

UNSILENCE AN EXPRESSIVE INSTRUMENT

TAZVERIK[®] (tazemetostat) demonstrated meaningful and sustained responses for relapsed or refractory (R/R) follicular lymphoma (FL) patients, in both MT and WT *EZH2* populations studied¹

TAZVERIK is indicated for the treatment of:

- Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an *EZH2* mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
- Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).¹

Important Safety Information

TAZVERIK increases the risk of developing secondary malignancies, including T-cell lymphoblastic lymphoma, myelodysplastic syndrome, and acute myeloid leukemia. Monitor patients long-term for the development of secondary malignancies.

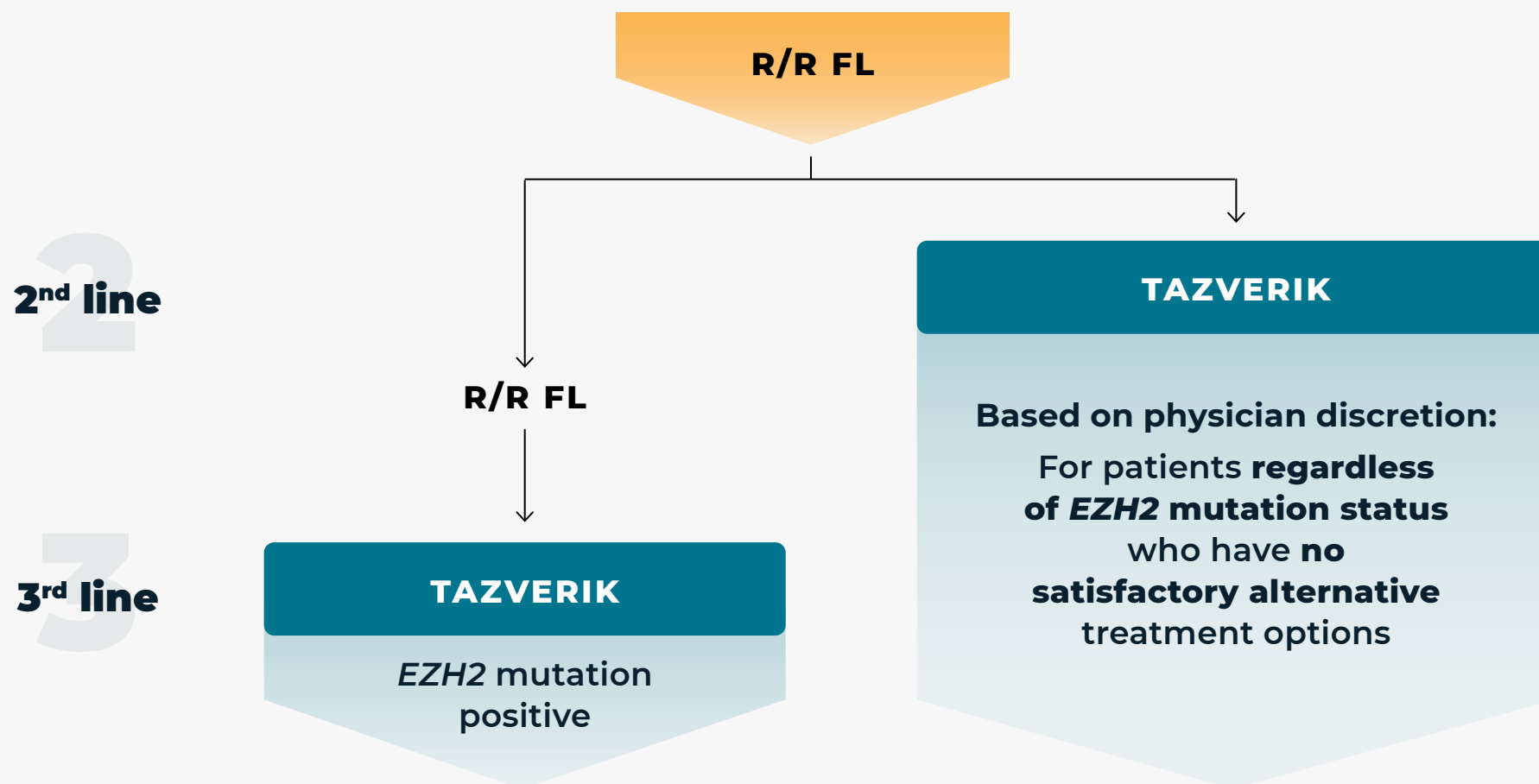
TAZVERIK can cause fetal harm. Advise patients of potential risk to a fetus and to use effective non-hormonal contraception.

The most common (≥20%) adverse reactions are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea, and abdominal pain.

EZH2=enhancer of zeste homologue 2; MT=mutant type; WT=wild type.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

WHEN IS TAZVERIK APPROPRIATE FOR YOUR R/R FL PATIENT?



FL=follicular lymphoma; R/R=relapsed or refractory.

