AVAILABLE AS AN ORAL SUSPENSION FOR CHILDREN AGE 1 TO <12 YEARS[1]

FOR THE FIRST TIME EVER

AS OF AUGUST 2022

IMBRUVICA® (ibrutinib): Safety and effectiveness have been established for children as young as 1 year of age with previously treated cGVHD[1-3]

This indication is supported by evidence from the iMAGINE study[1]

- **Pediatric patients under the age of 12 who developed cGVHD and have failed one or more lines of systemic therapy, have limited treatment options[1-3]**
- **Data from the iMAGINE trial (N=47) support that IMBRUVICA® produced a clinically meaningful response in pediatric patients with previously treated cGVHD[1]**

Once-daily IMBRUVICA® offers an oral suspension treatment option for children (ages 1-<12) with previously treated cGVHD[1]

INDICATION

IMBRUVICA® is a kinase inhibitor indicated for the treatment of:

- Adult and pediatric patients age 1 year and older with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage; infections; cardiac arrhythmias, cardiac failure, and sudden death; hypertension; cytopenias; second primary malignancies; tumor lysis syndrome; and embryo-fetal toxicity.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in adult or pediatric patients with cGVHD were fatigue (57%), anemia (49%)*, bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, musculoskeletal pain (30%), pyrexia (30%), muscle spasms (29%), stomatitis (29%), hemorrhage (26%), nausea (26%), abdominal pain (23%), pneumonia (23%), and headache (21%).

*Treatment-emergent decreases (all grades) were based on laboratory measurements.

cGVHD=chronic graft versus host disease.

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imbruvica® (ibrutinib)
420, 280, 140 mg tablets | 140, 70 mg capsules
70 mg/mL oral suspension

STUDY DESIGN: iMAGINE TRIAL

The iMAGINE trial study design[1,4]

An open-label, multicenter, single-arm, phase 1/2 study consisting of 47 patients aged 1 to <22 years with previously treated moderate or severe cGVHD.

Select Inclusion Criteria:

- Platelets ≥30 x 10^9/L and no transfusion for 7 days
- Absolute neutrophil count ≥1.0 x 10^9/L and off growth factor support for 7 days
- Total bilirubin ≥1.5x ULN (unless of non-hepatic origin or due to Gilbert's syndrome) or ≥3.0 x ULN if due to GVHD
- Estimated creatinine clearance ≥30 mL/min

Select Exclusion Criteria:

- Single-organ genitourinary involvement was the only manifestation of cGVHD

Select Patient Demographics:

- Median age of patients was 13 years (range: 1-19)
- Median time since diagnosis was 16.1 months
- Median number of prior cGVHD treatments was 2 (range: 1-12)
- Daily corticosteroid dose (prednisone or prednisone equivalent) at baseline was 0.47 mg/kg/day

Study Design Dosing:

- Patients 12 years of age and older (n=26): 420 mg taken orally once daily until disease progression
- Patients 1 to less than 12 years of age (n=21): starting dose of 120 mg/m², after 14 days of treatment 240 mg/m² taken orally once daily (up to a dose of 420 mg)

ALT=alanine transaminase, AST=aspartate aminotransferase, ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) occurred in 4.2% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA® in 27 clinical trials. Bleeding events of any grade including bruising and petechiae occurred in 39%, and excluding bruising and petechiae occurred in 23% of patients who received IMBRUVICA®, respectively.

The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA® increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA® without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding.

Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections: Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

Cardiac Arrhythmias, Cardiac Failure, and Sudden Death: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA® treatment.

