Contraindicated	Reduce VENCLEXTA dose to 70 mg
Other strong CYP3A inhibitor	Contraindicated	Reduce VENCLEXTA dose to 100 mg
Moderate CYP3A inhibitor	Reduce VENCLEXTA dose by at least 50%	
P-gp inhibitor		

[†]Consider alternative medications or reduce the VENCLEXTA dose as described in this table. CYP3A=cytochrome P450 3A; P-gp=P-glycoprotein.

- Resume the VENCLEXTA dose that was used prior to concomitant use of a strong or moderate CYP3A inhibitor or P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor

Dosage modifications for patients with severe hepatic impairment

- Reduce the VENCLEXTA once daily dose by 50% for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more closely for signs of toxicity

Please see Important Safety Information on pages 18 and 19. Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.



Summary of VEN+G safety data¹

1L CLL

The safety of VEN+G versus GClb was evaluated in an open-label, randomized, phase 3 study in patients with previously untreated CLL

- In the VEN+G arm, fatal adverse reactions that occurred in the absence of disease progression and within 28 days of the last VENCLEXTA treatment were reported in 2% (4/212) of patients. Serious adverse reactions were reported in 49% of patients in the VEN+G arm, most often due to febrile neutropenia and pneumonia (5% each)
- The median duration of exposure to VENCLEXTA was 10.5 months (range: 0 to 13.5 months). The median number of cycles was 6 for obinutuzumab and 12 for chlorambucil
- Adverse reactions led to treatment discontinuation in 16% of patients, dose reduction in 21%, and dose interruption in 74%
- Neutropenia led to dose interruption of VENCLEXTA in 41% of patients, reduction in 13%, and discontinuation in 2%

Common (≥10%) adverse reactions in patients treated with VEN+G				
Adverse Reaction by Body System	VEN+G		GClb	
	All Grades (%) n=212	Grade ≥3 (%) n=212	All Grades (%) n=214	Grade ≥3 (%) n=214
Blood and lymphatic system disorders				
Neutropenia*	60	56	62	52
Anemia*	17	8	20	7
Gastrointestinal disorders				
Diarrhea	28	4	15	1
Nausea	19	0	22	1
Constipation	13	0	9	0
Vomiting	10	1	8	1
General disorders and administration site conditions				
Fatigue*	21	2	23	1
Infections and infestations				
Upper respiratory tract infection*	17	1	17	1

*Includes multiple adverse reaction terms.

For common laboratory abnormalities data, please see Table 10 in the VENCLEXTA full Prescribing Information.

During treatment with single-agent VENCLEXTA after completion of VEN+G combination treatment:

- The most common (all grades) adverse reaction (≥10% of patients) reported was neutropenia (26%)
- The most common grade ≥3 adverse reactions (≥2% of patients) were neutropenia (23%) and anemia (2%)

Please see Important Safety Information on pages 18 and 19. Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.



Summary of VEN+R safety data¹

R/R CLL

The safety of VEN+R versus BR was evaluated in the open-label, randomized, phase 3 MURANO study in patients with CLL who had received at least one prior therapy

- In the VEN+R arm, fatal adverse reactions that occurred in the absence of disease progression and within 30 days of the last VENCLEXTA treatment and/or 90 days of last rituximab treatment were reported in 2% (4/194) of patients. Serious adverse reactions were reported in 46% of patients in the VEN+R arm, with the most frequent ($\geq 5\%$) being pneumonia (9%)
- At the time of data analysis, the median duration of exposure was 22 months in the VEN+R arm compared with 6 months in the BR arm
- Discontinuation due to any adverse events occurred in 16% of patients on VEN+R compared with 10% of patients on BR
- Dose reductions due to adverse events occurred in 15% of patients in both arms
- Dose interruptions due to adverse events occurred in 71% of patients on VEN+R compared with 40% of patients on BR
- In the VEN+R arm, neutropenia led to dose interruption of VENCLEXTA in 46% of patients and discontinuation in 3%, and thrombocytopenia led to discontinuation in 3% of patients

Common ($\geq 10\%$) adverse reactions in patients treated with VEN+R				
Adverse Reaction by Body System	VEN+R		BR	
	All Grades (%) n=194	Grade ≥ 3 (%) n=194	All Grades (%) n=188	Grade ≥ 3 (%) n=188
Blood and lymphatic system disorders				
Neutropenia*	65	62	50	44
Anemia*	16	11	23	14
Gastrointestinal disorders				
Diarrhea	40	3	17	1
Nausea	21	1	34	1
Constipation	14	<1	21	0
Infections and infestations				
Upper respiratory tract infection*	39	2	23	2
Lower respiratory tract infection*	18	2	10	2
Pneumonia*	10	7	14	10
General disorders and administration site conditions				
Fatigue*	22	2	26	<1

*Includes multiple adverse reaction terms.
BR=bendamustine + rituximab.

