COPIKTRA® (duvelisib)

Your guide to dosing and managing adverse reactions

COPIKTRA is indicated for the treatment of adult patients with:

- Relapsed or refractory CLL or SLL after ≥2 prior therapies
- Relapsed or refractory FL after ≥2 prior systemic therapies. Accelerated approval was based on ORR and continued approval may be contingent upon confirmatory trials

CLL, chronic lymphocytic leukemia; FL, follicular lymphoma; ORR, overall response rate; SLL, small lymphocytic lymphoma.

IMPORTANT SAFETY INFORMATION

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

- Fatal and/or serious infections occurred in 31% (4% fatal) 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% (<1% fatal) of COPIKTRA-treated patients. Monitor for the development of severe diarrhea or colitis. Withhold COPIKTRA.
- Fatal and/or serious cutaneous reactions occurred in 5% (<1% fatal) of COPIKTRA-treated patients. Withhold COPIKTRA.
- Fatal and/or serious pneumonitis occurred in 5% (<1% fatal) 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

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.

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

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

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.

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.

Copiktra® (duvelisib) 15mg | 25mg capsules

IMPORTANT SAFETY INFORMATION (cont'd)

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 (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia and cough.

FL

Serious adverse reactions were reported in 58% of patients and most often involved diarrhea or colitis, pneumonia, renal insufficiency, rash, and sepsis. The most common adverse reactions (≥20% of patients) were diarrhea or colitis, nausea, fatigue, musculoskeletal pain, rash, neutropenia, cough, anemia, pyrexia, headache, mucositis, abdominal pain, vomiting, transaminase elevation, and thrombocytopenia.

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):

1 oral capsule (monotherapy)

2 doses per day (BID)

3 3L treatment of CLL/SLL and FL*

*COPIKTRA is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after ≥2 prior therapies and for relapsed or refractory FL after ≥2 prior systemic therapies. Accelerated approval in FL was based on ORR and continued approval may be contingent upon confirmatory trials.

3L, third-line.

Dosing guidelines:

- COPIKTRA is an oral, chemo-free monotherapy taken in 28-day cycles until disease progression or unacceptable toxicity
- The recommended dose is 25 mg BID
- The capsules should be swallowed whole. Advise patients not to open, break, or chew the capsules
- Advise patients that if a dose is missed by fewer than 6 hours, to take the missed dose right away and take the next dose as usual
- If a dose is missed by more than 6 hours, advise patients to wait and take the next dose at the usual time

Copiktra® (duvelisib) 15mg | 25mg capsules

COPIKTRA® (duvelisib) is available in 2 dosage strengths

The COPIKTRA dose is taken twice daily, without food restrictions

Recommended dose

25 mg

Dose to help manage adverse reactions

15 mg

Dose modifications:

- Reduce the dose of COPIKTRA to 15 mg BID when coadministered with strong CYP3A4 inhibitors (eg, ketoconazole)
- Dose modification and toxicity management guidelines are available for select adverse reactions observed with COPIKTRA. **Please see the adverse reaction management tables on pages 15-19 for specific dose modification information**

Prophylaxis recommendations:

- Provide prophylaxis for PJP during treatment with COPIKTRA
- Following completion of COPIKTRA treatment, continue PJP prophylaxis until the absolute CD4+ T-cell count is greater than 200 cells/µL
- Withhold COPIKTRA in patients with suspected PJP of any grade, and permanently discontinue if PJP is confirmed
- Consider prophylactic antivirals during COPIKTRA treatment to prevent CMV infection, including CMV reactivation

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for CLL/SLL recommend PJP prophylaxis with sulfamethoxazole/trimethoprim or equivalent during treatment with duvelisib and until the absolute CD4+ T-cell count is >200 cells/µL.[1]*

*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.

BID, twice daily; CMV, cytomegalovirus; PJP, *Pneumocystis jirovecii* pneumonia.

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

COPIKTRA may be a convenient option for your patients

Oral COPIKTRA offers patients the convenience of taking their treatment

At home

or

While away[2]

Patients don't need to travel to a clinic to receive treatment, which can help avoid[2]:

- Finding transportation and parking
- Time spent waiting for the IV setup and infusion

Review the COPIKTRA dosing and side effect information with your patients

- The starter kit is a helpful resource to get your patients started on treatment and includes a patient-friendly reference card that explains how to take the medication

Ask your sales representative for a patient starter kit.

