Duvelisib (COPIKTRA) is NCCN recommended.†*
See page 12

1L 2L **3L COPIKTRA®** (duvelisib) for CLL/SLL

COPIKTRA is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after ≥2 prior therapies.

Patient Profile Guide

*National Comprehensive Cancer Network® (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.
CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma; 1L, first-line; 2L, second-line; 3L, third-line.

IMPORTANT SAFETY INFORMATION

WARNING: FATAL AND SERIOUS TOXICITIES: INFECTIONS, DIARRHEA OR COLITIS, CUTANEOUS REACTIONS, and PNEUMONITIS

- **Fatal and/or serious infections occurred in 31% of COPIKTRA-treated patients. Monitor for signs and symptoms of infection. Withhold COPIKTRA if infection is suspected.**
- **Fatal and/or serious diarrhea or colitis occurred in 18% of COPIKTRA-treated patients. Monitor for the development of severe diarrhea or colitis. Withhold COPIKTRA.**
- **Fatal and/or serious cutaneous reactions occurred in 5% of COPIKTRA-treated patients. Withhold COPIKTRA.**
- **Fatal and/or serious pneumonitis occurred in 5% of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.**

Find more information on incidence and time to onset of fatal and/or serious adverse reactions on page 2.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

Copiktra® (duvelisib) 15mg | 25mg capsules

IMPORTANT SAFETY INFORMATION

Incidence of serious (including fatal) adverse reactions and time to onset

Adverse reactions N=442	Serious (including fatal)	Fatal	Median onset (all grades)	75% of events occurred by
Infections*	31%	18/442, 4%	3 months	6 months
Diarrhea or colitis	18%	1/442, <1%	4 months	8 months
Cutaneous reactions†	5%	2/442, <1%	3 months	6 months
Pneumonitis	5%	1/442, <1%	4 months	9 months

*The most common serious infections were pneumonia, sepsis, and lower respiratory tract infections. Serious, including fatal, *Pneumocystis jirovecii* pneumonia (PJP) occurred in 1% of patients. Cytomegalovirus (CMV) reactivation/infection occurred in 1% of patients.

†Fatal cases included drug reaction with eosinophilia and systemic symptoms (DRESS) and toxic epidermal necrolysis (TEN). Presenting features for cutaneous reaction serious events were primarily described as pruritic, erythematous, or maculo-papular. Less common presenting features include exanthem, desquamation, erythroderma, skin exfoliation, keratinocyte necrosis, and papular rash.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infections: Serious, including fatal (4%), infections occurred in 31% of patients receiving COPIKTRA (N=442). The most common serious infections were pneumonia, sepsis, and lower respiratory infections. Median time to onset of any grade infection was 3 months, with 75% of cases occurring within 6 months. Treat infections prior to initiation of COPIKTRA. Advise patients to report new or worsening signs and symptoms of infection. Cases of *Pneumocystis jirovecii* pneumonia (PJP) (1%) and cytomegalovirus (CMV) reactivation/infection (1%) occurred in patients taking COPIKTRA. Provide prophylaxis for PJP during treatment and following completion of treatment until the absolute CD4+ T cell count is greater than 200 cells/μL. Consider prophylactic antivirals during COPIKTRA treatment to prevent CMV infection including CMV reactivation.

Diarrhea or Colitis: Serious, including fatal (<1%), diarrhea or colitis occurred in 18% of patients receiving COPIKTRA (N=442). Median time to onset of any grade diarrhea or colitis was 4 months, with 75% of cases occurring by 8 months. The median event duration was 0.5 months. Advise patients to report any new or worsening diarrhea.

Cutaneous Reactions: Serious, including fatal (<1%), cutaneous reactions occurred in 5% of patients receiving COPIKTRA (N=442). Fatal cases included drug reaction with eosinophilia and systemic symptoms (DRESS) and toxic epidermal necrolysis (TEN). Median time to onset of any grade cutaneous reaction was 3 months with a median event duration of 1 month. Presenting features for the serious events were primarily described as pruritic, erythematous, or maculo-papular. Less common presenting features include exanthem, desquamation, erythroderma, skin exfoliation, keratinocyte necrosis, and papular rash. Advise patients to report new or worsening cutaneous reactions.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Pneumonitis: Serious, including fatal (<1%), pneumonitis without an apparent infectious cause occurred in 5% of patients receiving COPIKTRA (N=442). Median time to onset of any grade pneumonitis was 4 months with 75% of cases occurring within 9 months. The median event duration was 1 month with 75% of cases resolving by 2 months.

