HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BRUKINSA safely and effectively. See full prescribing information for BRUKINSA.

BRUKINSA® (zanubrutinib) capsules, for oral use
Initial U.S. Approval: 2019

——————RECENT MAJOR CHANGES——————
Indications and Usage (1.5) 3/2024

——————INDICATIONS AND USAGE——————
BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with:
- Mantle cell lymphoma (MCL) who have received at least one prior therapy. (1.1)
  This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Waldenström's macroglobulinemia (WM). (1.2)
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti–CD20-based regimen. (1.3)
  This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). (1.4)
- Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy. (1.5)
  This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

——————DOSAGE AND ADMINISTRATION——————
- Recommended dosage: 160 mg orally twice daily or 320 mg orally once daily; swallow whole with water and with or without food. (2.1)
- Reduce BRUKINSA dose in patients with severe hepatic impairment. (2.2, 8.7)
- Advise patients not to open, break, or chew capsules. (2.1)
- Manage toxicity using treatment interruption, dose reduction, or discontinuation. (2.4)

——————DOSAGE FORMS AND STRENGTHS——————
Capsules: 80 mg. (3)

——————CONTRAINDICATIONS——————
None. (4)

——————WARNINGS AND PRECAUTIONS——————
- Hemorrhage: Monitor for bleeding and manage appropriately. (5.1)
- Infections: Monitor patients for signs and symptoms of infection, including opportunistic infections, and treat as needed. (5.2)
- Cytopenias: Monitor complete blood counts during treatment. (5.3)
- Second Primary Malignancies: Other malignancies have developed including skin cancers and non-skin carcinomas. Monitor and advise patients to use sun protection. (5.4)
- Cardiac Arrhythmias: Monitor for signs and symptoms of arrhythmias and manage appropriately. (5.5)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise women of the potential risk to a fetus and to use effective contraception. (5.6)

——————ADVERSE REACTIONS——————
The most common adverse reactions (≥30%), including laboratory abnormalities, are neutrophil count decreased, platelet count decreased, upper respiratory tract infection, hemorrhage, and musculoskeletal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact BeiGene at 1-877-828-5596 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

——————DRUG INTERACTIONS——————
- CYP3A Inhibitors: Modify BRUKINSA dose with moderate or strong CYP3A inhibitors as described. (2.3, 7.1)
- CYP3A Inducers: Avoid coadministration with strong or moderate CYP3A inducers. Dose adjustment may be recommended with moderate CYP3A inducers. (2.3, 7.1)

——————USE IN SPECIFIC POPULATIONS——————
Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 3/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Mantle Cell Lymphoma

BRUKINSA is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

This indication is approved under accelerated approval based on overall response rate *[see Clinical Studies (14.1)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

1.2 Waldenström's Macroglobulinemia

BRUKINSA is indicated for the treatment of adult patients with Waldenström's macroglobulinemia (WM) *[see Clinical Studies (14.2)]*.

1.3 Marginal Zone Lymphoma

BRUKINSA is indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti–CD20-based regimen.

This indication is approved under accelerated approval based on overall response rate *[see Clinical Studies (14.3)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

1.4 Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

BRUKINSA is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) *[see Clinical Studies (14.4)]*.

1.5 Follicular Lymphoma

BRUKINSA is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.

This indication is approved under accelerated approval based on response rate and durability of response *[see Clinical Studies (14.5)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of BRUKINSA for monotherapy or in combination with obinutuzumab is 160 mg taken orally twice daily or 320 mg taken orally once daily until disease progression or unacceptable toxicity.

BRUKINSA can be taken with or without food. Advise patients to swallow capsules whole with water. Advise patients not to open, break, or chew the capsules. If a dose of BRUKINSA is missed, it should be taken as soon as possible on the same day with a return to the normal schedule the following day.

2.2 Dosage Modification for Use in Hepatic Impairment

The recommended dosage of BRUKINSA for patients with severe hepatic impairment is 80 mg orally twice daily *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

2.3 Dosage Modifications for Drug Interactions

Recommended dosage modifications of BRUKINSA for drug interactions are provided in Table 1 *[see Drug Interactions (7.1)]*.

Table 1: Dosage Modifications for Use with CYP3A Inhibitors or Inducers

Coadministered Drug	**Recommended BRUKINSA Dosage** (Starting Dose: 160 mg twice daily or 320 mg once daily)
Clarithromycin 250 mg twice daily[a]	80 mg twice daily[b]
Clarithromycin 500 mg twice daily	80 mg once daily[b]
Posaconazole suspension 100 mg once daily	80 mg twice daily[b]
Posaconazole suspension dosage higher than 100 mg once daily Posaconazole delayed-release tablets 300 mg once daily Posaconazole intravenous 300 mg once daily	80 mg once daily[b]
Other strong CYP3A inhibitor	80 mg once daily[b]
Moderate CYP3A inhibitor	80 mg twice daily[b]
Strong CYP3A inducer	Avoid concomitant use.
Moderate CYP3A inducer	Avoid concomitant use. If these inducers cannot be avoided, increase BRUKINSA dose to 320 mg twice daily.

[a] Since clarithromycin 250 mg twice daily acts as a moderate CYP3A inhibitor, it is recommended that patients be administered clarithromycin 250 mg twice daily with 80 mg BRUKINSA twice daily *[see Clinical Pharmacology (12.3)]*.