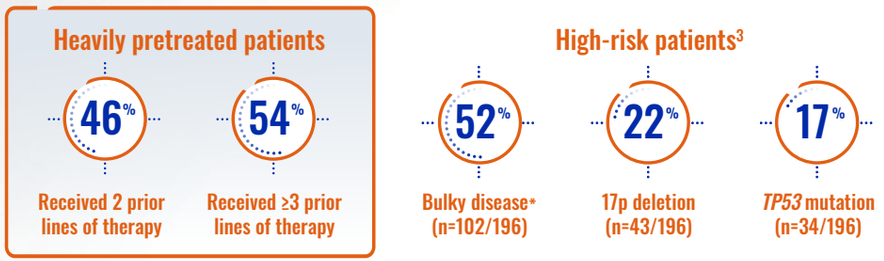
IV, intravenous.

Copiktra® (duvelisib) 15mg | 25mg capsules

COPIKTRA® (duvelisib) clinical trial experience

DUO trial: CLL/SLL

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.



- 69% of patients had unmutated IGHV (n=135/196) and 58% of patients had Rai stage III or IV (n=70/121)[3]

Primary endpoint: 16.4-month median PFS with COPIKTRA (n=95; SE: 2.1) vs 9.1-month median PFS with ofatumumab (n=101; SE: 0.5)

- 60% risk reduction with COPIKTRA (HR: 0.40; SE: 0.2)

In the overall study population, patients with CLL/SLL received COPIKTRA 25 mg orally twice daily (n=158)		
11.6 months median duration of treatment	**49% of patients** were exposed for ≥1 year	**29% of patients** had their dose reduced due to adverse reactions†

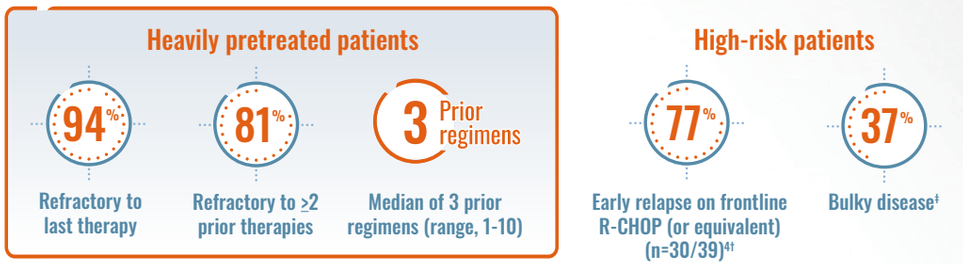
- Serious adverse reactions were reported in 73% of CLL/SLL patients (n=115/158) and most often involved infection (38% of patients; n=60/158) and diarrhea or colitis (23% of patients; n=36/158)
- The most common adverse reactions with COPIKTRA (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia, and cough

*Baseline lesion ≥5 cm.
†Most often due to diarrhea or colitis and rash.
HR, hazard ratio; IGHV, immunoglobulin heavy chain variable; PFS, progression-free survival; SE, standard error.

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

DYNAMO trial: FL[4]

DYNAMO was a single-arm, open-label trial with a primary endpoint of ORR in patients with measurable iNHL who were refractory* to rituximab (monotherapy or in combination) and to either chemotherapy or radioimmunotherapy. Efficacy in FL (n=83) was based on ORR and DOR as assessed by IRC. Safety was based on 4 clinical trials (N=442). Accelerated approval may be contingent upon confirmatory trials.