For common laboratory abnormalities data, please see Table 12 in the VENCLEXTA full Prescribing Information.

During treatment with single-agent VENCLEXTA after completion of VEN+R combination treatment:

- The most common (all grades) adverse reactions ($\geq 10\%$ patients) reported were upper respiratory tract infection (21%), diarrhea (19%), neutropenia (16%), and lower respiratory tract infection (11%)
- The most common grade 3 or 4 adverse reactions ($\geq 2\%$ patients) were neutropenia (12%) and anemia (3%)

Please see Important Safety Information on pages 18 and 19. Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.



Supporting patients who have been prescribed VENCLEXTA

Patient support programs

Serious illnesses come with many challenges. Getting VENCLEXTA shouldn't be one of them.

We believe every person should get the VENCLEXTA they have been prescribed, and we offer programs to make this happen.

If your patients:



Need help understanding their insurance coverage and related financial responsibilities, **VENCLEXTA Access Solutions** is here to help.



Do not have insurance coverage or have financial concerns and meet certain eligibility criteria, the **Genentech Patient Foundation*** may be able to provide free medicine.



Have insurance and need help paying for their medicine, **Affordability Options** may be available:

- The Genentech Oncology[®] Co-pay Assistance Program[†]
- Referrals to independent co-pay assistance foundations[‡]

The Genentech Patient Resource Center can help answer questions and connect you to the right Genentech patient support service. Call (877) GENENTECH (877-436-3683) to get started.

*To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine must have pursued all other forms of financial assistance and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet different income requirements.

[†]Eligibility criteria apply. Not valid for patients using federal or state government programs to pay for their medications. Patient must be taking the Genentech medication for an FDA-approved indication. See full terms and conditions at CopolyAssistanceNow.com.

[‡]VENCLEXTA Access Solutions does not influence or control the operations or eligibility criteria of any independent co-pay assistance foundation and cannot guarantee co-pay assistance after a referral from VENCLEXTA Access Solutions. The foundations to which we refer patients are not exhaustive or indicative of VENCLEXTA Access Solutions' endorsement or financial support. There may be other foundations to support the patient's disease state.



Supporting patients who have been prescribed VENCLEXTA (cont'd)

VENCOMPASS®



Providing product-related support for patients taking VENCLEXTA

This program is intended to provide product-related education and support to your patients taking VENCLEXTA for an approved use during the ramp-up phase and throughout their therapy. VENCOMPASS does not provide medical advice and will direct patients to speak with their healthcare provider for all treatment-related questions. Information provided is based on the full Prescribing Information and Medication Guide for VENCLEXTA.

VENCOMPASS Nurses* have experience in cancer care and can provide support through:

- Hydration, dosing, and weekly laboratory reminders
- Answering product-specific questions
- Providing available information regarding additional resources for patients

*VENCOMPASS Nurses do not provide medical advice and are trained to direct patients to speak with their healthcare professional about any treatment-related questions.

For VENCOMPASS, please visit
www.VENCLEXTA.com
or call (844) 9-COMPASS/
(844) 926-6727 for more information.



Important Safety Information for VENCLEXTA

Contraindication

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).

Tumor Lysis Syndrome

- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.
- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.

Neutropenia

- In patients with CLL, Grade 3 or 4 neutropenia developed in 63% to 64% of patients and Grade 4 neutropenia developed in 31% to 33% of patients treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients treated with VENCLEXTA in combination and monotherapy studies.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF).

Infections

- Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.

Immunization

- Do not administer live attenuated vaccines prior to, during, or after treatment with VENCLEXTA until B-cell recovery occurs. Advise patients that vaccinations may be less effective.