[b] Modify or interrupt zanubrutinib dose as recommended for adverse reactions *[see Dosage and Administration (2.4)]*.

After discontinuation of a CYP3A inhibitor or moderate CYP3A inducer, resume previous dose of BRUKINSA *[see Dosage and Administration (2.1, 2.2) and Drug Interactions (7.1)]*.

2.4 Dosage Modifications for Adverse Reactions

Recommended dosage modifications of BRUKINSA for Grade 3 or higher adverse reactions are provided in Table 2.

Table 2: Recommended Dosage Modifications for Adverse Reaction

Adverse Reaction	**Adverse Reaction Occurrence**	**Dosage Modification** (Starting Dose: 160 mg twice daily or 320 mg once daily)
Hematological toxicities *[see Warnings and Precautions (5.3)]*		
Grade 3 or Grade 4 febrile neutropenia Platelet count decreased to 25,000-50,000/mm^3 with significant bleeding Neutrophil count decreased to <500/mm^3 (lasting more than 10 consecutive days) Platelet count decreased to <25,000/mm^3 (lasting more than 10 consecutive days)	First	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 160 mg twice daily or 320 mg once daily.
	Second	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 80 mg twice daily or 160 mg once daily.
	Third	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 80 mg once daily.
	Fourth	Discontinue BRUKINSA
Non-hematological toxicities *[see Warnings and Precautions (5.5) and Adverse Reactions (6.1)]*		
Severe or life-threatening non-hematological toxicities[a]	First	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 160 mg twice daily or 320 mg once daily.[a]
	Second	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 80 mg twice daily or 160 mg once daily.
	Third	Interrupt BRUKINSA Once toxicity has resolved to Grade 1 or lower or baseline: Resume at 80 mg once daily.
	Fourth	Discontinue BRUKINSA.

[a] Evaluate the benefit-risk before resuming treatment at the same dosage for Grade 4 non-hematological toxicity.

Asymptomatic lymphocytosis in CLL and MCL should not be regarded as an adverse reaction, and these patients should continue taking BRUKINSA.

Refer to the obinutuzumab prescribing information for management of obinutuzumab toxicities.

3 DOSAGE FORMS AND STRENGTHS

Capsules: Each 80 mg capsule is a size 0, white to off-white opaque capsule marked with "ZANU 80" in black ink.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hemorrhage

Fatal and serious hemorrhage has occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher hemorrhage including intracranial and gastrointestinal hemorrhage, hematuria, and hemothorax was reported in 3.8% of patients treated with BRUKINSA in clinical trials, with fatalities occurring in 0.2% of patients. Bleeding of any grade, excluding purpura and petechiae, occurred in 32% of patients.

Bleeding has occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Coadministration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days before and after surgery depending upon the type of surgery and the risk of bleeding.

5.2 Infections

Fatal and serious infections (including bacterial, viral, or fungal infections) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher infections occurred in 26% of patients, most commonly pneumonia (7.9%), with fatal infections occurring in 3.2% of patients. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, *pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

5.3 Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (21%), thrombocytopenia (8%), and anemia (8%) based on laboratory measurements, developed in patients treated with BRUKINSA *[see Adverse Reactions (6.1)].* Grade 4 neutropenia occurred in 10% of patients, and Grade 4 thrombocytopenia occurred in 2.5% of patients.

Monitor complete blood counts regularly during treatment and interrupt treatment, reduce the dose, or discontinue treatment as warranted *[see Dosage and Administration (2.4)]*. Treat using growth factor or transfusions, as needed.

5.4 Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 14% of patients treated with BRUKINSA. The most frequent second primary malignancy was non-melanoma skin cancers (8%), followed by other solid tumors in 7% of the patients (including melanoma in 1% of patients) and hematologic malignancies (0.7%). Advise patients to use sun protection and monitor patients for the development of second primary malignancies.

5.5 Cardiac Arrhythmias

Serious cardiac arrhythmias have occurred in patients treated with BRUKINSA. Atrial fibrillation and atrial flutter were reported in 4.4% of patients treated with BRUKINSA,

including Grade 3 or higher cases in 1.9% of patients. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher ventricular arrhythmias were reported in 0.3% of patients.

Monitor for signs and symptoms of cardiac arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea, chest discomfort), manage appropriately *[see Dosage and Administration (2.4)]*, and consider the risks and benefits of continued BRUKINSA treatment.

5.6 Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity, including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and for 1 week after the last dose. Advise men to avoid fathering a child during treatment and for 1 week after the last dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus *[see Use in Specific Populations (8.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in more detail in other sections of the labeling:

- Hemorrhage *[see Warnings and Precautions (5.1)]*
- Infections *[see Warnings and Precautions (5.2)]*
- Cytopenias *[see Warnings and Precautions (5.3)]*
- Second Primary Malignancies *[see Warnings and Precautions (5.4)]*
- Cardiac Arrhythmias *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data in the WARNINGS AND PRECAUTIONS reflect exposure to BRUKINSA in nine monotherapy and 2 combination clinical trials, administered at 160 mg twice daily in 1608 patients and at 320 mg once daily in 121 patients. Among these 1729 patients, the median duration of exposure was 27.6 months, 78% of patients were exposed for at least 12 months, and 60% of patients were exposed for at least 24 months.