TAZVERIK is indicated for the treatment of:

- Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
- Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).¹

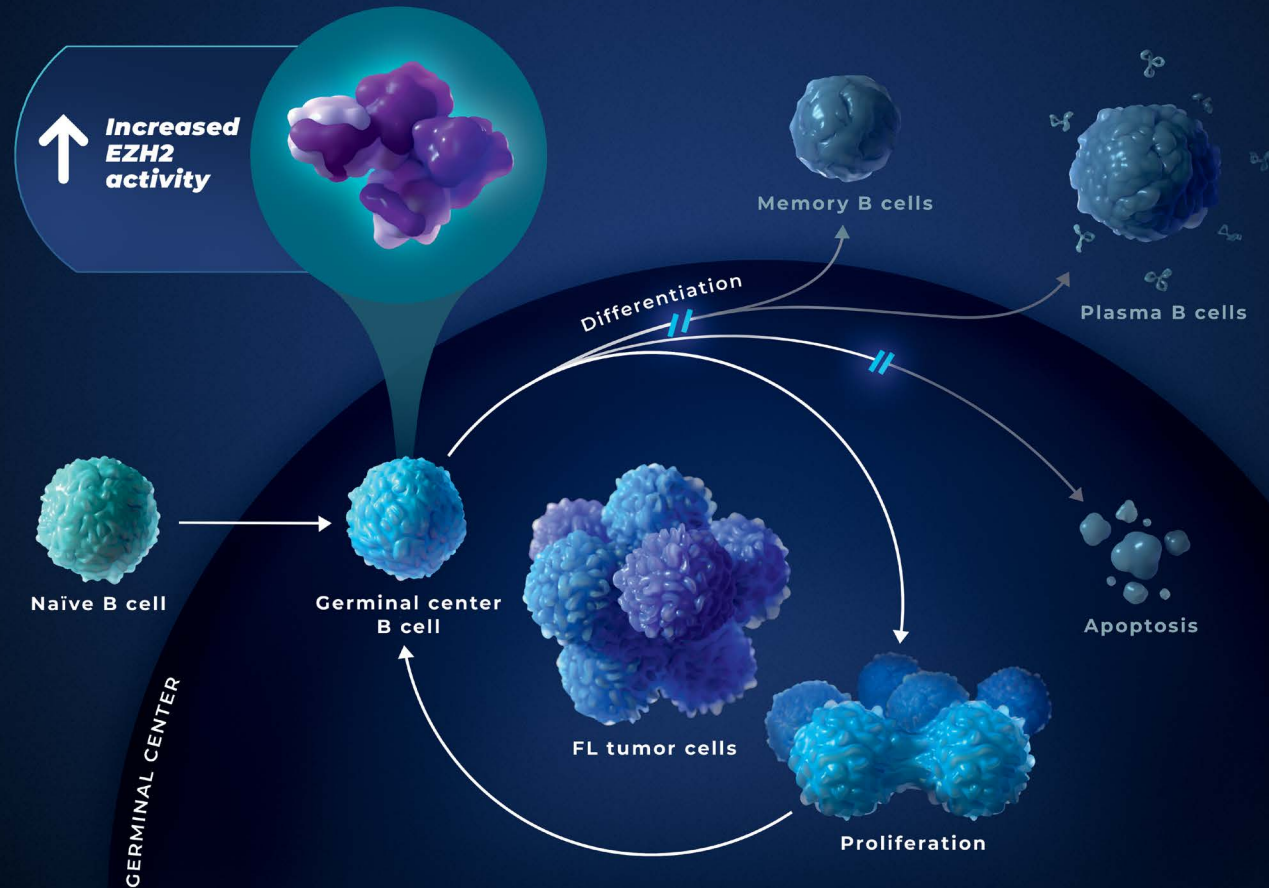
Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

