Indication: VENCLEXTA is indicated in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

DOSING AND ADMINISTRATION GUIDE

1L AML Treatment[1]

#1 PRESCRIBED THERAPY FOR NEWLY DIAGNOSED AML PATIENTS INELIGIBLE FOR INTENSIVE CHEMO[2]*

*Based on rolling 3-month IQVIA LAAD claims data for newly diagnosed, intensive chemo-ineligible AML patients, identified through their use of a low-intensity regimen (analysis period April 2021-March 2024).

NCCN RECOMMENDED

National Comprehensive Cancer Network® (NCCN®) recommends venetoclax (VENCLEXTA®) plus azacitidine for AML patients[3†]

For patients ≥18 years of age who are not candidates for intensive induction chemotherapy in first-line AML regardless of mutation status:

VEN+AZA | NCCN CATEGORY 1 PREFERRED

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Principles of Venetoclax Use with HMA or LDAC include:

- Bone marrow assessment recommended for response assessment on Days 21-28 of Cycle 1
- Patients in remission may require 7- to 14-day breaks to allow for hematologic recovery

†See NCCN Guidelines for AML, Version 3.2024, for complete recommendations and principles. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

1L=first line; VEN+AZA=venetoclax + azacitidine; HMA=hypomethylating agent; LDAC=low-dose cytarabine.

Select Important Safety Information

- Tumor lysis syndrome (TLS), including fatal events and renal failure requiring dialysis, has occurred in patients treated with VENCLEXTA. The risk of TLS is a continuum based on multiple factors, particularly reduced renal function, tumor burden, and type of malignancy. Assess all patients for risk, including evaluation of tumor burden and comorbidities, and provide prophylaxis for TLS, including hydration and anti-hyperuricemics. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases. Interrupt dosing if needed; when restarting VENCLEXTA follow dose modification guidance in the Prescribing Information.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during ramp-up phase, and requires VENCLEXTA dose reduction.
- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor blood counts and for signs of infection; manage as medically appropriate.
- Baseline neutrophil counts worsened in 95% to 100% of patients treated with VENCLEXTA in combination with azacitidine or decitabine or low-dose cytarabine. Neutropenia can recur with subsequent cycles.
- Fatal and serious infections such as pneumonia and sepsis have occurred in patients with VENCLEXTA. Monitor patients for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and 4 infection until resolution.
- 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 use effective contraception during treatment and for 30 days after the last dose.

See more on 1L AML assessment & management

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

USING THIS GUIDE

This guide provides PI-based direction for initiation, assessment, and management for select VENCLEXTA regimens, including safety, dosing, dose adjustments, and management of select cytopenias

Initiation[1]

- Evaluate TLS risk in all patients and provide prophylactic measures
- 3-day dose ramp-up for VEN+HMA or 4-day dose ramp-up for VEN+LDAC. Monitor blood chemistries
- Dose-reduce for concomitant use with P-gp inhibitors or strong or moderate CYP3A inhibitors or for severe hepatic impairment

Assessment[1]

- Assess and monitor for common and serious adverse reactions (ARs)
- Bone marrow assessment as clinically indicated
  - In AML clinical trials, bone marrow assessment was conducted following Cycle 1 treatment to assess for remission

Management[1]

- Manage hematologic ARs with dose modifications based on remission status*
  - May include VENCLEXTA pause or change in VENCLEXTA duration
- Manage non-hematologic ARs with dose modifications*

*See Table 6 in the full Prescribing Information for dose modifications.

This content is not a substitute for independent medical judgment.

PI=Prescribing Information; TLS=tumor lysis syndrome; P-gp=P-glycoprotein; CYP3A=cytochrome P450 3A.