Hepatotoxicity: Grade 3 and 4 ALT and/or AST elevation developed in 8% and 2%, respectively, of patients receiving COPIKTRA (N=442). Two percent of patients had both an ALT or AST > 3 X ULN and total bilirubin > 2 X ULN. Median time to onset of any grade transaminase elevation was 2 months with a median event duration of 1 month. Monitor hepatic function during treatment with COPIKTRA.

Neutropenia: Grade 3 or 4 neutropenia occurred in 42% of patients receiving COPIKTRA (N=442), with Grade 4 neutropenia occurring in 24% of all patients. Median time to onset of grade ≥3 neutropenia was 2 months. Monitor neutrophil counts at least every 2 weeks for the first 2 months of COPIKTRA therapy, and at least weekly in patients with neutrophil counts < 1.0 Gi/L (Grade 3-4).

Embryo-Fetal Toxicity: COPIKTRA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus and conduct pregnancy testing before initiating COPIKTRA treatment. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose.

ADVERSE REACTIONS

B-cell Malignancies Summary

Fatal adverse reactions within 30 days of the last dose occurred in 8% (36/442) of patients treated with COPIKTRA 25 mg BID. Serious adverse reactions were reported in 289 patients (65%). The most frequent serious adverse reactions that occurred were infection (31%), diarrhea or colitis (18%), pneumonia (17%), rash (5%), and pneumonitis (5%). The most common adverse reactions (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain and anemia.

CLL/SLL

Fatal adverse reactions within 30 days of the last dose occurred in 12% (19/158) of patients treated with COPIKTRA and in 4% (7/155) of patients treated with ofatumumab. Serious adverse reactions were reported in 73% (115/158) of patients treated with COPIKTRA and most often involved infection (38%; 60/158) and diarrhea or colitis (23%; 36/158). The most common adverse reactions with COPIKTRA (≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia and cough.

For specific information on the management of the adverse reactions above, please review *Dose Modifications for Adverse Reactions* within the full Prescribing Information.

DRUG INTERACTIONS

CYP3A Inducers: Coadministration with a strong CYP3A inducer may reduce COPIKTRA efficacy. Avoid coadministration with strong CYP3A4 inducers.

CYP3A Inhibitors: Coadministration with a strong CYP3A inhibitor may increase the risk of COPIKTRA toxicities. Reduce COPIKTRA dose to 15 mg BID when coadministered with a strong CYP3A4 inhibitor.

CYP3A Substrates: Coadministration of COPIKTRA with sensitive CYP3A4 substrates may increase the risk of toxicities of these drugs. Consider reducing the dose of the sensitive CYP3A4 substrate and monitor for signs of toxicities of the coadministered sensitive CYP3A substrate.

To report Adverse Reactions, contact FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch and Secura Bio, Inc. at 1-844-973-2872.

Please see accompanying full Prescribing Information, including Boxed Warning.

Copiktra® (duvelisib) 15mg | 25mg capsules

Experience the efficacy of COPIKTRA® (duvelisib) in 3L CLL/SLL

Heavily pretreated patients

46% Received 2 prior lines of therapy

54% Received ≥3 prior lines of therapy

High-risk patients[2]

52% Bulky disease* (n=102/196)

22% 17p deletion (n=43/196)