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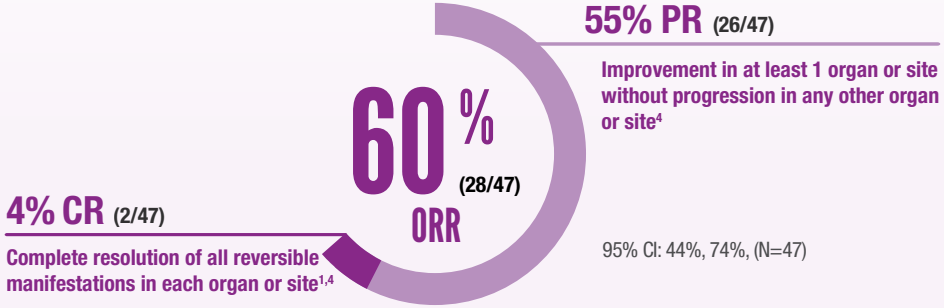
EFFICACY IN CHILDREN AGE 1 TO <22 YEARS WITH cGVHD WHO HAVE FAILED ONE OR MORE LINES OF THERAPY[1]

Approximately 6 out of 10 patients responded to treatment with IMBRUVICA®[1] based on Overall Response Rate (ORR)

- The efficacy of IMBRUVICA®* was established based on responses evaluated through Week 25 where overall response included complete response or partial response according to the 2014 National Institutes of Health Consensus Development Project Response Criteria

Overall Response Rate*



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hypertension: Hypertension occurred in 19% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from a subset of these patients (N=1,124), the median time to onset was 5.9 months (range, 0 to 24 months). In a long-term safety analysis over 5 years of 1,284 patients with B-cell malignancies treated for a median of 36 months (range, 0 to 98 months), the cumulative rate of hypertension increased over time. The prevalence for Grade 3 or greater hypertension was 4% (year 0-1), 7% (year 1-2), 9% (year 2-3), 9% (year 3-4), and 9% (year 4-5); the overall incidence for the 5-year period was 11%. Monitor blood pressure in patients treated with IMBRUVICA®, initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

Cytopenias: In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, grade 3 or 4 neutropenia occurred in 23% of patients, grade 3 or 4 thrombocytopenia in 8% and grade 3 or 4 anemia in 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (3.9%), occurred among the 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in adult or pediatric patients with cGVHD were fatigue (57%), anemia (49%)*, bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, musculoskeletal pain (30%), pyrexia (30%), muscle spasms (29%), stomatitis (29%), hemorrhage (26%), nausea (26%), abdominal pain (23%), pneumonia (23%), and headache (21%).

*Skin, mouth, liver, upper and lower GI, esophagus, lung, eye, and joint/fascia were the organs/sites considered in evaluating overall response.

CI=confidence interval, CR=complete response, ORR=overall response rate, PR=partial response.

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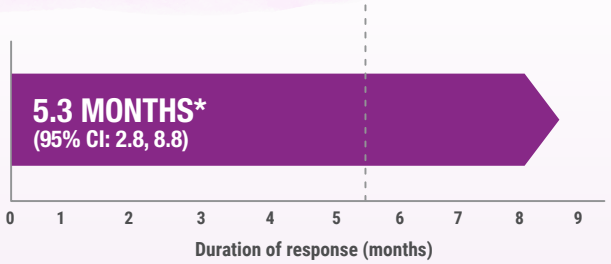
EFFICACY IN CHILDREN AGE 1 TO <22 YEARS WITH cGVHD WHO HAVE FAILED ONE OR MORE LINES OF THERAPY[1] (Cont'd)

Time to response/duration of response[2]

Time to first response:

Median time to first response was 0.9 months (range: 0.9, 6.1)

Median duration of response



The median time from first response to death or new systemic therapies for cGVHD was 14.8 months (95% CI: 4.6, not evaluable).