NCCN RECOMMENDED

Consistent with the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Principles of Venetoclax Use with HMA or LDAC[3†]

†See NCCN Guidelines for AML, Version 3.2024, for complete principles. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Important Safety Information

Tumor Lysis Syndrome

- Tumor lysis syndrome (TLS), including fatal events and renal failure requiring dialysis, has occurred in patients treated with VENCLEXTA.
- VENCLEXTA can cause rapid reduction in tumor and thus poses a risk for TLS at initiation and during the ramp-up phase in all patients. 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.
- In patients with AML who followed the current 3-day ramp-up dosing schedule and the TLS prophylaxis and monitoring measures, the rate of TLS was 1.1% in patients who received VENCLEXTA in combination with azacitidine. In patients with AML who followed a 4-day ramp-up dosing schedule and the TLS prophylaxis and monitoring measures, the rate of TLS was 5.6% and included deaths and renal failure in patients who received VENCLEXTA in combination with low-dose cytarabine.
- The risk of TLS is a continuum based on multiple factors, particularly reduced renal function, tumor burden, and type of malignancy.
- Assess all patients for risk and provide appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases. Interrupt dosing if needed; when restarting VENCLEXTA follow dose modification guidance in the Prescribing Information.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during the ramp-up phase, and requires VENCLEXTA dose reduction.

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

VIALE-A studied newly diagnosed AML patients who were ≥75 years of age or had comorbidities that precluded the use of intensive induction chemotherapy[1]

VIALE-A

A randomized (2:1), double-blind, placebo-controlled, multicenter, phase 3 study that evaluated the efficacy and safety of VENCLEXTA in combination with azacitidine (VEN+AZA; N=286) vs placebo with azacitidine (PBO+AZA; N=145) in adults with newly diagnosed AML who were ≥75 years of age, or had comorbidities (based on at least one of the following criteria: baseline ECOG performance status of 2–3, severe cardiac or pulmonary comorbidity, moderate hepatic impairment, CrCl <45 mL/min, or other comorbidity) that precluded the use of intensive induction chemotherapy. Patients received VENCLEXTA 400 mg orally once daily on Days 1-28 following completion of the ramp-up dosing schedule or placebo in combination with azacitidine 75 mg/m^2 on Days 1-7 of each 28-day cycle beginning on Cycle 1, Day 1 until disease progression or unacceptable toxicity. The primary endpoint was overall survival.

Select clinical endpoints[1,4]

Primary endpoint:

OS
OVERALL SURVIVAL

Select secondary endpoints:

- CR
- CR+CRh
- CR+CRh by initiation of Cycle 2

Efficacy was based on OS, measured from the date of randomization to death from any cause[1]

Overall survival, median number of months and (95% CI): 14.7 (11.9, 18.7) for VEN+AZA vs 9.6 (7.4, 12.7) for AZA; HR=0.66 (0.52, 0.85); *P*<0.001

Response rates:

- **CR (95% CI):** 37% (31, 43) for VEN+AZA vs 18% (12, 25) for AZA; *P*<0.001
- **CR+CRh (95% CI):** 65% (59, 70) for VEN+AZA vs 23% (16, 30) for AZA; *P*<0.001

CR was defined as absolute neutrophil count (ANC) >1,000/microliter, platelets >100,000/microliter, RBC transfusion independence, and bone marrow with <5% blasts. Absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease. CRh was defined as <5% of blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/microliter and ANC >500/microliter).

Additional studies

VIALE-C phase 3 trial: VEN+LDAC vs LDAC[1]

The efficacy and safety of VENCLEXTA in combination with low-dose cytarabine (VEN+LDAC; N=143) versus placebo with low-dose cytarabine (PBO+LDAC; N=68) was evaluated in VIALE-C, a double-blind randomized trial in patients with newly diagnosed AML. **In the VIALE-C trial, VEN+LDAC did not significantly improve OS versus placebo plus LDAC**.

M14-358 phase 1b trial: VEN+AZA or VEN+DEC[1]

VENCLEXTA was studied in a non-randomized, open-label trial that evaluated the efficacy of VENCLEXTA in combination with AZA (N=84) or DEC (N=31) in patients with newly diagnosed AML. Overall survival benefit was not evaluated for VENCLEXTA in combination with decitabine.

PBO=placebo; ECOG=Eastern Cooperative Oncology Group; CrCl=creatinine clearance; CR=complete remission; CRh=complete remission with partial hematologic recovery; CI=confidence interval; HR=hazard ratio; RBC=red blood cell.

Important Safety Information (cont'd)

Neutropenia

- In patients with AML, baseline neutrophil counts worsened in 95% to 100% of patients treated with VENCLEXTA in combination with azacitidine or decitabine or low-dose cytarabine. Neutropenia can recur with subsequent cycles.
- Monitor complete blood counts. Interrupt dosing for severe neutropenia. Resume at same dose then reduce duration based on remission status and first or subsequent occurrence of neutropenia. Consider supportive measures including antimicrobials and 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 for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and 4 infection until resolution and resume at same dose.

VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

VENCLEXTA IS FDA-APPROVED REGARDLESS OF MUTATION STATUS

Complete the guidance checklist for tumor lysis syndrome (TLS)[1]

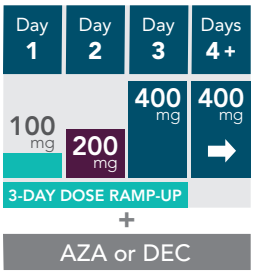
Assess patient-specific factors for level of risk of TLS and provide prophylactic hydration and anti-hyperuricemics to patients prior to first dose of VENCLEXTA and continue during ramp-up to reduce risk of TLS:

- ☐ **Confirm** that the patient's white blood cell count is **less than 25 × 10^9/L.** Cytoreduction prior to treatment may be required.
- ☐ **Provide appropriate prophylactic measures** including adequate hydration and anti-hyperuricemic agents prior to first VENCLEXTA dose, and continue during ramp-up phase.
- ☐ **Assess blood chemistry** (potassium, uric acid, phosphorus, calcium, and creatinine) and correct pre-existing abnormalities prior to initiation of treatment with VENCLEXTA.
- ☐ **Monitor blood chemistries** for TLS at pre-dose, 6 to 8 hours after each new dose during ramp-up, and 24 hours after reaching final dose.
- ☐ **For patients with risk factors** for TLS (eg, circulating blasts, high burden of leukemia involvement in bone marrow, elevated pretreatment LDH levels, or reduced renal function), consider additional measures, including increased laboratory monitoring and reducing VENCLEXTA starting dose.

Initiate AML dosing with a 3- or 4-day dose ramp-up for VEN regimens[1]

VENCLEXTA is taken orally once daily in combination with AZA, DEC, or LDAC

- Continue treatment until disease progression or unacceptable toxicity



- If dosing **in combination with azacitidine**, administer azacitidine at 75 mg/m^2, IV or subcutaneously, once daily on Days 1–7 of each 28-day cycle beginning on Cycle 1, Day 1
- If dosing **in combination with decitabine**, administer decitabine at 20 mg/m^2, IV, once daily on Days 1–5 of each 28-day cycle beginning on Cycle 1, Day 1

- If dosing **in combination with low-dose cytarabine**, follow the 4-day dose ramp-up schedule, for VENCLEXTA (Day 1: 100 mg, Day 2: 200 mg, Day 3: 400 mg, Day 4+: 600 mg) and administer low-dose cytarabine at 20 mg/m^2 subcutaneously once daily on Days 1-10 of each 28-day cycle beginning on Cycle 1, Day 1

LDH=lactate dehydrogenase; IV=intravenous.

Important Safety Information (cont'd)

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 use effective contraception during treatment with VENCLEXTA and for 30 days after the last dose.

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

Reduce the VENCLEXTA dose for drug-drug interactions and hepatic impairment[1]

Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including risk of TLS. See below for dose modifications based on drug-drug interactions.

Dose modifications with select inhibitors

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

	Initiation and ramp-up phase				Steady daily dose (after ramp-up phase)
	Day 1	Day 2	Day 3	Day 4	
Posaconazole	10 mg	20 mg	50 mg	70 mg	Reduce VENCLEXTA dose to 70 mg
Other strong CYP3A inhibitor*	10 mg	20 mg	50 mg	100 mg	Reduce VENCLEXTA dose to 100 mg

For moderate CYP3A† and P-gp inhibitors,‡ reduce the VENCLEXTA dose by at least 50%.

*Ceritinib, clarithromycin, cobicistat, elvitegravir, idelalisib, itraconazole, ketoconazole, lopinavir, nefazodone, ritonavir.[5§]
†Aprepitant, ciprofloxacin, conivaptan, crizotinib, diltiazem, dronedarone, erythromycin, fluconazole, imatinib.[5§]
‡Amiodarone, cyclosporine, dronedarone, quinidine, ranolazine, verapamil.[5§]
§This is not an exhaustive list and is intended only to complement, not replace, clinical judgment during treatment of patients with VENCLEXTA. Please refer to the FDA website for more examples.