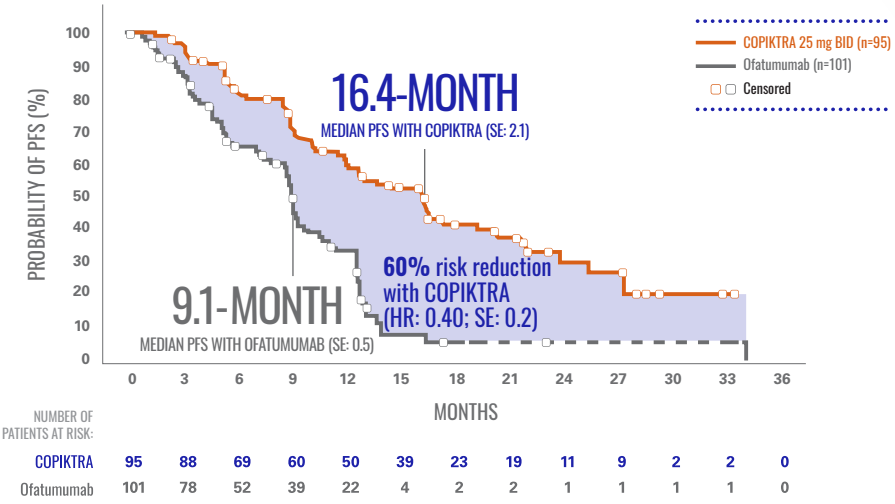
17% *TP53* mutation (n=34/196)

- 69% of patients had unmutated IGHV (n=135/196) and 58% of patients had Rai stage III or IV (n=70/121)[2]

Study features:

DUO was a randomized, open-label, superiority trial comparing COPIKTRA to ofatumumab with a primary endpoint of PFS in adult patients with CLL/SLL who received at least 1 prior therapy (N=319). The approval of COPIKTRA in CLL/SLL was based on a subset analysis of patients with at least 2 prior lines of therapy where the risk:benefit ratio appeared greater in this more heavily pretreated population (n=196). Safety was based on the overall study population (see full Prescribing Information for a detailed study description).

COPIKTRA demonstrated >7-month median PFS advantage vs ofatumumab (n=196)†



COPIKTRA decreased the risk of progression in those with del(17p) and/or *TP53* (n=59/196; HR: 0.36)[3‡]

*Baseline lesion ≥5 cm.[2]
†Kaplan-Meier estimate.
‡This analysis was not powered to show statistical significance in PFS across this prespecified subgroup.[4]

BID, twice daily; HR, hazard ratio; IGHV, immunoglobulin heavy chain variable; PFS, progression-free survival; SE, standard error.

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Established safety profile

Adverse reactions occurring in patients with B-cell malignancies receiving COPIKTRA 25 mg BID

Data reflect exposure to COPIKTRA across 4 clinical trials totaling 442 patients with previously treated hematologic malignancies.

Adverse reactions	COPIKTRA 25 mg BID (N=442)	
	Any grade (%)	Grade ≥3 (%)
Most common adverse reactions (≥20%)		
Diarrhea or colitis*†	50	23
Neutropenia*	34	30
Rash*‡	31	9
Fatigue*	29	5
Pyrexia	26	2
Cough*	25	<1
Nausea*	24	<1
Upper respiratory tract infection*	21	<1
Pneumonia*§	21	15
Anemia*	20	11
Musculoskeletal pain*	20	1
Additional safety[5]		
Bleeding‖	16	3
Arthralgia	10	<1
Hyperglycemia	6	2
Hypertension	5	<1
Atrial fibrillation	3	<1
Tumor lysis syndrome	<1	<1

Adverse reactions can be managed with dose reduction, treatment hold, or discontinuation of COPIKTRA (see Prescribing Information for more detail)

*Grouped term for reactions with multiple preferred terms.

†Diarrhea or colitis includes the preferred terms: colitis, enterocolitis, colitis microscopic, colitis ulcerative, diarrhea, diarrhea hemorrhagic.

‡Rash includes the preferred terms: dermatitis (including allergic, exfoliative, perivascular), erythema (including multiforme), rash (including exfoliative, erythematous, follicular, generalized, macular and papular, pruritic, pustular), TEN and toxic skin eruption, DRESS, drug eruption, SJS.

§Pneumonia includes the preferred terms: all preferred terms containing "pneumonia" except for "pneumonia aspiration," bronchopneumonia, bronchopulmonary aspergillosis.

‖Bleeding includes bruising and petechia.[5]

SJS, Stevens-Johnson syndrome.

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Not an actual patient.

Joseph,* aged 70

Substitute teacher at nearby high school. Married, with 3 grown sons. Tutors neighborhood kids in his spare time. Enjoys attending sporting events.