Improvement in patient-reported symptom bother

50% (13/26)

ORR results were supported by exploratory analyses of patient-reported symptom bother which showed at least a 7-point decrease in Lee Symptom Scale overall summary score through Week 25 in 50% of patients age 12 years and older†

*Median duration of response was calculated from first response to progression, death, or new systemic therapy for chronic GVHD.
†The Lee Symptom Scale assesses the severity of cGVHD by directly measuring patient symptom burden based on manifestations of the disease (skin, energy, lung, nutritional status, psychological functioning, eye, and mouth).[5]

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

The most common Grade 3 or higher adverse reactions (≥5%) reported in adult or pediatric patients with cGVHD were pneumonia (14%), anemia (13%)*, fatigue (12%), pyrexia (11%), diarrhea (10%), neutropenia (10%)*, sepsis (10%), osteonecrosis (9%), stomatitis (9%), hypokalemia (7%), headache (5%), and musculoskeletal pain (5%).

Discontinuation of IMBRUVICA® treatment due to an adverse reaction occurred in 24% of adult patients and 23% of pediatric patients. Adverse reactions leading to dose reduction occurred in 26% of adult patients and 19% of pediatric patients.

*Treatment-emergent decreases (all grades) were based on laboratory measurements.

DRUG INTERACTIONS

CYP3A Inhibitors: Co-administration of IMBRUVICA® with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA® are recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA® if strong inhibitors are used short-term (e.g., for ≤ 7 days). Avoid grapefruit and Seville oranges during IMBRUVICA® treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

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SAFETY IN PEDIATRIC PATIENTS WITH cGVHD WHO HAVE FAILED ONE OR MORE LINES OF THERAPY[1]

In the iMAGINE trial

Median duration of exposure was 7.1 months (range: 0.2, 25.9 months)[1]

Adverse reactions reported in ≥10% of patients aged 1 to <22 years with cGVHD in iMAGINE[1]

Body System	Adverse Reactions	Previously Treated (N=47)	
		All grades (%)	Grade 3 or 4 (%)
General disorders and administration site conditions	Pyrexia	30	11
Musculoskeletal and connective tissue disorders	Musculoskeletal pain*	30	2
	Osteonecrosis	11	9
Gastrointestinal disorders	Diarrhea	28	2
	Abdominal pain*	23	4
	Stomatitis*	23	9
	Vomiting	19	2
	Nausea	19	4
Infections and infestations	Pneumonia*	23	13
	Skin infection*	17	4
	Sepsis*	11	9†
Nervous system disorders	Headache	21	2
Skin and subcutaneous tissue disorders	Rash*	19	2
	Pruritus	13	0
	Petechiae	13	0
Respiratory, thoracic and mediastinal disorders	Cough	19	2
Vascular Disorders	Hemorrhage*	17	0
	Hypertension*	11	4
Blood and lymphatic system disorders	Hypokalemia	15	6
	Hypogammaglobulinemia*	11	0
Cardiac Disorders	Sinus tachycardia	11	0
Investigations	Alanine aminotransferase increased	11	2

The system organ class and individual ADR preferred terms are sorted in descending frequency order.

*Includes multiple ADR terms.
†Includes 1 event with a fatal outcome.
ADR=adverse drug reaction.

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SAFETY IN PEDIATRIC PATIENTS WITH cGVHD WHO HAVE FAILED ONE OR MORE LINES OF THERAPY[1] (Cont'd)

In the iMAGINE trial (Cont'd)

Select hematologic laboratory abnormalities (≥10%) that worsened from baseline in patients who received IMBRUVICA® in the iMAGINE trial[1]

	IMBRUVICA® (N=47)	
	All Grades (%)	Grades 3 or 4 (%)
Hemoglobin decreased	49	13
Platelets decreased	21	4
Neutrophils decreased	13	6

Treatment-emergent Grade 4 neutropenia occurred in 3% of patients.