Ensure additional measures for other potential drug interactions[1]

- ☐ **Reduce the VENCLEXTA dose** and monitor more frequently for adverse reactions.
- ☐ **Avoid grapefruit products, Seville oranges, and starfruit** during treatment with VENCLEXTA, as they contain inhibitors of CYP3A.
- ☐ **Avoid concomitant use of VENCLEXTA with strong CYP3A inducers or moderate CYP3A inducers.** Concomitant use of VENCLEXTA with strong CYP3A inducers decreases VENCLEXTA exposure, which may decrease VENCLEXTA efficacy.
- ☐ **Monitor international normalized ratio (INR) more frequently in patients using warfarin** concomitantly with VENCLEXTA. Concomitant use of VENCLEXTA increases warfarin exposure, which may increase the risk of bleeding.
- ☐ **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. Concomitant use of VENCLEXTA increases exposure of P-gp substrates, which may increase toxicities of these substrates.

Dose modifications for patients with severe hepatic impairment[1]

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

Important Safety Information (cont'd)

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.

VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

A tolerable, manageable, and predictable safety profile[1]

No additional warnings or precautions for VENCLEXTA were observed in the AML trials.

The safety profile of VEN+AZA was consistent with the known side effect profile of both agents.

Adverse reactions (≥10%) in patients with AML who received VEN+AZA with a difference between arms of ≥5% for all grades or ≥2% for Grade 3 or 4 reactions compared with PBO+AZA*

Adverse reaction by body system					
		VEN+AZA (N=283)		PBO+AZA (N=144)	
Body system	**Adverse reaction**	**All Grades (%)**	**Grade 3 or 4 (%)**	**All Grades (%)**	**Grade 3 or 4 (%)**
Gastrointestinal disorders	Nausea	44	2	35	<1
	Diarrhea†	43	5	33	3
	Vomiting†	30	2	23	<1
	Stomatitis†	18	1	13	0
	Abdominal pain†	18	<1	13	0
Blood and lymphatic system disorders	Febrile neutropenia	42	42	19	19
Musculoskeletal and connective tissue disorders	Musculoskeletal pain†	36	2	28	1
General disorders and administration site conditions	Fatigue†	31	6	23	2
	Edema†	27	<1	19	0
Vascular disorders	Hemorrhage†	27	7	24	3
	Hypotension†	12	5	8	3
Metabolism and nutrition disorders	Decreased appetite†	25	4	17	<1
Skin and subcutaneous tissue disorders	Rash†	25	1	15	0
Infections and infestations	Sepsis† (excluding fungal)	22	22	16	14
	Urinary tract infection†	16	6	9	6
Respiratory, thoracic and mediastinal disorders	Dyspnea†	18	4	10	2
Nervous system disorders	Dizziness†	17	<1	8	<1

*Patients who received at least one dose of either treatment.
†Includes multiple adverse reaction terms.

Hematologic laboratory abnormalities

New or worsening Grade 3 or 4 hematologic laboratory abnormalities (≥10%) in VIALE-A with a difference between arms of ≥2% for VEN+AZA vs PBO+AZA, respectively: neutrophils decreased 98% vs 81%, platelets decreased 88% vs 80%, lymphocytes decreased 71% vs 39%, hemoglobin decreased 57% vs 52%.

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

Duration of exposure and serious adverse reactions[1,4,6]

Patients maintained treatment with VEN in the VEN+AZA arm for a median of 7.6 months[1]

Median duration of exposure to VEN or PBO

VEN+AZA[1]	PBO+AZA[6]
7.6	**4.3**
months (range: <0.1-30.7)	**months** (range: 0.1-24.0)

Median number of cycles

VEN+AZA[4]	PBO+AZA[4]
7.0	**4.5**
cycles (range: 1.0-30.0)	**cycles** (range: 1.0-26.0)

Rate of serious adverse reactions				
	VEN+AZA (N=283)[1]		PBO+AZA (N=144)[4,6]	
	(%) occurrence	Most frequent adverse reaction(s)	(%) occurrence	Most frequent adverse reaction(s)
Serious ARs	83	≥5%: febrile neutropenia (30%), pneumonia (22%), sepsis (excluding fungal; 19%), hemorrhage (6%)	73	≥5%: pneumonia (22%), febrile neutropenia (10%), sepsis (8%)
Fatal ARs	23	≥2%: pneumonia (4%), sepsis (excluding fungal; 3%), hemorrhage (2%)	20	≥2%: sepsis (4%), pneumonia (2%)