ECOG 1 **Rai stage III**

Medical history—CLL diagnosed 4.5 years ago

Reason for latest office visit—Patient presented with severe fatigue and pain in the upper-left portion of his abdomen. Physical examination revealed multiple enlarged lymph nodes. Imaging showed widespread bulky lymphadenopathy with no signs suggesting Richter's syndrome. LDH levels were found to be slightly elevated.

1st Line

Ibrutinib

- PR within 5 months
- Maintained response for 42 months before showing signs of progression

2nd Line

Venetoclax and **rituximab**

- After first relapse, 5-week dose ramp-up on venetoclax
- 6-month treatment regimen of venetoclax in combination with rituximab

Current

CLL appears to be refractory to treatment and imaging shows residual lymph node enlargement

***Representative patient profile.**

ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; PR, partial response.

HIGH RISK (cont'd)

Comorbidities:

None

Notable lab findings
Hemoglobin: 9.8 g/dL [normal range: 13.8-17.2 g/dL][6]
WBC: 70 × 10^9/L [normal range: 4.5-11.0 × 10^9/L][7]
ALC: 62 × 10^9/L [normal range: 0.9-2.90 × 10^9/L][8]
Platelet: 94 × 10^9/L [normal range: 150-400 × 10^9/L][9]

Cytogenetics:

FISH: del(17p)

"Hearing I was high risk worried me, but I'm ready to take the next step in my treatment. I haven't had any chemo yet, and I'd like to keep it that way. I'm happy to hear there are other options that don't require infusions."

ALC, absolute lymphocyte count; FISH, fluorescence in situ hybridization; WBC, white blood cell.

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INTOLERANT TO CURRENT THERAPY

Not an actual patient.

Suzanne,* aged 58

Ultrasound technician. Married, with 2 college-aged daughters. An avid reader who looks forward to her monthly book club meetings.

ECOG 1 **Rai stage IV**

Medical history—CLL diagnosed 4 years ago

Reason for latest office visit—Patient presented to her primary care physician with symptoms of chest pain, fatigue, and heart palpitations and was referred to her cardiologist. After several attempts to regulate and stabilize the atrial fibrillation without success, her cardiologist recommended further discussion with her oncologist to determine the best treatment option.

1st Line	2nd Line	Current
FCR • CR after 6 cycles • 24 months in remission before relapse	**Ibrutinib** • PR within 6 months • After 3 months on ibrutinib maintenance, patient developed atrial fibrillation that could not be managed with cardiology intervention	Hematologist discontinued treatment

***Representative patient profile.**

CR, complete response; FCR, Fludarabine+cyclophosphamide+rituximab.

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INTOLERANT TO CURRENT THERAPY (cont'd)

Comorbidities:

Chronic kidney disease

Notable lab findings
Hemoglobin: 11.4 g/dL [normal range: 12.1-15.1 g/dL][6]
WBC: 45 × 10^9/L [normal range: 4.5-11.0 × 10^9/L][7]
ALC: 41 × 10^9/L [normal range: 0.9-2.90 × 10^9/L][8]
Platelet: 90 × 10^9/L [normal range: 150-400 × 10^9/L][9]

Cytogenetics:

FISH: del(11q)

Mutational analysis:

***TP53* wild-type**
IGHV-mutated

"I had a side effect with my last treatment and my doctor recommended I switch to a different medication. I'm encouraged to hear that there are other options that may be the right fit for me, and I'm ready to move forward."

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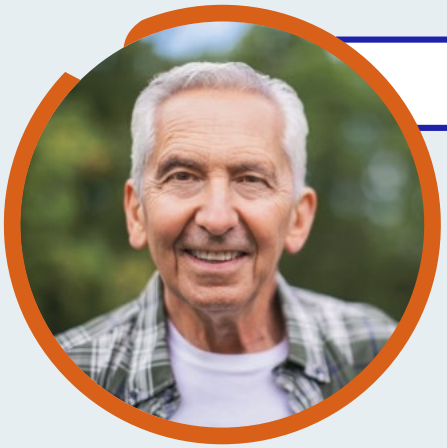

Not an actual patient.

Eddie,* aged 83

Retired accountant. Married, with 2 children and 4 grandchildren. Enjoys putting jigsaw puzzles together with his older grandchildren. Lives an hour away from the treatment clinic.