In this pooled safety population, the most common adverse reactions (≥30%), including laboratory abnormalities, were neutrophil count decreased (51%), platelet count decreased (41%), upper respiratory tract infection (38%), hemorrhage (32%), and musculoskeletal pain (31%).

Table 11: Adverse Reactions in ≥10% of Patients with Previously Untreated CLL/SLL and 17p Deletion in SEQUOIA

System Organ Class Preferred Term	CLL/SLL with 17p Deletion BRUKINSA (N=111)	
	All Grades (%)	Grade 3 or 4 (%)
Infections and infestations		
Upper respiratory tract infection[a]	38	0
Pneumonia[b]	20*	8
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[c]	38	2.7
Skin and subcutaneous tissue disorders		
Rash[d]	28	0
Bruising[e]	26	0.9
Vascular disorders		
Hemorrhage[f]	28	4.5
Hypertension[g]	11	5.4
Neoplasms		
Second primary malignancy[h]	22†	6
Gastrointestinal disorders		
Diarrhea	18	0.9
Nausea	16	0
Constipation	15	0
Abdominal pain[g]	12	1.8
Respiratory, thoracic, and mediastinal disorders		
Cough[g]	18	0
Dyspnea[g]	13	0
General disorders and administration site conditions		
Fatigue[i]	14	0.9
Nervous system disorders		
Headache	11	1.8

* Includes 1 fatal outcome.

† Includes non-melanoma skin cancer in 13%.

[a] Upper respiratory tract infection: upper respiratory tract infection, nasopharyngitis, sinusitis, rhinitis, pharyngitis, upper respiratory tract congestion, upper respiratory tract inflammation, viral upper respiratory tract infection, and related terms.

[b] Pneumonia: pneumonia, COVID-19 pneumonia, lower respiratory tract infection, and related terms including specific types of infection.

[c] Musculoskeletal pain: musculoskeletal pain, arthralgia, back pain, pain in extremity, myalgia, neck pain, bone pain.

[d] Rash: Rash, dermatitis, toxic skin eruption, and related terms.

[e] Bruising: all terms containing bruise, bruising, contusion, or ecchymosis.

[f] Hemorrhage: all terms containing hematoma, hemorrhage, hemorrhagic, and related terms indicative of bleeding.

[g] Includes multiple similar adverse reaction terms.
[h] Second primary malignancy: includes non-melanoma skin cancer, malignant solid tumors (including bladder, lung, renal, breast, prostate, ovarian, pelvis, and ureter), and malignant melanoma.
[i] Fatigue: fatigue, asthenia, and lethargy.

Clinically significant adverse reactions occurring in <10% of BRUKINSA recipients in this cohort included urinary tract infection (8%), edema (7%), atrial fibrillation or flutter (4.5%), and COVID-19 (3.6%).

Table 12 summarizes select laboratory abnormalities in this cohort.

Table 12: Select Laboratory Abnormalities (≥20%) that Worsened from Baseline in Patients with Previously Untreated CLL/SLL and 17p Deletion in SEQUOIA

Laboratory Abnormality[a]	BRUKINSA	
	All Grades (%)	Grade 3 or 4 (%)
Hematologic abnormalities		
Neutrophils decreased	42	19[b]
Hemoglobin decreased	26	3.6
Platelets decreased	23	0.9
Chemistry abnormalities		
Glucose increased[c]	52	6
Magnesium increased	31	0
Creatinine increased	27	0.9

[a] The denominator used to calculate the rate varied from 110 to 111 based on the number of patients with a baseline value and at least one post-treatment value. Grading is based on NCI CTCAE criteria.
[b] Grade 4, 9%.
[c] Non-fasting conditions.

ALPINE

The safety of BRUKINSA monotherapy was evaluated in patients with previously treated CLL/SLL in a randomized, multicenter, open-label, actively controlled trial *[see Clinical Studies (14.4)]*. In ALPINE, 324 patients received BRUKINSA monotherapy, 160 mg orally twice daily and 324 patients received ibrutinib monotherapy, 420 mg orally daily until disease progression or unacceptable toxicity.

In ALPINE, the median duration of exposure was 24 months for BRUKINSA. Adverse reactions leading to death in the BRUKINSA arm occurred in 24 (7%) patients. Adverse reactions leading to death that occurred in >1% of patients were pneumonia (2.8%) and COVID-19 infection (1.9%).

One hundred and four patients in the BRUKINSA arm (32%) reported ≥1 serious adverse reaction. Serious adverse reactions occurring in ≥5% of patients were pneumonia (10%), COVID-19 (7%), and second primary malignancies (5%).

Adverse reactions led to treatment discontinuation in 13% of patients, dose reduction in 11%, and dose interruption in 42%. The leading cause of treatment discontinuation was pneumonia. The leading causes of dose modification (≥5% of all patients) were respiratory infections (COVID-19, pneumonia) and neutropenia.

Table 13 summarizes select adverse reactions in ALPINE.