Primary endpoint: 42% ORR in heavily pretreated FL (n=35/83; 95% CI: 31-54)[§]

Patients with FL received COPIKTRA 25 mg orally twice daily (N=96)		
24 weeks median duration of treatment	**46% of patients** exposed for ≥6 months	**23% of patients** had their dose reduced due to an adverse reaction[‖]

- Serious adverse reactions were reported in 58% of patients with FL and most often involved diarrhea or colitis, pneumonia, renal insufficiency, rash, and sepsis
- The most common adverse reactions (≥20% of patients with FL) were diarrhea or colitis, nausea, fatigue, musculoskeletal pain, rash, neutropenia, cough, anemia, pyrexia, headache, mucositis, abdominal pain, vomiting, transaminase elevation, and thrombocytopenia

Median time to first dose modification or discontinuation was 4 months (range, 0.1 to 27 months)

*Refractory disease was defined as less than a partial remission or relapse within 6 months after the last dose.
†Early relapse was defined as no response during treatment, progressive disease in less than 2 years, or time to next treatment in less than 2 years.
‡Baseline lesion ≥5 cm.
§One patient achieved a complete response and 34 patients achieved partial responses.
‖Most often due to transaminase elevation, diarrhea or colitis, lipase increased, and infection.
CI, confidence interval; DOR, duration of response; iNHL, indolent non-Hodgkin lymphoma; IRC, independent review committee; R-CHOP, rituximab-cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone.

Copiktra® (duvelisib) 15mg | 25mg capsules

Additional data: dose modification patterns from an analysis of the phase 3 DUO trial in CLL/SLL

A retrospective analysis examined dose modifications and their impact on response to COPIKTRA[5]*

Study features and limitations (see DUO study description on page 8):

- Data from a retrospective analysis of patients who were dose interrupted or dose reduced in the phase 3 DUO trial (n=158)
- This analysis was not powered to show statistical significance in these subsets

Dose modifications[5]

- Dose interruptions (DI) occurred more frequently than dose reductions (DR) in patients treated with COPIKTRA (80% vs 27%)
- The most common adverse events of special interest (AESIs) resulting in DI or DR included diarrhea or colitis, infection, cutaneous reactions, neutropenia, hepatotoxicity (transaminase elevation), and pneumonitis†
  - In most cases, AESIs did not lead to discontinuation‡
- The median time to first DI and DR occurred within the first 6 months of treatment (DI, 4 months [range, 0.1 to 25 months]; DR, 5 months [range, 1 to 23 months])
  - DI typically coincided with time to onset of AESIs (median time to onset across AESIs after starting COPIKTRA ranged from 2.2 to 4.3 months)
- The median durations of DI and DR were 2 weeks (range, 1 day to 19 weeks) and 17 weeks (range, 2 days to 98 weeks), respectively

*Response was assessed before and after dose modifications, and PFS was assessed in patients with and without dose modifications. Response was analyzed using descriptive statistics, and PFS was estimated using Kaplan-Meier methods.

†AESIs related to COPIKTRA were defined as groupings of infections, diarrhea, colitis, neutropenia, cutaneous reactions, alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) elevation, and pneumonitis.

‡Discontinuations occurred in ≤10% of COPIKTRA-treated patients (10% diarrhea/colitis, 7% infections, 4% cutaneous reactions, 3% pneumonitis, 1% neutropenia, 1% transaminase elevation).

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

Impact of dose interruptions (DI)[6]

- Among patients who received ≥2 prior therapies (n=93) and responded to COPIKTRA (n=75/93), median time to first response occurred prior to DI
- Response status improved or remained stable in most patients who had ≥1 DI when followed by 3 or more weeks of COPIKTRA
  - 74% after DI of >1 week (n=26/35)
  - 63% after DI of >2 weeks (n=19/30)

Similar median PFS in patients with and without DI within the first 3 months of therapy[7]

DI duration	≥1 DI	No DI
>1 week	20.5 months (n=16; 95% CI: 5.9-NE)	16.5 months (n=68; 95% CI: 12.8-24)
>2 weeks	22.1 months (n=12; 95% CI: 5.9-NE)	16.5 months (n=72; 95% CI: 12.8-21.9)

Impact of dose reductions (DR)[6]

- Among patients who received ≥2 prior therapies (n=93) and responded to COPIKTRA (n=75/93), median time to first response occurred prior to DR
- Response to COPIKTRA was maintained in 50% of patients for ≥90 days after DR (n=6/12)

PFS was maintained in patients with DR vs those without DR within the first 3 months of therapy[7]