EZH2 PLAYS A CRITICAL ROLE IN NORMAL B-CELL DEVELOPMENT & FOLLICULAR LYMPHOMA²⁻⁷

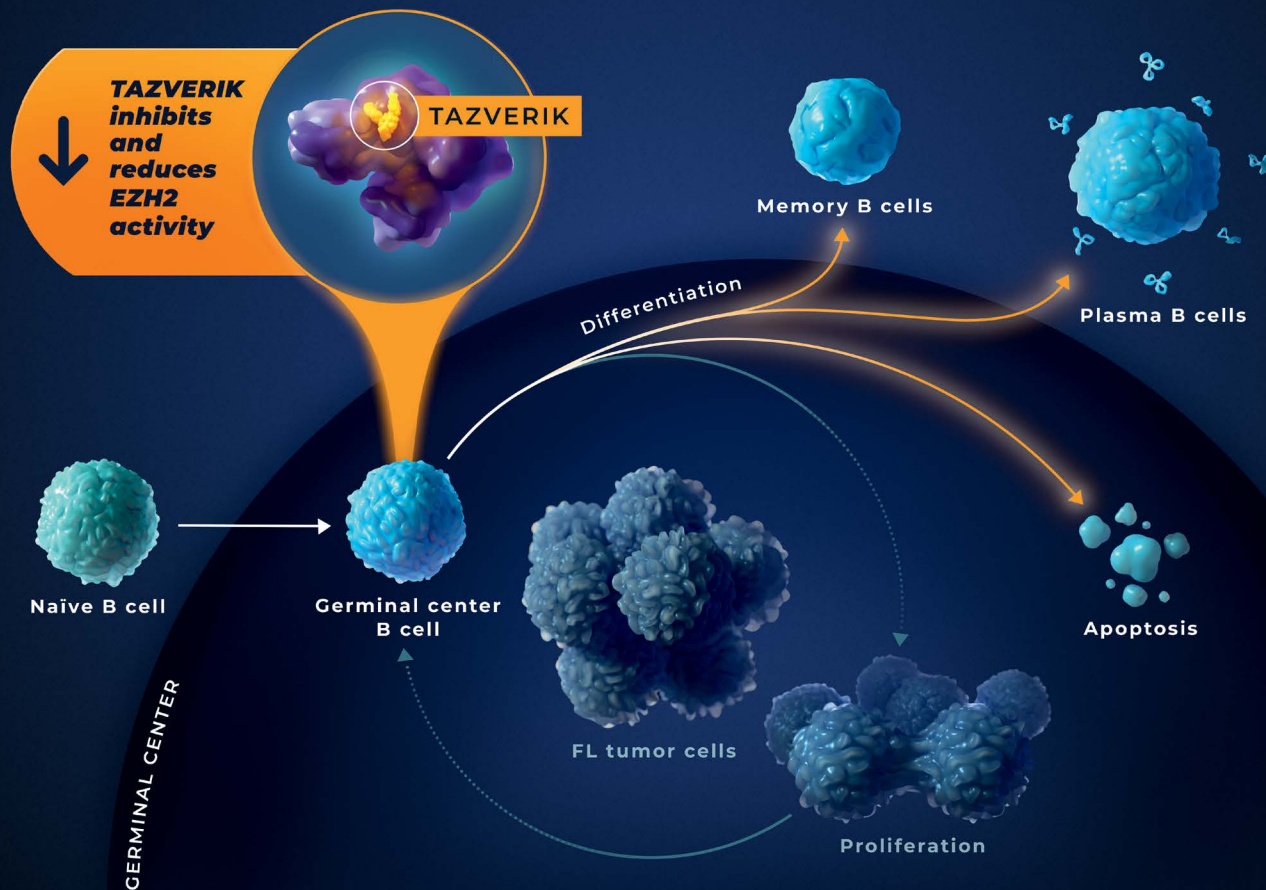
- **EZH2 is an epigenetic regulator of B-cell identity** in the germinal center²

- Through appropriate and timely silencing of genes involved in differentiation, negative cell cycle regulation, and apoptosis, EZH2 allows developing germinal center B cells to proliferate transiently and survive²⁻⁴

- **FL is caused by heterogeneous combinations of oncogenic hits, leading to high EZH2 activity.** This results in B cells locked in a proliferative germinal center state and the accumulation of malignant B cells^{2,3,5,6}



SELECTIVELY INHIBITING BOTH MT AND WT EZH2 MAY RESTORE EXPRESSION OF GENES THAT ALLOW FOR GERMINAL CENTER EXIT^{1,2,5-7}



- **Inhibition of EZH2 activity** may suppress aberrant B-cell proliferation and allow for the expression of genes that lead to B-cell differentiation and germinal center exit^{1,2}

- Regardless of oncogenic mutation, **FL tumors have a critical dependence on EZH2** for growth and survival^{1,2}

MOA=mechanism of action;
MOD=mechanism of disease;
MT=mutant type; WT=wild type.

Important Safety Information (continued)

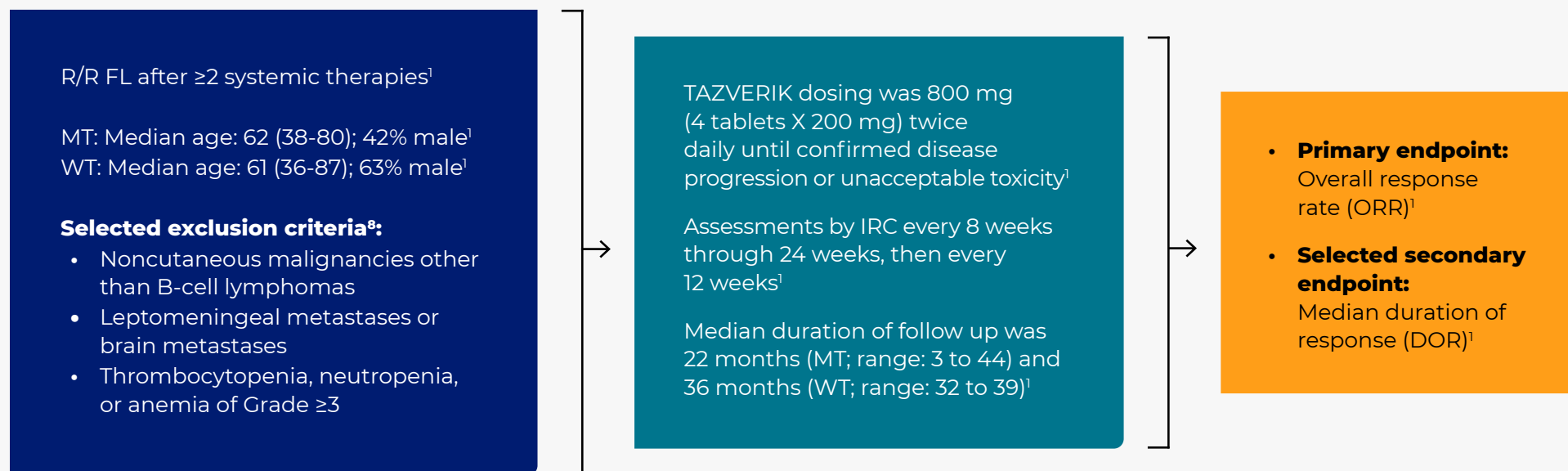
Warnings and Precautions

• Secondary Malignancies

The risk of developing secondary malignancies is increased following treatment with TAZVERIK. Across clinical trials of 729 adults who received TAZVERIK 800 mg twice daily, myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) occurred in 0.7% of patients. One pediatric patient developed T-cell lymphoblastic lymphoma (T-LBL). Monitor patients long-term for the development of secondary malignancies.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

STUDY DESIGN: A SINGLE-ARM, PHASE 2 TRIAL OF RELAPSED OR REFRACTORY FL PATIENTS



IRC=independent review committee.