Discontinuation, reduction, and interruption rates of VEN or PBO[1,6]				
	VEN	VEN+AZA	PBO	PBO+AZA
	(%) occurrence	Most frequent adverse reaction(s)	(%) occurrence	Most frequent adverse reaction(s)
ARs leading to permanent drug discontinuation	24	≥2%: sepsis (excluding fungal; 3%), pneumonia (2%)	20	≥2%: sepsis (4%), pneumonia (3%), thrombocytopenia (2%), malignant neoplasm progression (2%)
ARs leading to dose reductions	3	pneumonia (0.7%)	4	pneumonia (1%)
ARs leading to dose interruptions	72	≥5%: febrile neutropenia (20%), neutropenia (20%), pneumonia (14%), sepsis (excluding fungal; 11%), thrombocytopenia (10%)	57	≥5%: pneumonia (13%), neutropenia (10%)

- In the VEN+AZA arm, among patients who achieved bone marrow clearance of leukemia, 53% (114/216)* underwent dose interruptions for ANC <500/microliter[1,7]
- Once bone marrow assessment confirmed a remission, defined as less than 5% leukemia blasts with cytopenia, VENCLEXTA or placebo was interrupted up to 14 days or until ANC ≥500/microliter and platelet count ≥50,000/microliter[1]
- Azacitidine was resumed on the same day as VENCLEXTA or placebo following interruption[1]
- Azacitidine dose reduction was implemented in the clinical trial for management of hematologic toxicity[1]

*Of patients who achieved a morphologic leukemia-free state of response or better.[7]

AR=adverse reaction.

VENCLEXTA® venetoclax tablets 10mg, 50mg, 100mg

Responses for CR and CRh were reached at different times throughout treatment; management of Grade 4 neutropenia or thrombocytopenia differs before and after remission is achieved[1]

In AML clinical trials, bone marrow assessment was conducted following Cycle 1 treatment. Once bone marrow assessment confirmed a remission,* VENCLEXTA or placebo was interrupted up to 14 days or until ANC ≥500/microliter and platelet count ≥50,000/microliter.

For patients with resistant disease at the end of Cycle 1, a bone marrow assessment was performed after Cycle 2 or 3 and as clinically indicated.[1]

*Defined as less than 5% leukemia blasts with cytopenia.[1]

See page 3 of this guide for select secondary endpoint results (CR and CR+CRh).

In VIALE-A, median time to first response of CR or CRh was 1.0 months (range: 0.6-14.3 months) with VEN+AZA treatment; some patients achieved CR or CRh in later cycles[1]

Secondary endpoint: CR+CRh by initiation of Cycle 2[4,8]

- **40%** (n=114/286) with VEN+AZA (95% CI: [34, 46]; *P*<0.001)

In an exploratory post hoc analysis of CR+CRh in the VEN+AZA ITT population[8]

- **47%** (134/286) achieved CR+CRh by the beginning of Cycle 3
- **50%** (143/286) achieved CR+CRh by the beginning of Cycle 4

ITT=intention to treat.

When treating AML with VENCLEXTA regimens, monitor blood counts frequently through resolution of cytopenias. Dose modification and interruptions for cytopenias are dependent on remission status.[1]

- See facing page for information to help manage patients who experience cytopenias and non-hematologic toxicities

Important Safety Information (cont'd)