Efficacy endpoint	≥1 DR	No DR
Median PFS	27.6 months (n=7; 95% CI: 4.4-27.6)	16.4 months (n=77; 95% CI: 12.1-20.5)

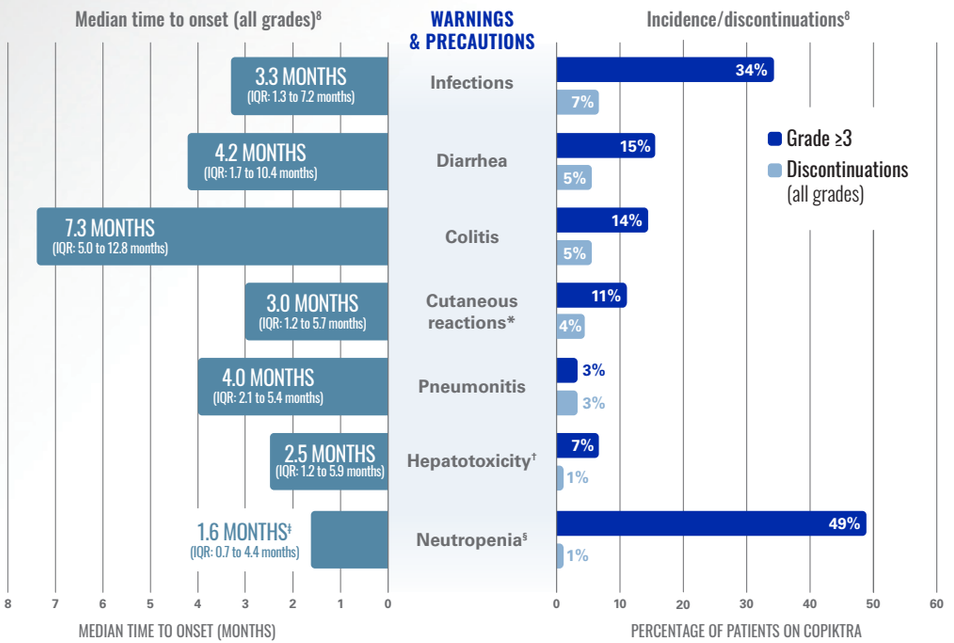
In this retrospective analysis, DI or DR did not notably impact efficacy outcomes with COPIKTRA and may contribute to the effective management of TEAEs[5]

NE, not evaluated; TEAEs, treatment-emergent adverse events.

Copiktra® (duvelisib) 15mg | 25mg capsules

Incidence of adverse reactions and discontinuation rates in CLL/SLL

36% of patients with CLL/SLL (n=57/158) discontinued COPIKTRA, most often due to diarrhea or colitis, infection, and rash



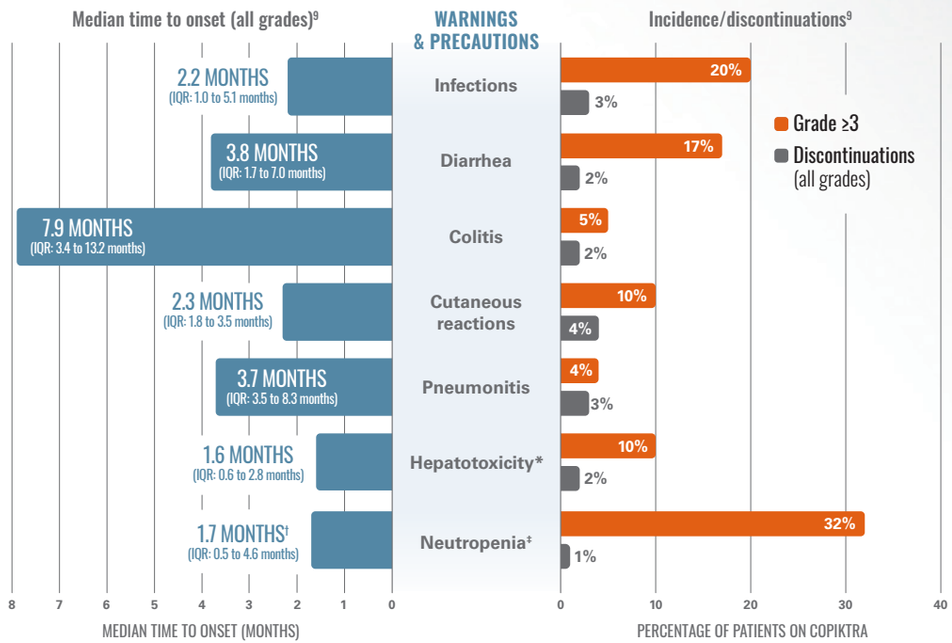
- COPIKTRA is indicated for the treatment of adult patients with relapsed or refractory CLL or SLL after ≥2 prior therapies
- Median adverse event duration for diarrhea or colitis was 0.5 months (range, 1 day to 29 months); 1 month, respectively, for hepatotoxicity (range, 1 day to 16 months), pneumonitis, and cutaneous reactions (range, 1 day to 37 months)‖