Important Safety Information (continued)

Warnings and Precautions

• Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, TAZVERIK can cause fetal harm when administered to pregnant women. There are no available data on TAZVERIK use in pregnant women to inform the drug-associated risk. Administration of tazemetostat to pregnant rats and rabbits during organogenesis resulted in dose-dependent increases in skeletal developmental abnormalities in both species beginning at maternal exposures approximately 1.5 times the adult human exposure (area under the plasma concentration time curve [AUC_{0-45h}]) at the 800 mg twice daily dose.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

TAZVERIK® (tazemetostat) WAS STUDIED IN A HEAVILY PRETREATED FL PATIENT POPULATION



TAZVERIK was studied in an open-label, single-arm, multicenter, phase 2 trial with 6 cohorts of patients, including 2 cohorts with histologically-confirmed R/R FL^{1,8}

Enrolled 2 cohorts: EZH2 MT (n=45) and WT (n=54) patients¹

• Patients in the EZH2 MT cohort had the following mutations: Y646X [S,H,C] (36%), Y646F (29%), Y646N (27%), A682G (11%), and A692V (2%)

BASELINE DISEASE CHARACTERISTICS^{1,8}	MT EZH2 (n=45)	WT EZH2 (n=54)
ECOG PS 0 or 1, %	100	91
ECOG PS 2, %*	0	7
POD24, %	42	59
Median time from initial diagnosis, years	4.7	6.3
Median number of lines of prior systemic therapy (range)	2 (1 to 11)	3 (1 to 8)
Refractory to rituximab, %	49	59
Double refractory to rituximab, %†	20	28
Refractory to last therapy, %	49	41
Prior stem cell transplant, %	9	39

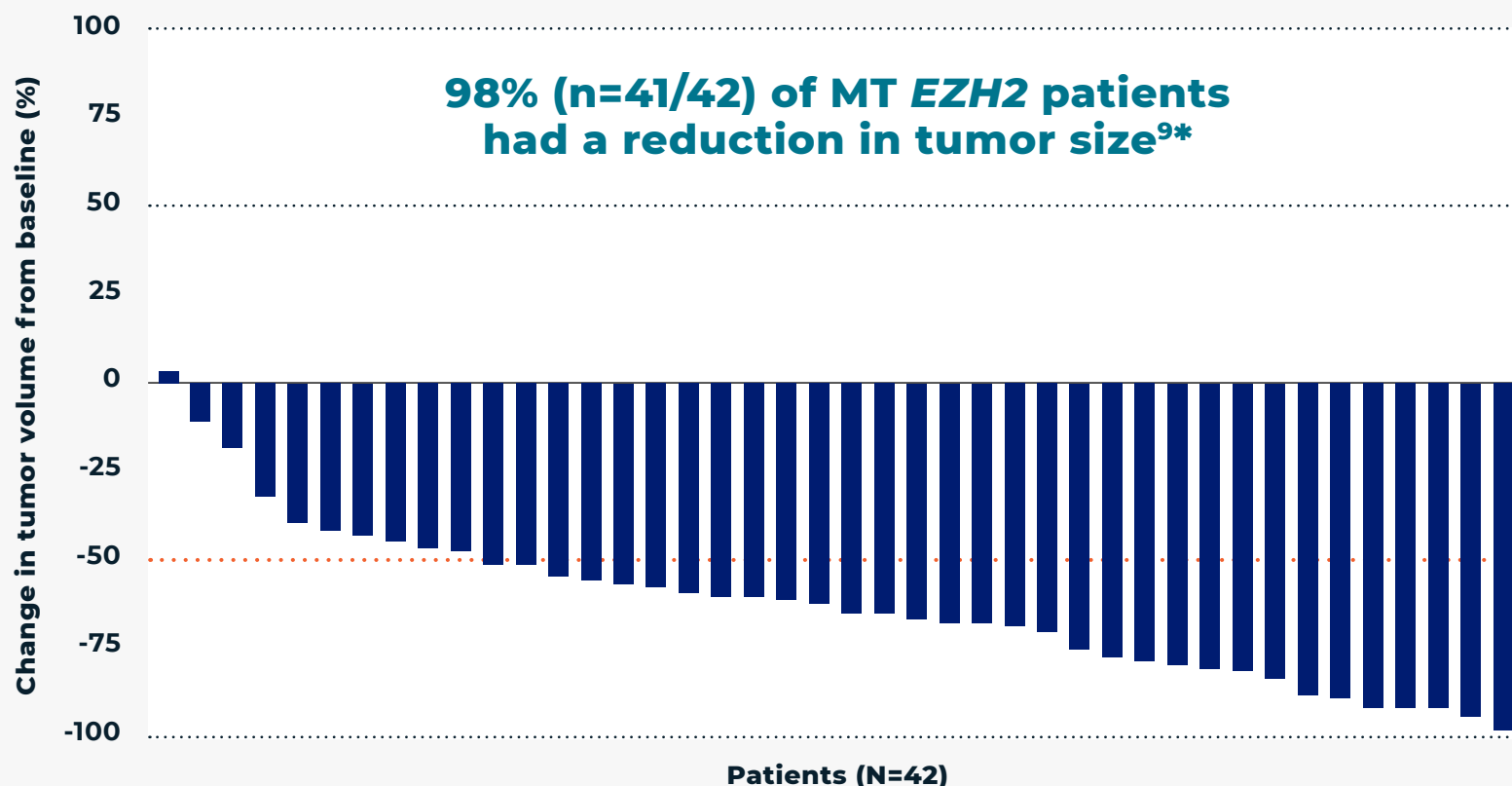
ECOG PS=Eastern Cooperative Oncology Group Performance Status; MT=mutant type; POD24=early progression within 24 months following front-line therapy; WT=wild type.