Adverse Reactions

- **In patients with AML receiving combination therapy with azacitidine,** the most frequent serious adverse reactions (≥5%) were febrile neutropenia (30%), pneumonia (22%), sepsis (excluding fungal; 19%), and hemorrhage (6%). The most common adverse reactions including hematological abnormalities (≥30%) of any grade were neutrophils decreased (98%), platelets decreased (94%), lymphocytes decreased (91%), hemoglobin decreased (61%), nausea (44%), diarrhea (43%), febrile neutropenia (42%), musculoskeletal pain (36%), pneumonia (33%), fatigue (31%), and vomiting (30%). Fatal adverse reactions occurred in 23% of patients who received VENCLEXTA in combination with azacitidine, with the most frequent (≥2%) being pneumonia (4%), sepsis (excluding fungal; 3%), and hemorrhage (2%).
- **In patients with AML receiving combination therapy with decitabine,** the most frequent serious adverse reactions (≥10%) were sepsis (excluding fungal; 46%), febrile neutropenia (38%), and pneumonia (31%). The most common adverse reactions including hematological abnormalities (≥30%) of any grade were neutrophils decreased (100%), lymphocytes decreased (100%), white blood cells decreased (100%), platelets decreased (92%), hemoglobin decreased (69%), febrile neutropenia (69%), fatigue (62%), constipation (62%), musculoskeletal pain (54%), dizziness (54%), nausea (54%), abdominal pain (46%), diarrhea (46%), pneumonia (46%), sepsis (excluding fungal; 46%), cough (38%), pyrexia (31%), hypotension (31%), oropharyngeal pain (31%), edema (31%), and vomiting (31%). One (8%) fatal adverse reaction of bacteremia occurred within 30 days of starting treatment.
- **In patients with AML receiving combination therapy with low-dose cytarabine,** the most frequent serious adverse reactions (≥10%) were pneumonia (17%), febrile neutropenia (16%), and sepsis (excluding fungal; 12%). The most common adverse reactions including hematological abnormalities (≥30%) of any grade were platelets decreased (97%), neutrophils decreased (95%), lymphocytes decreased (92%), hemoglobin decreased (63%), nausea (42%), and febrile neutropenia (32%). Fatal adverse reactions occurred in 23% of patients who received VENCLEXTA in combination with LDAC, with the most frequent (≥5%) being pneumonia (6%) and sepsis (excluding fungal; 7%).

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

Recommended dose modifications for cytopenias and non-hematologic adverse reactions in AML[1]

Managing Grade 4 neutropenia with or without fever or infection, or Grade 4 thrombocytopenia

Is the patient in remission?*†

NO

▶ **STAY ON VENCLEXTA REGIMEN:** In most instances, do not interrupt the VENCLEXTA regimen due to cytopenias prior to achieving remission

YES

❚❚ **DELAY SUBSEQUENT** cycle of VENCLEXTA regimen and monitor blood counts

For 1st occurrence (lasting at least 7 days)

▶ **RESUME VENCLEXTA** therapy at 400 mg‡ in combination with azacitidine or decitabine or at 600 mg‡ in combination with low-dose cytarabine upon resolution to Grade 1 or 2 and resume 28-day treatment cycle

For subsequent occurrences (lasting at least 7 days)

▶ **RESUME VENCLEXTA** therapy at 400 mg‡ in combination with azacitidine or decitabine or at 600 mg‡ in combination with low-dose cytarabine upon resolution to Grade 1 or 2

▼ **REDUCE TREATMENT CYCLE** by 7 days for each subsequent cycle *(eg, for 2nd occurrence, VENCLEXTA would be dosed for 21 days of a 28-day cycle)*

In an exploratory post hoc analysis of VIALE-A[8]

- 75% of patients in remission† (139/186) had at least 1 pause in dosing lasting ≥7 days

For any occurrence of Grade 3 or 4 non-hematologic toxicities

❚❚ **INTERRUPT VENCLEXTA** if not resolved with supportive care

▶ **RESUME VENCLEXTA** at the same dose upon resolution to Grade 1 or baseline level

*Recommend bone marrow evaluation.
†Defined as less than 5% leukemia blasts with cytopenia.[1]
‡Dose may vary based on drug-drug interactions or severe hepatic impairment.