*Cutaneous reactions was defined as the onset of rash.
†Hepatotoxicity was defined as an elevation in ALT and/or AST.
‡Median time to onset based on grade ≥3 neutropenia.
§Grade ≥3 neutropenia was defined as an absolute neutrophil count <1.0 Gi/L.
‖For B-cell malignancies (N=442).
IQR, interquartile range (25th to 75th percentile).

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

Incidence of adverse reactions and discontinuation rates in FL

29% of patients with FL (n=28/96) discontinued COPIKTRA, most often due to diarrhea or colitis and rash



- COPIKTRA is indicated for the treatment of adult patients with relapsed or refractory FL after ≥2 prior systemic therapies. Accelerated approval was based on ORR and continued approval may be contingent upon confirmatory trials
- Median duration of exposure was 9 months (range, 0.1-53 months), with 36% of patients (n=160/442) having at least 1 year of exposure

*Hepatotoxicity was defined as an elevation in ALT and/or AST.
†Median time to onset based on grade ≥3 neutropenia.
‡Grade ≥3 neutropenia was defined as an absolute neutrophil count <1.0 Gi/L.

Copiktra® (duvelisib) 15mg | 25mg capsules

Recommended dosing modifications to manage adverse reactions

COPIKTRA oral monotherapy offers flexible dosing

Initial dose	 25 mg BID
Dose reduction	 15 mg BID
Subsequent dose modification	**DISCONTINUE** COPIKTRA if patient is unable to tolerate 15 mg BID

Adverse reactions can generally be managed by dose interruption, dose reduction, or discontinuation[5]

Assessing the severity of adverse reactions[10]

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only
Grade 2	Moderate; limiting age-appropriate instrumental activities of daily living (ADL)
Grade 3	Severe or medically significant but not immediately life-threatening; disabling; limiting self-care ADL
Grade 4	Life-threatening consequences

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

Nonhematologic adverse reaction management

Grade	Recommended management
INFECTIONS	
Grade 3 or higher infection	**WITHHOLD UNTIL RESOLVED** **RESUME AT THE SAME OR REDUCED DOSE**
Clinical CMV infection or viremia (positive PCR or antigen test)	**WITHHOLD UNTIL RESOLVED** **RESUME AT THE SAME OR REDUCED DOSE** • If resumed, monitor patients for CMV reactivation (by PCR or antigen test) at least monthly
	Additional considerations: Consider prophylactic antivirals during treatment to prevent CMV infection and reactivation • In the clinical trials, most patients who received prophylaxis received acyclovir or valacyclovir[11]
PJP	**WITHHOLD** until evaluated for suspected PJP **DISCONTINUE** for confirmed PJP Provide prophylaxis for PJP during treatment
	Additional considerations: • Following completion of COPIKTRA, continue prophylaxis until the absolute CD4+ T-cell count is greater than 200 cells/μL • Most patients in the trials received sulfamethoxazole/trimethoprim[11]

CMV, cytomegalovirus; PCR, polymerase chain reaction; PJP, *Pneumocystis jirovecii* pneumonia.