*ECOG PS was missing for one WT patient.

†And an alkylating agent or purine nucleoside antagonist.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

IN THE STUDY, TAZVERIK DEMONSTRATED EFFICACY REGARDLESS OF EZH2 MUTATION STATUS



**69%
ORR**
(n=29/42; 95%
CI: 53%–82%)^{1,9†}

**10.9
months**
median DOR

(range: 0.0+ to 22.1+)
(n=29/42; 95% CI: 7.2–NE)

The data for this cohort were
not yet mature at the time
of assessment.

The ORR included **12%** (n=5/42) of patients with a **complete response** and **57%** (n=24/42) with a **partial response**.

CI=confidence interval; ORR=overall response rate; DOR=duration of response; NE= not estimable.

*The tumor size was measured based on the maximum reduction in the sum of the products of the perpendicular diameters.

†According to the International Working Group Non-Hodgkin Lymphoma (IWG-NHL) criteria as assessed by independent review committee.

Important Safety Information (continued)

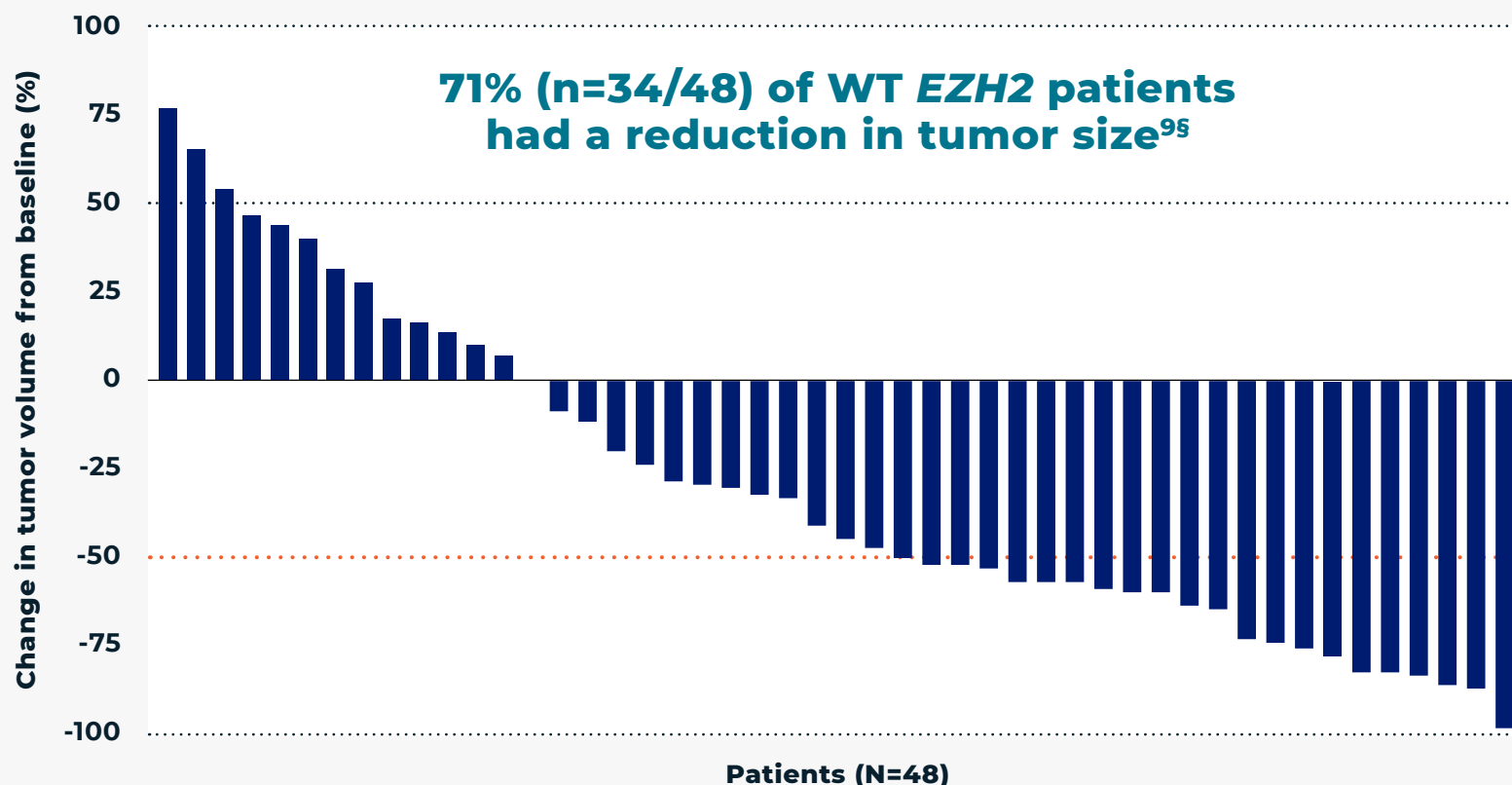
Warnings and Precautions

• Embryo-Fetal Toxicity (continued)

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TAZVERIK and for 6 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with TAZVERIK and for 3 months after the final dose.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

IN THE STUDY, TAZVERIK DEMONSTRATED EFFICACY REGARDLESS OF EZH2 MUTATION STATUS



**34%
ORR**
(n=18/53; 95%
CI: 22%–48%)^{1,9†}

**13.0
months**
median DOR

(range: 1.0 to 22.5+)
(n=18/53; 95% CI: 5.6–NE)

The ORR included **4%** (n=2/53) of patients with a **complete response** and **30%** (n=16/53) with a **partial response**.

†According to the International Working Group Non-Hodgkin Lymphoma (IWG-NHL) criteria as assessed by independent review committee.

§The tumor size was measured based on the maximum reduction in the sum of the products of the perpendicular diameters. Tumor response was unevaluable in 5 out of 53 WT *EZH2* patients in the intent-to-treat population.

Important Safety Information (continued)

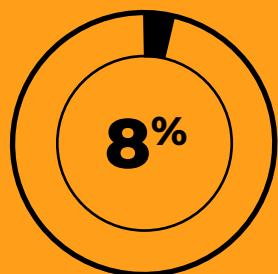
Adverse Reactions

In 99 clinical study patients with relapsed or refractory follicular lymphoma receiving TAZVERIK 800 mg twice daily: Serious adverse reactions occurred in 30% of patients who received TAZVERIK. Serious adverse reactions occurring in $\geq 2\%$ were general physical health deterioration, abdominal pain, pneumonia, sepsis, and anemia. The most common ($\geq 20\%$) adverse reactions were fatigue (36%), upper respiratory tract infection (30%), musculoskeletal pain (22%), nausea (24%), and abdominal pain (20%).