Table 13: Adverse Reactions in ≥10% of Patients with Relapsed or Refractory CLL/SLL Who Received BRUKINSA in ALPINE

System Organ Class Preferred Term	BRUKINSA (N=324)		Ibrutinib (N=324)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Infections and infestations				
Upper respiratory tract infection[a]	27	1.2	22	1.2
Pneumonia[b]	18*	9	19†	11
COVID-19[c]	14*	7	10†	4.6
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[d]	26	0.6	28	0.6
Vascular disorders				
Hemorrhage[e]	24*	2.5	26†	3.7
Hypertension[f]	19	13	20	13
Skin and subcutaneous tissue disorders				
Rash[g]	20	1.2	21	0.9
Bruising[h]	16	0	14	0
Gastrointestinal disorders				
Diarrhea	14	1.5	22	0.9
General disorders				
Fatigue[i]	13	0.9	14	0.9
Respiratory, thoracic, and mediastinal disorders				
Cough[f]	11	0.3	11	0
Nervous system disorders				
Dizziness[f]	10	0	7	0

***** Includes fatal outcomes: pneumonia (9 patients), COVID-19 (8 patients), and hemorrhage (1 patient).

† Includes fatal outcomes: pneumonia (10 patients), COVID-19 (9 patients), and hemorrhage (2 patients).

[a] Upper respiratory tract infection: upper respiratory tract infection, sinusitis, pharyngitis, rhinitis, nasopharyngitis, laryngitis, tonsillitis, and related terms.

[b] Pneumonia: Pneumonia, COVID-19 pneumonia, lower respiratory tract infection, lung infiltration, and related terms including specific types of infection.

[c] COVID-19: COVID-19, COVID-19 pneumonia, postacute COVID-19 syndrome, SARS-CoV-2 test positive.

[d] Musculoskeletal pain: musculoskeletal pain, arthralgia, back pain, pain in extremity, myalgia, neck pain, spinal pain, bone pain, and musculoskeletal discomfort.

[e] Hemorrhage: all terms containing hematoma, hemorrhage, hemorrhagic, and related terms indicative of bleeding.

[f] Includes multiple similar adverse reaction terms.

[g] Rash: Rash, Dermatitis, and related terms.

[h] Bruising: all terms containing bruise, bruising, contusion, or ecchymosis.

[i] Fatigue: asthenia, fatigue, lethargy.

Clinically relevant adverse reactions in <10% of patients who received BRUKINSA included urinary tract infection (9%), supraventricular arrhythmias (9%) including atrial fibrillation or flutter (4.6%), abdominal pain (8%), headache (8%), pruritus (6.2%), constipation (5.9%), and edema (4.6%).

Table 14 summarizes select laboratory abnormalities in ALPINE.

Table 14: Select Laboratory Abnormalities (≥20%) that Worsened from Baseline in Patients Who Received BRUKINSA in ALPINE

Laboratory Abnormality[a]	BRUKINSA		Ibrutinib	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Hematologic abnormalities				
Neutrophils decreased	43	15	33	16
Hemoglobin decreased	28	4	32	3.7
Lymphocytes increased	24	19	26	19
Platelets decreased	22	4	24	3.4
Chemistry abnormalities				
Glucose increased	52	5	29	2.8
Creatinine increased	26	0	23	0
Phosphate decreased	21	2.5	13	2.2
Calcium decreased	21	0.6	29	0

[a] The denominator used to calculate the rate was 321 in the BRUKINSA arm, and varied from 320 to 321 in the ibrutinib arm, based on the number of patients with a baseline value and at least one post-treatment value. Grading is based on NCI CTCAE criteria.

Follicular Lymphoma

The safety of BRUKINSA in combination with obinutuzumab was evaluated in 143 adult patients with relapsed or refractory follicular lymphoma (FL) in study BGB-3111-212 (ROSEWOOD), a randomized, multicenter, open-label trial *[see Clinical Studies (14.5)]*. The trial required an absolute neutrophil count ≥1 × 10^9/L, platelet count ≥50 × 10^9/L, and CLcr ≥30 mL/min and excluded patients requiring a strong CYP3A inhibitor or inducer.

Patients were randomized to receive either BRUKINSA 160 mg twice daily until disease progression or unacceptable toxicity plus obinutuzumab (n=143) or obinutuzumab monotherapy (n=71). Obinutuzumab was dosed at 1,000 mg intravenously on Days 1, 8, and 15 of Cycle 1; on Day 1 of Cycles 2 to 6; and then every 8 weeks for up to 20 doses. At the discretion of the investigator, obinutuzumab was administered intravenously on Day 1 (100 mg) and on Day 2 (900 mg) of Cycle 1 instead of 1,000 mg on Day 1 of Cycle 1.

In patients who received BRUKINSA in combination with obinutuzumab, the median age was 63, 49% were female, 63% were White, and 21% were Asian. Most patients (97%) had an ECOG performance status of 0 to 1. The median duration of BRUKINSA treatment was 12 months, with 24% of patients treated for at least 2 years.

Serious adverse reactions occurred in 35% of patients who received BRUKINSA in combination with obinutuzumab. Serious adverse reactions in ≥5% of patients included pneumonia (11%) and

COVID-19 (10%). Fatal adverse reactions occurred in 4.2% of patients, with the leading cause of death being COVID-19 (2.1%).

Adverse reactions led to permanent discontinuation of BRUKINSA in 17% of patients, dose reduction in 9%, and dose interruption in 40%. Adverse reactions leading to permanent discontinuation in ≥2% of patients were pneumonia, COVID-19, and second primary malignancy. The leading causes of BRUKINSA dosage modification (42% of all patients) were pneumonia, COVID-19, thrombocytopenia, and neutropenia.