VENCLEXTA® venetoclax tablets 10mg, 50mg, 100mg

Advise patients[1]:

Of the risks and review the Medication Guide with patients before they start VENCLEXTA

Of the potential risk of TLS, particularly at treatment initiation, during the ramp-up phase, and with resumption after an interruption and to immediately report any signs and symptoms associated with this event (fever, chills, nausea, vomiting, confusion, shortness of breath, seizure, irregular heartbeat, dark or cloudy urine, unusual tiredness, muscle pain, and/or joint discomfort) to their health care provider (HCP) for evaluation

Let patients know that they can expect their HCP to:
- Do tests to check their risk of getting TLS before they start taking VENCLEXTA
- Do blood tests to check for TLS when they first start treatment and during treatment with VENCLEXTA
- Delay or decrease their dose, or stop treatment with VENCLEXTA if they have side effects

To be adequately hydrated every day when taking VENCLEXTA to reduce the risk of TLS. The recommended volume is 6 to 8 glasses (approximately 56 ounces total) of water each day. Patients should drink water starting 2 days before and on the day of the first dose, and every time the dose is increased

To take VENCLEXTA orally once daily with a meal and water at approximately the same time each day

To swallow tablets whole, and to not chew, crush, or break the tablets. To tell their HCP if they struggle to swallow 100-mg VENCLEXTA tablets. Their HCP should deliver the recommended VENCLEXTA dosage using the appropriate strength (eg, patients can take two 50-mg tablets or ten 10-mg tablets instead of one 100-mg tablet as needed)

To keep VENCLEXTA in its original container to protect from moisture. VENCLEXTA should be stored at or below 86°F (30°C)

Of the importance of keeping scheduled appointments for blood work or other laboratory tests

To contact their HCP immediately if they develop a fever or any signs of infection. Advise patients of the need for periodic monitoring of blood counts and that dosing may be paused

To take VENCLEXTA exactly as prescribed and not to change their dose or stop taking VENCLEXTA unless they are told to do so by their doctor

Please see additional Important Safety Information throughout.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

Missed dose[1]

If a patient misses a dose by <u>less than 8 hours</u> from the time it is usually taken

The patient should take the missed dose right away and take the next dose as usual.

If a patient misses a dose by <u>more than 8 hours</u>

The patient should not take the missed dose and should take the next dose at the usual time.

If a <u>patient vomits</u> following dosing

No additional dose should be taken that day. The next prescribed dose should be taken at the usual time the next day.

Important Safety Information (cont'd)

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. Consider alternative medications or adjust VENCLEXTA dosage and monitor more frequently for adverse reactions. 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.
- Monitor international normalized ratio (INR) more frequently in patients receiving warfarin.
- 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.

Lactation

- Advise nursing women not to breastfeed during treatment with VENCLEXTA and for 1 week after the last dose.

Females and Males of Reproductive Potential

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

Hepatic Impairment

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

References: 1. VENCLEXTA [package insert]. North Chicago, IL: AbbVie Inc. **2.** Data on file, Genentech Inc. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed May 17, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med*. 2020;383(7):617-629. **5.** US Food and Drug Administration. For healthcare professionals | FDA's examples of drugs that interact with CYP enzymes and transporter systems. Updated March 8, 2024. Accessed April 17, 2024. https://www.fda.gov/drugs/drug-interactions-labeling/healthcare-professionals-fdas-examples-drugs-interact-cyp-enzymes-and-transporter-systems. **6.** Data on file, ABVRRTI71272. AbbVie Inc. **7.** Data on file, ABVRRTI71500. AbbVie Inc. **8.** Data on file, ABVRRTI71211. AbbVie Inc.

VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

VENCLEXTA PATIENT SUPPORT PROGRAMS

VENCLEXTA Access Solutions

Genentech Access Solutions can help your patients:

- Better understand their coverage
- Find financial assistance options
- Learn how to get the VENCLEXTA they have been prescribed
- Understand which specialty pharmacy their health insurance plan requires
- Enroll in additional support options in the event of a coverage delay

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

The completion and submission of coverage- or reimbursement-related documentation are the responsibility of the patient and healthcare provider. Genentech and AbbVie make no representation or guarantee concerning coverage or reimbursement for any service or item. Genentech provides coverage and reimbursement services to patients to help them understand benefits, coverage, and reimbursement.

The Genentech Oncology Co-pay Assistance Program

The Genentech Oncology Co-pay Assistance Program provides 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
CopayAssistanceNow.com

*Eligibility criteria apply. Not valid for patients using federal or state government programs to pay for their Genentech medicine. Patients must be taking the Genentech medicine for an FDA-approved indication. Please visit the Co-pay Program website for the full list of Terms and Conditions.

Visit **venclextahcp.com/aml** or contact a rep to learn more.

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

abbvie | Genentech
A Member of the Roche Group

VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

US-VENA-240047/June 2024