23% of previously treated pediatric and young adult (aged 1 to <22 years) patients who received IMBRUVICA® in the iMAGINE study discontinued treatment due to adverse reactions[1]

- Adverse reactions which resulted in permanent discontinuation in at least 2 patients included hemorrhage
- Adverse reactions leading to dose reduction occurred in 19% of patients
- Adverse reactions which required dose reduction in at least 2 patients included stomatitis

The safety and effectiveness of IMBRUVICA® in pediatric patients for indications other than cGVHD have not been established.[1]

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EMBRACE AN FDA-APPROVED, cGVHD TREATMENT DEVELOPED FOR CHILDREN

Dosing and administration[1]

Patients 1 to less than 12 years of age: 240 mg/m^2 taken orally once daily (up to a dose of 420 mg)

Patients 12 years and older: 420 mg taken orally once daily

- Administer IMBRUVICA® until cGVHD progression, recurrence of an underlying malignancy, or unacceptable toxicity. When a patient no longer requires therapy for the treatment of cGVHD, IMBRUVICA® should be discontinued considering the medical assessment of the individual patient
- Recommended dosage based on body surface area (BSA) for patients 1 to less than 12 years of age using either IMBRUVICA® capsules/tablets or oral suspension
- Tablets or capsules should be taken orally with a glass of water. Do not open, break, or chew the capsules. Do not cut, crush, or chew the tablets

See full Prescribing Information for oral suspension administration instructions.

In the iMAGINE trial[1,4]

Approximately 6 out of 10 patients responded to treatment with IMBRUVICA®

- ORR* was 60% (28/47) in pediatric patients aged 1 to <22 years with cGVHD who failed one or more lines of systemic therapy with 95% CI (44%, 74%)
  - 55% (26/47) experienced a PR to treatment with IMBRUVICA®
  - 4% (2/47) experienced CR, resulting in a complete resolution of all reversible manifestations of cGVHD

IMBRUVICA® was evaluated for safety and tolerability in pediatric patients with cGVHD who failed 1 or more systemic therapies

IMPORTANT SAFETY INFORMATION (continued)

SPECIFIC POPULATIONS

Pediatric Use: The safety and effectiveness of IMBRUVICA® have not been established for the treatment of cGVHD after failure of one or more lines of therapy in pediatric patients less than 1 year of age. The safety and effectiveness of IMBRUVICA® in pediatric patients have not been established in CLL/SLL, CLL/SLL with 17p deletion, WM, or in patients with mature B-cell non-Hodgkin lymphoma.

In the randomized population from a study that included 35 patients (26 pediatric patients age 5 to less than 17 years) with previously treated mature B-cell non-Hodgkin lymphoma, major hemorrhage and discontinuation of chemoimmunotherapy due to adverse reactions occurred more frequently in the ibrutinib plus chemoimmunotherapy arm compared to the chemoimmunotherapy alone arm.

*Evaluated through Week 25 visit where overall response included complete response or partial response according to the 2014 National Institutes of Health Consensus Development Project Response Criteria.
cGVHD=chronic graft versus host disease, CI=confidence interval, CR=complete response, ORR=overall response rate, PR=partial response.

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The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA® increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA® without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding.

Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections: Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

Cardiac Arrhythmias, Cardiac Failure, and Sudden Death: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA® treatment.

Hypertension: Hypertension occurred in 19% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from a subset of these patients (N=1,124), the median time to onset was 5.9 months (range, 0 to 24 months). In a long-term safety analysis over 5 years of 1,284 patients with B-cell malignancies treated for a median of 36 months (range, 0 to 98 months), the cumulative rate of hypertension increased over time. The prevalence for Grade 3 or greater hypertension was 4% (year 0-1), 7% (year 1-2), 9% (year 2-3), 9% (year 3-4), and 9% (year 4-5); the overall incidence for the 5-year period was 11%. Monitor blood pressure in patients treated with IMBRUVICA®, initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

Please click here for the full Prescribing Information.

Cytopenias: In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, grade 3 or 4 neutropenia occurred in 23% of patients, grade 3 or 4 thrombocytopenia in 8% and grade 3 or 4 anemia in 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (3.9%), occurred among the 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in adult or pediatric patients with cGVHD were fatigue (57%), anemia (49%)*, bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, musculoskeletal pain (30%), pyrexia (30%), muscle spasms (29%), stomatitis (29%), hemorrhage (26%), nausea (26%), abdominal pain (23%), pneumonia (23%), and headache (21%).