Table 15 summarizes adverse reactions in BGB-3111-212.

Table 15: Adverse Reactions in ≥10% of Patients with Relapsed or Refractory FL Who Received BRUKINSA in Study BGB-3111-212

System Organ Class Preferred Term	BGB-3111-212			
	BRUKINSA + Obinutuzumab (N=143)		Obinutuzumab (N=71)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
General disorders and administration site conditions				
Fatigue[a,b]	27	1.4	25	1.4
Pyrexia	13	0	20	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[a,c]	22	3.5	23	1.4
Vascular disorders				
Hemorrhage[a,d]	20	1.4	10	1.4
Gastrointestinal disorders				
Diarrhea	18	2.8	17	1.4
Constipation	13	0	9	0
Abdominal pain[a]	11	2.1	11	0
Infections and infestations				
Upper respiratory tract infection[a,e]	17	2.8	10	0
Pneumonia[a,f,*]	15	13	11	7
COVID-19[a,*]	13	9	11	4.2
Herpes virus infection[g]	11	2.1	1.4	0
Urinary tract infection[h]	10	1.4	7	0
Respiratory, thoracic, and mediastinal disorders				
Cough[a]	14	0	14	0
Dyspnea[a,*]	11	2.1	13	0
Skin and subcutaneous tissue disorders				
Rash[a,i]	11	0	14	0

***** Includes fatal outcomes: COVID-19 (3 patients), pneumonia (2 patients), dyspnea (1 patient).

[a] Includes multiple related terms.

[b] Fatigue: Fatigue, asthenia, and lethargy.

[c] Musculoskeletal pain: Back pain, musculoskeletal pain, musculoskeletal discomfort, noncardiac chest pain, neck pain, pain in extremity, myalgia, spinal pain, bone pain, arthralgia, and related terms.

[d] Hemorrhage: All terms containing hematoma, hemorrhage, hemorrhagic, and related terms indicative of bleeding.
[e] Upper respiratory tract infection: Upper respiratory tract infection, sinusitis, pharyngitis, laryngitis, rhinitis, nasopharyngitis, laryngopharyngitis, tonsillitis bacterial, and related terms.
[f] Pneumonia: Pneumonia, COVID-19 pneumonia, lung infiltration, lung consolidation, and related terms including specific types of infection.
[g] Herpes virus infection: Herpes viral infection, herpes zoster, herpes simplex, herpes simplex reactivation, varicella, and Epstein-Barr viremia.
[h] Urinary tract infection: Urinary tract infection, cystitis, pyelonephritis, and related terms.
[i] Rash: Rash, erythema, dermatitis, drug eruption, skin reaction, and related terms.

Clinically relevant adverse reactions in <10% of patients who received BRUKINSA in combination with obinutuzumab included bruising, edema, pruritus, petechiae, vomiting, headache, arthralgia, hypertension, sepsis, cardiac arrhythmias, renal insufficiency, febrile neutropenia, transaminase elevation, and pneumonitis.

Table 16: Select Laboratory Abnormalities (≥20%) that Worsened from Baseline in Patients Who Received BRUKINSA in Study BGB-3111-212

Laboratory Abnormality[a]	BGB-3111-212			
	BRUKINSA + Obinutuzumab		Obinutuzumab	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Hematologic abnormalities				
Platelets decreased	65	11	43	11
Neutrophils decreased	47	17	42	14
Hemoglobin decreased	31	0.8	23	0
Lymphocytes decreased	30	11	51	25
Chemistry				
Glucose increased[b]	53	8	41	9
Alanine aminotransferase increased	23	0	28	0
Phosphate decreased	21	0.8	14	0

[a] The denominator used to calculate the rate was 122 in the BRUKINSA + obinutuzumab arm, and varied from 56 to 58 in the obinutuzumab arm, based on the number of patients with a baseline value and at least one post-treatment value. Grading is based on NCI CTCAE criteria.
[b] Nonfasting conditions.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on BRUKINSA

Table 17: Drug Interactions that Affect Zanubrutinib

Moderate and Strong CYP3A Inhibitors	
Clinical Impact	• Coadministration with a moderate or strong CYP3A inhibitor increases zanubrutinib C_{max} and AUC *[see Clinical Pharmacology (12.3)]* which may increase the risk of BRUKINSA toxicities.
Prevention or management	• Reduce BRUKINSA dosage when coadministered with

Moderate and Strong CYP3A Inhibitors	
	moderate or strong CYP3A inhibitors *[see Dosage and Administration (2.3)]*.
Moderate and Strong CYP3A Inducers	
Clinical Impact	• Coadministration with a moderate or strong CYP3A inducer decreases zanubrutinib C_{max} and AUC *[see Clinical Pharmacology (12.3)]* which may reduce BRUKINSA efficacy.
Prevention or management	• Avoid coadministration of BRUKINSA with strong CYP3A inducers *[see Dosage and Administration (2.3)]*. • Avoid coadministration of BRUKINSA with moderate CYP3A inducers *[see Dosage and Administration (2.3)]*. If these inducers cannot be avoided, increase BRUKINSA dosage to 320 mg twice daily *[see Dosage and Administration (2.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animals, BRUKINSA can cause fetal harm when administered to pregnant women. There are no available data on BRUKINSA use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of zanubrutinib to pregnant rats during the period of organogenesis was associated with fetal heart malformation at approximately 5-fold human exposures *(see Data)*. Women should be advised to avoid pregnancy while taking BRUKINSA. If BRUKINSA is used during pregnancy, or if the patient becomes pregnant while taking BRUKINSA, the patient should be apprised of the potential hazard to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Embryo-fetal development toxicity studies were conducted in both rats and rabbits. Zanubrutinib was administered orally to pregnant rats during the period of organogenesis at doses of 30, 75, and 150 mg/kg/day. Malformations in the heart (2 or 3-chambered hearts) were noted at all dose levels in the absence of maternal toxicity. The dose of 30 mg/kg/day is approximately 5 times the exposure (AUC) in patients receiving the recommended dose of 160 mg twice daily.