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

MAJORITY OF PATIENTS WERE ABLE TO STAY ON THE FULL DOSE OF TAZVERIK DURING THE TRIAL¹

DISCONTINUATIONS



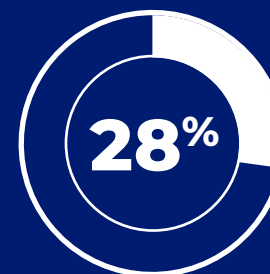
of patients
permanently discontinued
treatment due to
an adverse reaction.
The adverse reaction
resulting in permanent
discontinuation in $\geq 2\%$
of patients was second
primary malignancy.¹

REDUCTIONS



of patients
receiving TAZVERIK
required **dose reductions**
due to an
adverse reaction.¹

INTERRUPTIONS



of patients
receiving TAZVERIK
required **dose interruptions**
due to an adverse reaction.
Adverse reactions requiring
dosage interruptions
in $\geq 3\%$ of patients
were thrombocytopenia
and fatigue.¹

The most common ($\geq 20\%$) adverse reactions were fatigue (36%), upper respiratory tract infection (30%), musculoskeletal pain (22%), nausea (24%), and abdominal pain (20%).¹

30% of patients in the TAZVERIK clinical trial experienced serious adverse reactions. Serious adverse reactions occurring in $\geq 2\%$ of patients taking TAZVERIK included general physical health deterioration, abdominal pain, pneumonia, sepsis, and anemia.¹

TAZVERIK does not have a boxed warning or REMS requirement.

REMS=Risk Evaluation and Mitigation Strategy.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

TAZVERIK WAS GENERALLY WELL-TOLERATED ACROSS CLINICALLY DIVERSE FL PATIENTS (N=99)¹



Adverse reactions (≥10%) in patients with relapsed or refractory FL who received TAZVERIK¹

ADVERSE REACTION	ALL GRADES (%)	GRADE 3 OR 4 (%)
General		
Fatigue ^a	36	5
Pyrexia	10	0
Infections		
Upper respiratory tract infection ^b	30	0
Lower respiratory tract infection ^c	17	0
Urinary tract infection ^d	11	2
Gastrointestinal		
Nausea	24	1
Abdominal pain ^e	20	3
Diarrhea	18	0
Vomiting	12	1
Musculoskeletal and connective tissue		
Musculoskeletal pain ^f	22	1
Skin and subcutaneous tissue		
Alopecia	17	0
Rash ^g	15	0
Respiratory and mediastinal system		
Cough ^h	17	0
Nervous system		
Headache ⁱ	13	0

≤5% of patients experienced grade 3 or 4 adverse reactions.¹

^aIncludes fatigue and asthenia

^bIncludes laryngitis, nasopharyngitis, pharyngitis, rhinitis, sinusitis, upper respiratory tract infection, viral upper respiratory tract infection