Embryo-Fetal Toxicity

- VENCLEXTA may cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to avoid pregnancy during treatment.

Increased Mortality in Patients with Multiple Myeloma when VENCLEXTA is Added to Bortezomib and Dexamethasone

- In a randomized trial (BELLINI; NCT02755597) in patients with relapsed or refractory multiple myeloma, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.



Important Safety Information for VENCLEXTA (cont'd)

Adverse Reactions

- **In patients with CLL receiving combination therapy with obinutuzumab**, serious adverse reactions were most often due to febrile neutropenia and pneumonia (5% each). The most common adverse reactions ($\geq 20\%$) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%).
- **In patients with CLL receiving combination therapy with rituximab**, the most frequent serious adverse reaction ($\geq 5\%$) was pneumonia (9%). The most common adverse reactions ($\geq 20\%$) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), and nausea (21%).
- **In patients with CLL/SLL receiving monotherapy**, the most frequent serious adverse reactions ($\geq 5\%$) were pneumonia (9%), febrile neutropenia (5%), and sepsis (5%). The most common adverse reactions ($\geq 20\%$) of any grade were neutropenia (50%), diarrhea (43%), nausea (42%), upper respiratory tract infection (36%), anemia (33%), fatigue (32%), thrombocytopenia (29%), musculoskeletal pain (29%), edema (22%), and cough (22%).

Drug Interactions

- Concomitant use with a P-gp inhibitor or a strong or moderate CYP3A inhibitor increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including the risk of TLS. Adjust VENCLEXTA dosage and closely monitor patients for signs of VENCLEXTA toxicities. Resume the VENCLEXTA dosage that was used prior to concomitant use of a P-gp inhibitor or a strong or moderate CYP3A inhibitor 2 to 3 days after discontinuation of the inhibitor.

- Patients should avoid grapefruit products, Seville oranges, and starfruit during treatment as they contain inhibitors of CYP3A.
- Avoid concomitant use of strong or moderate CYP3A inducers.
- Avoid concomitant use of VENCLEXTA with a P-gp substrate. If concomitant use is unavoidable, separate dosing of the P-gp substrate at least 6 hours before VENCLEXTA.
- Monitor international normalized ratio (INR) closely in patients receiving warfarin.

Lactation

- Advise nursing women to discontinue breastfeeding during treatment with VENCLEXTA.

Females and Males of Reproductive Potential

- Advise females of reproductive potential to use effective contraception during treatment with VENCLEXTA and for at least 30 days after the last dose.
- Based on findings in animals, male fertility may be compromised by treatment with VENCLEXTA.

Hepatic Impairment

- Reduce the dose of VENCLEXTA for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more closely for signs of toxicity. No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.



IMPORTANT INFORMATION



Providing product-related support for patients taking VENCLEXTA

Dedicated VENCLEXTA® support from VENCOMPASS Nurses*

(844) 9-COMPASS/(844) 926-6727 | www.VENCLEXTA.com

*This program is intended to support your patients taking VENCLEXTA for an approved use during the ramp-up phase and throughout their therapy. VENCOMPASS is not intended to replace your medical advice. All information to be provided will be based on full Prescribing Information and Medication Guide.

VENCLEXTA Access Solutions

Your Resource for Access and Reimbursement Support

(888) 249-4918 | www.Genentech-Access.com/VENCLEXTA

Oncology® Co-pay Card

Genentech co-pay programs provide financial assistance to eligible commercially insured patients to help with their co-pays, co-insurance or other out-of-pocket (OOP) costs.

(855) MY-COPAY/(855) 692-6729 CopolyAssistanceNow.com/VENCLEXTA

Contact your AbbVie or Genentech representative
to learn more about VENCLEXTA or ask questions about treatment initiation

Please see Important Safety Information on pages 18 and 19.

Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

References: 1. VENCLEXTA Prescribing Information. 2. Data on file, AbbVie Inc. ABVVRTI69608. 3. Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med.* 2019;380(23):2225-2236. doi:10.1056/NEJMoa1815281 4. GAZYVA Prescribing Information, March 2020. 5. Seymour JF, Kipps TJ, Eichhorst B, et al. Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med.* 2018;378(12):1107-1120. doi:10.1056/NEJMoa1713976. 6. Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med.* 2019;380(23):2225-2236 doi:10.1056/NEJMoa1815281

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