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Discontinuation of IMBRUVICA® treatment due to an adverse reaction occurred in 24% of adult patients and 23% of pediatric patients. Adverse reactions leading to dose reduction occurred in 26% of adult patients and 19% of pediatric patients.

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DRUG INTERACTIONS

CYP3A Inhibitors: Co-administration of IMBRUVICA® with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA® are recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA® if strong inhibitors are used short-term (e.g., for ≤ 7 days). Avoid grapefruit and Seville oranges during IMBRUVICA® treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Pediatric Use: The safety and effectiveness of IMBRUVICA® have not been established for the treatment of cGVHD after failure of one or more lines of therapy in pediatric patients less than 1 year of age. The safety and effectiveness of IMBRUVICA® in pediatric patients have not been established in CLL/SLL, CLL/SLL with 17p deletion, WM, or in patients with mature B-cell non-Hodgkin lymphoma.

In the randomized population from a study that included 35 patients (26 pediatric patients age 5 to less than 17 years) with previously treated mature B-cell non-Hodgkin lymphoma, major hemorrhage and discontinuation of chemoimmunotherapy due to adverse reactions occurred more frequently in the ibrutinib plus chemoimmunotherapy arm compared to the chemoimmunotherapy alone arm.

Hepatic Impairment: Patients with cGVHD: Avoid use of IMBRUVICA® in patients with total bilirubin level > 3x upper limit of normal (ULN) (unless of non-hepatic origin or due to Gilbert's syndrome). Reduce recommended dose when administering IMBRUVICA® to patients with total bilirubin level > 1.5 to 3x ULN (unless of non-hepatic origin or due to Gilbert's syndrome).

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EMBRACE AN FDA-APPROVED, cGVHD TREATMENT DEVELOPED FOR CHILDREN

IMBRUVICA® is the first and only once-daily treatment for pediatric cGVHD in patients age 1 to <12 years after failure of 1 or more systemic therapies[1-3]

imbruvica® By Your Side Patient Support

To learn more about IMBRUVICA® By Your Side patient support, call:
1-888-YourSide (1-888-968-7743) Monday-Friday, 8:00 AM-8:00 PM

Eligible patients may pay as little as $0

Eligible patients may pay as little as $0 per prescription of IMBRUVICA®. Rules and maximum limits apply. Patients currently using the IMBRUVICA® Copay Card are not eligible for retroactive billing or reimbursement of previous copays. The IMBRUVICA® Copay Card is available to patients with commercial prescription coverage for IMBRUVICA® who meet eligible criteria. The IMBRUVICA® Copay Card cannot be used by patients receiving prescription reimbursement under federal, state, or government-funded insurance programs, including Medicare Part D, Medicare Advantage Plan, Medicaid, Medigap, VA DOD and TRICARE, or where prohibited by law or the patient's health insurance provider. The IMBRUVICA® Copay program may be updated or discontinued at any time without notice.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage; infections; cardiac arrhythmias, cardiac failure, and sudden death; hypertension; cytopenias; second primary malignancies; tumor lysis syndrome; and embryo-fetal toxicity.

ADVERSE REACTIONS

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*Treatment-emergent decreases (all grades) were based on laboratory measurements.

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References:

1. IMBRUVICA® (ibrutinib) Prescribing Information. **2.** JAKAFI® (ruxolitinib) Prescribing Information. **3.** REZUROCK® (belumosudil) Prescribing Information. **4.** Data on file. **5.** Lee S, Cook EF, Soiffer R, et al. Development and validation of a scale to measure symptoms of chronic graft-versus-host disease. *Biol Blood Marrow Transplant.* 2002;8(8):444–452.

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