^cIncludes bronchitis, lower respiratory tract infection, tracheobronchitis

^dIncludes cystitis, urinary tract infection, urinary tract infection staphylococcal

^eIncludes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper

^fIncludes back pain, limb discomfort, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, myalgia, neck pain, non-cardiac chest pain, pain in extremity, pain in jaw, spinal pain

^gIncludes erythema, rash, rash erythematous, rash generalized, rash maculo-papular, rash pruritic, rash pustular, skin exfoliation

^hIncludes cough and productive cough

ⁱIncludes headache, migraine, sinus headache

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

LABORATORY PARAMETERS WERE MOSTLY MANAGEABLE DURING THE TRIAL¹

Select laboratory abnormalities ($\geq 10\%$) worsening from baseline in patients with R/R FL who received TAZVERIK¹



LABORATORY ABNORMALITY	TAZVERIK*	
	ALL GRADES (%)	GRADE 3 OR 4 (%)
Hematology		
Decreased lymphocytes	57	18
Decreased hemoglobin	50	8
Decreased platelets	50	7
Decreased white blood cells	41	9
Decreased neutrophils	20	7
Chemistry		
Increased glucose	53	10
Increased aspartate aminotransferase	24	0
Increased alanine aminotransferase	21	2.3
Increased alkaline phosphatase	18	1.0
Increased creatinine	17	0

TAZVERIK does not require special supportive care or monitoring.

*The denominator used to calculate the rate varied from 88 to 96 based on the number of patients with a baseline value and at least one post-treatment value.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

TAZVERIK OFFERS ORAL, TWICE-DAILY DOSING

TAZVERIK
(tazemetostat) tablets
200 mg



Recommended dose of 800 mg (4 x 200 mg tablets) taken orally, twice daily, until disease progression or unacceptable toxicity.¹



with or without food

1st dose



Tablets are actual size.

2nd dose



Swallow tablets whole. Do not cut, crush, or chew tablets.

Do not take an additional dose if a dose is missed or vomiting occurs after taking TAZVERIK, but continue with the next scheduled dose.¹

CYP3A=Cytochrome P450 (CYP)3A.

How supplied: 240-count bottle

NDC number (10 digit): 72607-100-00

NDC number (11 digit): 72607-0100-00

NDC=National Drug Code

Important Safety Information (continued)

Drug Interactions

Avoid coadministration of strong or moderate CYP3A inhibitors with TAZVERIK. If coadministration of moderate CYP3A inhibitors cannot be avoided, reduce TAZVERIK dose.

Avoid coadministration of moderate and strong CYP3A inducers with TAZVERIK, which may decrease the efficacy of TAZVERIK.

Coadministration of TAZVERIK with CYP3A substrates, including hormonal contraceptives, can result in decreased concentrations and reduced efficacy of CYP3A substrates.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

GUIDANCE FOR DOSE MODIFICATION AND REDUCTION



Recommended dose reductions of TAZVERIK for adverse reactions¹

DOSE REDUCTION	DOSAGE	DOSE ADJUSTMENTS NOT RECOMMENDED FOR PATIENTS WITH:
First	600 mg twice daily	mild to severe renal impairment, including end-stage renal disease.¹
Second	400 mg twice daily*	mild hepatic impairment. TAZVERIK has not been studied in patients with moderate or severe hepatic impairment.^{1†}

*Permanently discontinue TAZVERIK in patients who are unable to tolerate 400 mg orally twice daily.¹

†Mild=total bilirubin > 1 to 1.5 times ULN or AST > ULN; moderate=total bilirubin > 1.5 to 3 times ULN; severe=total bilirubin > 3 times ULN.¹

AST=aspartate aminotransferase; ULN=upper limit of normal.

Recommended dose reductions of TAZVERIK for moderate CYP3A inhibitors¹

CURRENT DOSAGE	ADJUSTED DOSAGE
800 mg orally twice daily	400 mg orally twice daily
600 mg orally twice daily	400 mg for first dose and 200 mg for second dose
400 mg orally twice daily	200 mg orally twice daily

Please see additional Important Safety Information on the following pages and refer to the full [Prescribing Information](#).

GUIDANCE FOR DOSE MODIFICATION AND REDUCTION (continued)

Recommended dosage modifications of TAZVERIK for adverse reactions¹

ADVERSE REACTION	SEVERITY	DOSAGE MODIFICATION
Neutropenia	Neutrophil count less than $1 \times 10^9/L$	- Withhold until neutrophil count is greater than or equal to $1 \times 10^9/L$ or baseline. - For first occurrence, resume at same dose. - For second and third occurrence, resume at reduced dose. - Permanently discontinue after fourth occurrence.
Thrombocytopenia	Platelet count less than $50 \times 10^9/L$	- Withhold until platelet count is greater than or equal to $75 \times 10^9/L$ or baseline. - For first and second occurrence, resume at reduced dose. - Permanently discontinue after third occurrence.
Anemia	Hemoglobin less than 8 g/dL	Withhold until improvement to at least Grade 1 or baseline, then resume at same or reduced dose.
Other adverse reactions	Grade 3	- Withhold until improvement to at least Grade 1 or baseline. - For first and second occurrence, resume at reduced dose. - Permanently discontinue after third occurrence.
	Grade 4	- Withhold until improvement to at least Grade 1 or baseline. - For first occurrence, resume at reduced dose. - Permanently discontinue after second occurrence.