Administration of zanubrutinib to pregnant rabbits during the period of organogenesis at 30, 70, and 150 mg/kg/day resulted in postimplantation loss at the highest dose. The dose of 150 mg/kg is approximately 32 times the exposure (AUC) in patients at the recommended dose and was associated with maternal toxicity.

In a pre and postnatal developmental toxicity study, zanubrutinib was administered orally to rats at doses of 30, 75, and 150 mg/kg/day from implantation through weaning. The offspring from the middle and high dose groups had decreased body weights preweaning, and all dose groups had adverse ocular findings (e.g., cataract, protruding eye). The dose of 30 mg/kg/day is approximately 5 times the AUC in patients receiving the recommended dose.

8.2 Lactation

Risk Summary

There are no data on the presence of zanubrutinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions from BRUKINSA in a breastfed child, advise lactating women not to breastfeed during treatment with BRUKINSA and for two weeks following the last dose.

8.3 Females and Males of Reproductive Potential

BRUKINSA can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating BRUKINSA therapy.

Contraception

Females

Advise female patients of reproductive potential to use effective contraception during treatment with BRUKINSA and for 1 week following the last dose of BRUKINSA. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Males

Advise men to avoid fathering a child while receiving BRUKINSA and for 1 week following the last dose of BRUKINSA.

8.4 Pediatric Use

Safety and effectiveness of BRUKINSA in pediatric patients have not been established.

8.5 Geriatric Use

Of the 1729 patients with MCL, MZL, WM, CLL/SLL, and FL in clinical studies with BRUKINSA, 59% were ≥65 years of age, and 21% were ≥75 years of age. Patients ≥65 years of age had numerically higher rates of Grade 3 or higher adverse reactions and serious adverse reactions (57% and 38%, respectively) than patients <65 years of age (51% and 29%, respectively). No overall differences in effectiveness were observed between younger and older patients.

8.6 Renal Impairment

No dosage modification is recommended in patients with mild, moderate, or severe renal impairment (CLcr ≥15 mL/min, estimated by Cockcroft-Gault). Monitor for BRUKINSA

adverse reactions in patients on dialysis *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

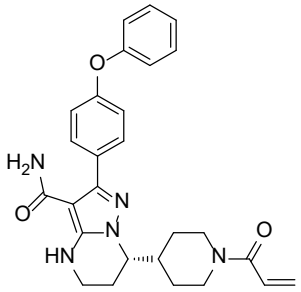
Dosage modification of BRUKINSA is recommended in patients with severe hepatic impairment *[see Dosage and Administration (2.2)]*. The safety of BRUKINSA has not been evaluated in patients with severe hepatic impairment. No dosage modification is recommended in patients with mild to moderate hepatic impairment. Monitor for BRUKINSA adverse reactions in patients with hepatic impairment *[see Clinical Pharmacology (12.3)]*.

11 DESCRIPTION

BRUKINSA (zanubrutinib) is a kinase inhibitor. The empirical formula of zanubrutinib is $C_{27}H_{29}N_5O_3$ and the chemical name is (*S*)-7-(1-acryloylpiperidin-4-yl)-2-(4-phenoxyphenyl)-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-3-carboxamide. Zanubrutinib is a white to off-white powder, with a pH of 7.8 in saturated solution. The aqueous solubility of zanubrutinib is pH dependent, from very slightly soluble to practically insoluble.

The molecular weight of zanubrutinib is 471.55 Daltons.

Zanubrutinib has the following structure:



Each BRUKINSA capsule for oral administration contains 80 mg zanubrutinib and the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and sodium lauryl sulfate. The capsule shell contains edible black ink, gelatin, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Zanubrutinib is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). Zanubrutinib forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. In nonclinical studies, zanubrutinib inhibited malignant B-cell proliferation and reduced tumor growth.

12.2 Pharmacodynamics

BTK Occupancy in PBMCs and Lymph Nodes

The median steady-state BTK occupancy in peripheral blood mononuclear cells was maintained at 100% over 24 hours at a total daily dose of 320 mg in patients with B-cell malignancies. The

median steady-state BTK occupancy in lymph nodes was 94% to 100% following the approved recommended dosage.

Cardiac Electrophysiology

At the approved recommended doses (160 mg twice daily or 320 mg once daily), there were no clinically relevant effects on the QTc interval. The effect of BRUKINSA on the QTc interval above the therapeutic exposure has not been evaluated.

12.3 Pharmacokinetics

Zanubrutinib maximum plasma concentration (C_{max}) and area under the plasma drug concentration over time curve (AUC) increase proportionally over a dosage range from 40 mg to 320 mg (0.13 to 1 time the recommended total daily dose). Limited systemic accumulation of zanubrutinib was observed following repeated administration.