Symbol key

✓	No change	▶	Resume at same dose	✕	Discontinue
▽	Withhold	▼	Resume at reduced dose		

Copiktra® (duvelisib) 15mg | 25mg capsules

Nonhematologic adverse reaction management (cont'd)

Grade	Recommended management
NONINFECTIOUS DIARRHEA OR COLITIS*	
Mild/moderate diarrhea (grade 1-2) Up to 6 stools per day over baseline and responsive to antidiarrheal agents OR **Colitis (grade 1)** Asymptomatic inflammation of the colon	**NO CHANGE IN DOSE** • **INITIATE** supportive therapy with antidiarrheal agents as appropriate • **MONITOR** at least weekly until resolved
	Additional considerations: In the 442 safety cohort, 50% of patients who experienced diarrhea or colitis (all grades) received treatment (n=113/222). Treatments included systemic steroids, antidiarrheal, anti-inflammatory agents, antibiotics, and antifungals. **The most common treatment was loperamide and budesonide**[12] • 87% of patients who were treated had an outcome of resolved or recovered
Mild/moderate diarrhea (grade 1-2) Up to 6 stools per day over baseline and unresponsive to antidiarrheal agents	**WITHHOLD UNTIL RESOLVED** • **INITIATE** supportive therapy with enteric acting steroids (eg, budesonide) • **MONITOR** at least weekly until resolved **RESUME AT REDUCED DOSE**
Abdominal pain, stool with mucus or blood, change in bowel habits, peritoneal signs OR **Severe diarrhea (grade 3)** >6 stools per day over baseline	**WITHHOLD UNTIL RESOLVED** • **INITIATE** supportive therapy with enteric acting steroids (eg, budesonide) or systemic steroids • **MONITOR** at least weekly until resolved **RESUME AT REDUCED DOSE** **DISCONTINUE** for recurrent grade 3 colitis or recurrent colitis of any grade
	Additional considerations: Perform a diagnostic workup to determine etiology, including colonoscopy
Life-threatening	**DISCONTINUE**

*Severe colitis is inflammation of the colon, including enterocolitis, microscopic colitis, and ulcerative colitis.

Grade	Recommended management
CUTANEOUS REACTIONS	
Grade 1-2	**NO CHANGE IN DOSE** • **INITIATE** supportive care with emollients, antihistamines (for pruritus), or topical steroids • **MONITOR** closely
	Additional considerations: Review all concomitant medications and **discontinue any medications potentially contributing to the event**
Grade 3	**WITHHOLD UNTIL RESOLVED** • **INITIATE** supportive care with emollients, antihistamines (for pruritus), or topical or systemic steroids • **MONITOR** at least weekly until resolved **RESUME AT REDUCED DOSE** **DISCONTINUE** if severe cutaneous reaction does not improve, worsens, or recurs
	Additional considerations: Presenting features for serious events were primarily pruritic, erythematous, and maculo-papular. Less common presenting features include exanthem, desquamation, erythroderma, skin exfoliation, keratinocyte necrosis, and papular rash
Life-threatening	**DISCONTINUE**
SJS, TEN, DRESS (Any grade)	**DISCONTINUE**

SJS, Stevens-Johnson syndrome.

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

Copiktra® (duvelisib) 15mg | 25mg capsules

Nonhematologic adverse reaction management (cont'd)

Grade	Recommended management
PNEUMONITIS WITHOUT SUSPECTED INFECTIOUS CAUSE	
Moderate (grade 2) symptomatic pneumonitis	**WITHHOLD UNTIL RESOLVED** • **TREAT** with systemic steroid therapy **RESUME AT REDUCED DOSE** if pneumonitis recovers to Grade 0 or 1 **DISCONTINUE** if noninfectious pneumonitis recurs or patient does not respond to steroid therapy
	Additional considerations: Withhold COPIKTRA in patients with new or progressive pulmonary signs and symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on a radiologic exam, or a decline by more than 5% in oxygen saturation; and evaluate for etiology
Severe (grade 3) or life-threatening pneumonitis	**DISCONTINUE** • **TREAT** with systemic steroid therapy
ALT/AST ELEVATION	
3 to 5 x upper limit of normal (ULN) (grade 2)	**NO CHANGE IN DOSE** • **MONITOR** at least weekly until return to <3 x ULN
>5 to 20 x ULN (grade 3)	**WITHHOLD** • **MONITOR** at least weekly until return to <3 x ULN **RESUME AT SAME DOSE** (first occurrence) **RESUME AT REDUCED DOSE** (subsequent occurrence)
>20 x ULN (grade 4)	**DISCONTINUE**