Important Safety Information (continued)

Lactation

Because of the potential risk for serious adverse reactions from TAZVERIK in the breastfed child, advise women not to breastfeed during treatment with TAZVERIK and for one week after the final dose.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.

RESOURCES AND INFORMATION TO SUPPORT YOUR PATIENTS' ACCESS TO TAZVERIK



PATIENT ASSISTANCE PROGRAM (PAP)

Patients may be eligible to receive a limited supply of free medication if they are uninsured, underinsured (based on program eligibility criteria), or are enrolled in Medicare Part D.



QUICK START PROGRAM

New patients may be eligible to receive a limited supply of free medication.



BRIDGE SUPPLY PROGRAM

Helping existing patients access medication should they experience a change or delay in drug coverage.



CO-PAY ASSISTANCE PROGRAM

Patients with commercial health insurance may be eligible to receive co-payment assistance from Epizyme to help reduce out-of-pocket costs for TAZVERIK*.

Disclaimer: All patient support is subject to eligibility criteria and program terms and conditions.

*This offer is not valid for cash-paying patients or patients currently enrolled in Medicare, Medicaid, or any other federal or state healthcare program. Limitations apply. Void where prohibited.

Epizyme **n.o.w.**SM
Patient & Product Support

If you are interested in learning more about any of the services mentioned, including eligibility requirements, visit **epizymenow.com** or contact EpizymeNOW Patient & Product Support at **1-833-4EPINOW (437-4669)**, Monday through Friday (9 AM - 6 PM ET).

References: **1.** TAZVERIK (tazemetostat) Prescribing Information. Cambridge, MA: Epizyme, Inc., July, 2020. **2.** Béguelin W, Popovic R, Teater M, et al. EZH2 is required for germinal center formation and somatic EZH2 mutations promote lymphoid transformation. *Cancer Cell*. 2013;23:677-692. **3.** Huet S, Sujobert P, Salles G. From genetics to the clinic: A translational perspective on follicular lymphoma. *Nat Rev Cancer*. 2018;18:224-239. **4.** Lue JK, Amengual JE. Emerging EZH2 inhibitors and their application in lymphoma. *Curr Hematol Malig Rep*. 2018;13:369-382. **5.** Mamessier E, Broussais-Guillaumot F, Chetaille B, et al. Nature and importance of follicular lymphoma precursors. *Haematologica*. 2014;9(5):802-810. **6.** Lackraj T, Goswami R, Kridel R. Pathogenesis of follicular lymphoma. *Best Pract Res Cl Ha*. 2018;31:2-14. **7.** Naradikian MS, Scholz JL, Oropallo MA, Cancro MP. Understanding B cell biology. In: Bosch X, Ramos-Casals M, Khamashta MA (eds.). *Drugs Targeting B-Cells in Autoimmune Diseases*. Springer;2014. **8.** Morschhauser F, Tilly H, Chaidos A, et al. Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial. *Lancet Oncol*. 2020;21(11):1433-1442. **9.** Data on file.

TAZVERIK: THE FIRST AND ONLY FDA-APPROVED EZH2 INHIBITOR FOR R/R FL PATIENTS¹

TAZVERIK
(tazemetostat) tablets
200 mg

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).¹



Oral twice-daily dose of 800 mg (4 x 200 mg tablets) can be taken with or without food¹



Overall response rates were achieved in heavily pretreated FL patients^{1,9}:

- **69% ORR in patients with MT EZH2** (n=29/42; 95% CI: 53%–82%)
- **34% ORR in patients with WT EZH2** (n=18/53; 95% CI: 22%–48%)



Sustained responses were demonstrated in both cohorts^{1,9}:

- **Median DOR of 10.9 months in patients with MT EZH2** (n=29/42; 95% CI: 7.2–NE; range: 0.0+ to 22.1+)*
- **Median DOR of 13.0 months in patients with WT EZH2** (n=18/53; 95% CI: 5.6–NE; range: 1.0 to 22.5+)



8% of patients permanently discontinued treatment due to an adverse reaction.¹

- **Secondary malignancies:** TAZVERIK increases the risk of developing secondary malignancies, including T-cell lymphoblastic lymphoma, myelodysplastic syndrome, and acute myeloid leukemia. Monitor patients long-term for the development of secondary malignancies.
- **Embryo-fetal toxicity:** TAZVERIK can cause fetal harm. Advise patients of potential risk to a fetus and to use effective non-hormonal contraception.



Tazemetostat (TAZVERIK®) is included in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-cell Lymphomas with a category 2A recommendation as an option for appropriate patients with R/R FL.[†]

*Duration of response data for the MT EZH2 subgroup are not yet mature.

†Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-cell Lymphomas V.2.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed February 23, 2021. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org). 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.

R/R=relapsed or refractory; FL=follicular lymphoma; EZH2=enhancer of zeste homologue 2; ORR=overall response rate; MT=mutant type; CI=confidence interval; WT=wild type; DOR=duration of response; NE=not estimable; NCCN=National Comprehensive Cancer Network.

Please see additional Important Safety Information on the following pages and refer to the full Prescribing Information.



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