The geometric mean (%CV) zanubrutinib steady-state daily AUC is 2,099 (42%) ng·h/mL following 160 mg twice daily and 1,917 (59%) ng·h/mL following 320 mg once daily. The geometric mean (%CV) zanubrutinib steady-state C_{max} is 295 (55%) ng/mL following 160 mg twice daily and 537 (55%) ng/mL following 320 mg once daily.

Absorption

The median t_{max} of zanubrutinib is 2 hours.

Effect of Food

No clinically significant differences in zanubrutinib AUC or C_{max} were observed following administration of a high-fat meal (approximately 1,000 calories with 50% of total caloric content from fat) in healthy subjects.

Distribution

The geometric mean (%CV) apparent volume of distribution (Vz/F) of zanubrutinib is 537 (73%) L. The plasma protein binding of zanubrutinib is approximately 94% and the blood-to-plasma ratio is 0.7 to 0.8.

Elimination

The mean half-life ($t_{½}$) of zanubrutinib is approximately 2 to 4 hours following a single oral zanubrutinib dose of 160 mg or 320 mg. The geometric mean (%CV) apparent oral clearance (CL/F) of zanubrutinib is 128 (58%) L/h.

Metabolism

Zanubrutinib is primarily metabolized by cytochrome P450(CYP)3A.

Excretion

Following a single radiolabeled zanubrutinib dose of 320 mg to healthy subjects, approximately 87% of the dose was recovered in feces (38% unchanged) and 8% in urine (less than 1% unchanged).

Specific Populations

No clinically significant differences in the pharmacokinetics of zanubrutinib were observed based on age (19 to 90 years), sex, race (Asian, White, and Other), body weight (36 to 144 kg),

In the BRUKINSA in combination with obinutuzumab arm, 5% had received lenalidomide plus rituximab, 21% had received stem cell transplantation, 53% had refractory disease to rituximab, and 37% had progression of disease within 24 months of the first systemic therapy.

Efficacy was based on overall response rate and duration of response, as determined by an IRC. Efficacy results are shown in Table 25. The median time to response in the BRUKINSA combination arm was 2.8 months (range 2.0 to 23.0 months).

Table 25: Efficacy Results per IRC in Patients with Relapsed or Refractory Follicular Lymphoma

Parameter	BRUKINSA + Obinutuzumab (N=145)	Obinutuzumab (N=72)
Overall response rate		
ORR, n (%)	100 (69)	33 (46)
(95% CI)[a]	(61, 76)	(34, 58)
CR	57 (39)	14 (19)
PR	43 (30)	19 (26)
Risk difference, % (95% CI)[b]	22.7 (9.0, 36.5)	
2-sided p-value[b,c]	0.0012	
Duration of response		
Median DOR (95% CI),[d] months	NE (25.3, NE)	14.0 (9.2, 25.1)

CI=Confidence interval, CR=complete response, DOR=duration of response, NE=not estimable, ORR=overall response rate, PR=partial response.

[a] Estimated using the Clopper-Pearson method.

[b] Estimated by stratified Cochran-Mantel-Haenszel method.

[c] Significance level, 0.05.

[d] Estimated by Kaplan-Meier method. Estimated median follow-up for DOR was 19.0 months overall.

The estimated DOR rate at 18 months was 69% (95% CI: 58, 78) in the BRUKINSA combination arm and 42% (95% CI: 23, 60) in the obinutuzumab monotherapy arm.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Package Size	Content	NDC Number
120-count	Bottle with a child-resistant cap containing 120 capsules 80 mg, white to off-white opaque capsule, marked with “ZANU 80” in black ink	72579-011-02

Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Patient Information).

Hemorrhage

Inform patients to report signs or symptoms of severe bleeding. Inform patients that BRUKINSA may need to be interrupted for major surgeries or procedures *[see Warnings and Precautions (5.1)]*.

Infections

Inform patients to report signs or symptoms suggestive of infection *[see Warnings and Precautions (5.2)]*.

Cytopenias

Inform patients that they will need periodic blood tests to check blood counts during treatment with BRUKINSA *[see Warnings and Precautions (5.3)]*.

Second Primary Malignancies

Inform patients that other malignancies have been reported in patients who have been treated with BRUKINSA, including skin cancer and other solid tumors. Advise patients to use sun protection and have monitoring for development of other cancers *[see Warnings and Precautions (5.4)]*.

Cardiac Arrhythmias

Counsel patients to report any signs of palpitations, lightheadedness, dizziness, fainting, shortness of breath, and chest discomfort *[see Warnings and Precautions (5.5)]*.

Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential hazard to a fetus and to use effective contraception during treatment and for 1 week after the last dose of BRUKINSA *[see Warnings and Precautions (5.6)]*. Advise males with female sexual partners of reproductive potential to use effective contraception during BRUKINSA treatment and for 1 week after the last dose of BRUKINSA *[see Use in Specific Populations (8.3)]*.

Lactation

Advise females not to breastfeed during treatment with BRUKINSA and for 2 weeks after the last dose *[see Use in Specific Populations (8.2)]*.

Administration Instructions

BRUKINSA may be taken with or without food. Advise patients that BRUKINSA capsules should be swallowed whole with a glass of water, without being opened, broken, or chewed *[see Dosage and Administration (2.1)]*.