ECOG 1 **Rai stage** III

Medical history—CLL diagnosed 4.5 years ago

Reason for latest office visit—Patient presented with a low-grade fever and complains of new-onset night sweats. Physical examinations revealed left cervical lymphadenopathy and splenomegaly. Imaging showed enlarged lymph nodes.

1st Line

Obinutuzumab and **chlorambucil**

- PR after 6 cycles
- Maintained response for 22 months before disease progression

2nd Line

Ibrutinib

- PR after 6 months

Current

Shows signs of disease progression at 2-year follow-up visit

***Representative patient profile.**

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FRAIL/ELDERLY (cont'd)

Comorbidities:

Osteoarthritis **Hypertension**

Notable lab findings
Platelet: 160 × 10^9/L [normal range: 150-400 × 10^9/L][9]
Hemoglobin: 10.4 g/dL [normal range: 13.8-17.2 g/dL][6]
WBC: 30 × 10^9/L [normal range: 4.5-11.0 × 10^9/L][7]
ALC: 26 × 10^9/L [normal range: 0.9-2.90 × 10^9/L][8]

Cytogenetics:

FISH: del(11q)

Mutational analysis:

IGHV-unmutated

"I liked my last treatment because I didn't have to go in for infusions and my wife got a break from driving me. I would prefer not to go back to an IV if there are oral options available."

IV, intravenous.

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DUVELISIB IS AN NCCN PREFERRED REGIMEN FOR ADULT PATIENTS WITH OR WITHOUT DEL(17P)/*TP53* MUTATION WITH RELAPSED OR REFRACTORY CLL OR SLL[1*†] (SEE FDA-APPROVED INDICATION BELOW)

For adults with relapsed or refractory CLL/SLL after at least 2 prior therapies,

Consider COPIKTRA® (duvelisib) for appropriate patients

Chemo-free oral monotherapy

- COPIKTRA oral monotherapy offers flexible dosing, with a 25-mg recommended dose and a 15-mg strength available to help manage adverse reactions[‡]
- With COPIKTRA, patients have the convenience of taking their treatment at home or while away (without food restrictions)[10]

Demonstrated clinical activity

- COPIKTRA provided 16.4-month median PFS vs 9.1 months with ofatumumab (HR: 0.40; SE: 0.2) in the DUO clinical trial (see description inside)[§]

Established safety profile

- Boxed Warning: Fatal and/or Serious adverse reactions included infections, diarrhea or colitis, cutaneous reactions, and pneumonitis
- Additional Warnings and Precautions include hepatotoxicity, neutropenia, and embryo-fetal toxicity
- Serious adverse reactions in CLL/SLL were reported in 73% of patients treated with COPIKTRA and most often involved infection and diarrhea or colitis
- The most common adverse reactions in CLL/SLL (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia, and cough

*See NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for specific recommendation.

†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.

‡COPIKTRA should be taken BID in 28-day cycles until disease progression or unacceptable toxicity.

§Kaplan-Meier estimate.

Please see the Boxed Warning on cover, Important Safety Information throughout, and the accompanying full Prescribing Information.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V.1.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed August 23, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Data on file, 015. **3.** Data on file, 009. **4.** Flinn IW, Hillmen P, Montillo M, et al. The phase 3 DUO trial: duvelisib vs ofatumumab in relapsed and refractory CLL/SLL. *Blood*. 2018;132(23):2446-2455. **5.** Data on file, 013. **6.** Hemoglobin. MedlinePlus Web site. https://medlineplus.gov/ency/article/003645.htm. Updated June 3, 2019. Accessed July 2, 2019. **7.** WBC count. MedlinePlus Web site. https://medlineplus.gov/ency/article/003643.htm. Updated June 3, 2019. Accessed July 2, 2019. **8.** Normal lab values. CLL Society Web site. https://cllsociety.org/toolbox/normal-lab-values/. Accessed August 23, 2019. **9.** Platelet count. MedlinePlus Web site. https://medlineplus.gov/ency/article/003647.htm. Updated June 3, 2019. Accessed July 2, 2019. **10.** Weingart SN, Brown E, Bach PB, et al. NCCN Task Force Report: oral chemotherapy. *J Natl Compr Canc Netw*. 2008;6(suppl 3):S1-S14.

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