COPIKTRA does not have any contraindications listed in the Prescribing Information

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

Hematologic adverse reaction management

Grade	Recommended management
NEUTROPENIA	
ANC 0.5 to 1.0 Gi/L	**NO CHANGE IN DOSE** • **MONITOR** ANC at least weekly
ANC <0.5 Gi/L	**WITHHOLD** • **MONITOR** ANC until >0.5 Gi/L **RESUME AT SAME DOSE** (first occurrence) **RESUME AT REDUCED DOSE** (subsequent occurrence)
	Additional considerations: In the trials, around 13% of patients received treatment with granulocyte colony stimulating factor for an event of neutropenia[12]
THROMBOCYTOPENIA	
Platelet count 25 to <50 Gi/L (grade 3) With grade 1 bleeding	**NO CHANGE IN DOSE** • **MONITOR** platelet counts at least weekly
Platelet count 25 to <50 Gi/L (grade 3) with grade 2 bleeding OR **Platelet count <25 Gi/L (grade 4)**	**WITHHOLD** • **MONITOR** platelet counts until ≥25 Gi/L and resolution of bleeding (if applicable) **RESUME AT SAME DOSE** (first occurrence) **RESUME AT REDUCED DOSE** (subsequent occurrence)

ANC, absolute neutrophil count.

Copiktra® (duvelisib) 15mg | 25mg capsules

Patient support services

Secura Care™ Patient Support Program offers help with insurance verification and patient support programs.†

The Patient Support Program includes:

- The Co-Pay Program offers quick and easy access to co-pay assistance for COPIKTRA.
- With the Co-Pay Program, eligible, commercially insured patients pay no more than $5 per month up to an annual maximum of $25,000 per calendar year.
- The Secura Bio Quickstart Program offers the first cycle of drug at no cost to eligible patients who have a delay of 5 days or more in obtaining prior authorization.
- Encourage your patients to find out if they are eligible for the Co-Pay Program by calling Secura Care™:
  844-9SECURA [(844) 973-2872] Monday to Friday 10:00 AM to 7:00 PM ET
- The Patient Assistance Program is available to support low-income and uninsured patients. Please have your patient contact Secura Care™ to understand if they qualify.

To access Secura Care™, please call:
844-9SECURA [(844) 973-2872] Monday to Friday 10:00 AM to 7:00 PM ET
Or visit our website at: https://securabio.com/patient-support-programs

† Limitations apply. This offer is not valid under Medicare, Medicaid, or any other federal or state program. Secura Bio, Inc. reserves the right to rescind, revoke, or amend this program without notice.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V.2.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed October 08, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** 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. **3.** Data on file,015. **4.** Flinn IW, Miller CB, Ardeshna KM, et al. DYNAMO: a phase II study of duvelisib (IPI-145) in patients with refractory indolent non-Hodgkin lymphoma [published online February 11, 2019]. *J Clin Oncol*. doi:10.1200/JCO.18.00915. **5.** Flinn IW, Montillo M, Illés Á, et al. Effect of dose modifi cationson response to duvelisib in patients with relapsed/refractory CLL/SLL in the DUO trial. Poster presented at: 2019 American Society of Clinical Oncology Annual Meeting; May 31-June 4, 2019; Chicago, IL. **6.** Data on file, 018. **7.** Data onfile, 019. **8.** Data on file,01 1. **9.** Data on file,008. **10.** Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. National Cancer Institute Web site. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_ Quick_ Reference_8.5x11.pdf. Published November 27, 2017. Accessed September 17, 2019. **11.** Data on file, 014. **12.** Data on file, 012.

SECURA BIO™
Secura Bio, Inc.
1995 Village Center Circle, Suite 128
Las Vegas, NV 89134

11/20 USCPR2007701

Copiktra® (duvelisib) 15mg | 25mg capsules