Missed Dose

Advise patients that if they miss a dose of BRUKINSA, they may still take it as soon as possible on the same day with a return to the normal schedule the following day *[see Dosage and Administration (2.1)]*.

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including over-the-counter medications, vitamins, and herbal products *[see Drug Interactions (7.1)]*.

Manufactured for:
BeiGene USA, Inc.
1840 Gateway Dr., FL 3
San Mateo, CA 94404

PATIENT INFORMATION
BRUKINSA® (BROO-kin-sah)
(zanubrutinib)
capsules

What is BRUKINSA?

BRUKINSA is a prescription medicine used to treat adults with:

- Mantle cell lymphoma (MCL) who have received at least one prior treatment for their cancer.
- Waldenström's macroglobulinemia (WM).
- Marginal zone lymphoma (MZL) when the disease has come back or did not respond to treatment and who have received at least one certain type of treatment.
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- Follicular lymphoma (FL), in combination with the medicine obinutuzumab, when the disease has come back or did not respond to treatment and who have received at least two prior treatments.

It is not known if BRUKINSA is safe and effective in children.

Before taking BRUKINSA, tell your healthcare provider about all of your medical conditions, including if you:

- have bleeding problems.
- have had recent surgery or plan to have surgery. Your healthcare provider may stop BRUKINSA for any planned medical, surgical, or dental procedure.
- have an infection.
- have or had heart rhythm problems.
- have high blood pressure.
- have liver problems, including a history of hepatitis B virus (HBV) infection.
- are pregnant or plan to become pregnant. BRUKINSA can harm your unborn baby. If you are able to become pregnant, your healthcare provider may do a pregnancy test before starting treatment with BRUKINSA.
  - **Females** should avoid getting pregnant during treatment and for 1 week after the last dose of BRUKINSA. You should use effective birth control (contraception) during treatment and for 1 week after the last dose of BRUKINSA.
  - **Males** should avoid getting female partners pregnant during treatment and for 1 week after the last dose of BRUKINSA. You should use effective birth control (contraception) during treatment and for 1 week after the last dose of BRUKINSA.
- are breastfeeding or plan to breastfeed. It is not known if BRUKINSA passes into your breast milk. Do not breastfeed during treatment with BRUKINSA and for 2 weeks after the last dose of BRUKINSA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking BRUKINSA with certain other medications may affect how BRUKINSA works and can cause side effects.

How should I take BRUKINSA?

- Take BRUKINSA exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking BRUKINSA unless your healthcare provider tells you to.
- Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking BRUKINSA if you develop certain side effects.
- Take BRUKINSA with or without food.
- Swallow BRUKINSA capsules whole with a glass of water. Do not open, break, or chew the capsules.
- If you miss a dose of BRUKINSA, take it as soon as you remember on the same day. Return to your normal schedule the next day.

What are the possible side effects of BRUKINSA?

BRUKINSA may cause serious side effects, including:

- **Bleeding problems (hemorrhage).** Bleeding problems are common with BRUKINSA, and can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs or symptoms of bleeding, including:
  - blood in your stools or black stools (looks like tar)
  - pink or brown urine
  - unexpected bleeding, or bleeding that is severe or you cannot control
  - increased bruising
  - dizziness
  - weakness
  - confusion

- vomit blood or vomit that looks like coffee grounds
- cough up blood or blood clots
- change in speech
- headache that lasts a long time

- **Infections** that can be serious and may lead to death. Tell your healthcare provider right away if you have fever, chills, or flu-like symptoms.
- **Decrease in blood cell counts** (white blood cells, platelets, and red blood cells). Your healthcare provider should do blood tests during treatment with BRUKINSA to check your blood counts.
- **Second primary cancers.** New cancers have happened in people during treatment with BRUKINSA, including cancers of the skin or other organs. Your healthcare provider will check you for other cancers during treatment with BRUKINSA. Use sun protection when you are outside in sunlight.
- **Heart rhythm problems** (atrial fibrillation, atrial flutter, and ventricular arrhythmias) that can be serious and may lead to death. Tell your healthcare provider if you have any of the following signs or symptoms:
  - your heartbeat is fast or irregular
  - feel lightheaded or dizzy
  - pass out (faint)
  - shortness of breath
  - chest discomfort

The most common side effects of BRUKINSA include:

- decreased white blood cell count
- decreased platelet count
- upper respiratory tract infection
- bleeding
- muscle, bone, or joint pain

These are not all the possible side effects of BRUKINSA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store BRUKINSA?

- Store BRUKINSA capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- BRUKINSA comes in a bottle with a child-resistant cap.

Keep BRUKINSA and all medicines out of the reach of children.

General information about the safe and effective use of BRUKINSA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use BRUKINSA for a condition for which it was not prescribed. Do not give BRUKINSA to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about BRUKINSA that is written for healthcare professionals.

What are the ingredients in BRUKINSA?

Active ingredient: zanubrutinib
Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and sodium lauryl sulfate.
Capsule shell contains edible black ink, gelatin, and titanium dioxide.

Manufactured for: BeiGene USA, Inc., 1840 Gateway Dr., FL 3, San Mateo, CA 94404

For more information, go to www.BRUKINSA.com or call 1-833-969-2463.

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 3/2024