רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

Venclexta 10, 50 and 100 mg tablets

ונקלקסטה 10, 50 ו-100 מ"ג טבליות

Film coated tablets

Venetoclax 10, 50 and 100 mg

חברת AbbVie Biopharmaceuticals Ltd. מבקשת להודיע כי העלון לרופא ולצרכן של התכשיר שבנדון עודכנו.
בהודעה זו מצוינים סעיפים בהם נעשה שינוי מהותי או שינוי המהווה החמרה. בהודעה זו ובעלונים המצורפים מידע שהתווסף מסומן באדום ומידע שהוסר מסומן ~~בכחול~~.

ההתוויות המאושרות לתכשיר:

VENCLEXTA is indicated for the treatment of:

1.1 Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

VENCLEXTA in combination with rituximab or as monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL), who have received at least one prior therapy.

VENCLEXTA in combination with obinutuzumab is indicated for the treatment of patients with previously untreated chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL).

1.2 Acute Myeloid Leukemia

VENCLEXTA in combination with a hypomethylating agent or in combination with low dose cytarabine is indicated for newly diagnosed patients with acute myeloid leukemia (AML) who are ineligible for intensive chemotherapy.

העלון לרופא עודכן בסעיפים הבאים:

RMP section:

~~Education and Communication to potential prescribers~~
~~The marketing of Venclexta is subject to a risk management plan (RMP). Prescribers of this product should undergo education and training regarding the product emphasizing important safety information.~~

Patient Quick Start Guide
The 'Patient Quick Start Guide', includes instructions regarding the correct medication schedule and safety information for CLL/SLL Patients. Please explain to the patient the need to review the guide before starting treatment. The 'Patient Quick Start Guide' is included in the 'CLL/SLL Starting Pack'.

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6.1 Clinical Trials Experience

Table 11~~and Table 12~~ presents adverse reactions ~~and laboratory abnormalities, respectively,~~ identified in the MURANO trial. ~~The MURANO trial was not designed to demonstrate a statistically significant difference in adverse reaction rates for VEN+R as compared with B+R, for any specific adverse reaction or laboratory abnormality.~~

Table 11. Common (≥10%) Adverse Reactions ~~Reported with ≥5% Higher All Grade or ≥2% Higher Grade ≥3 Incidence~~ in Patients Treated with VEN+R ~~Compared with B+R~~

Adverse Reaction by Body System	VENCLEXTA + Rituximab Followed by Single Agent VENCLEXTA (N=194)		Bendamustine + Rituximab (N=188)	
	All Grades (%)	Grade ≥3 (%)	All Grades (%)	Grade ≥3 (%)
Blood ~~&~~and lymphatic system disorders				
Neutropenia[a]	65	62	50	44
Anemia[a]	16	11	23	14
Gastrointestinal disorders				
Diarrhea	40	3	17	1
Nausea	21	1	34	1
Constipation	14	<1	21	0
Infections and~~&~~ infestations				
Upper respiratory tract infection[a]	39	2	23	2
Lower respiratory tract infection[a]	18	2	10	2
Pneumonia[a]	10	7	14	10
~~**Musculoskeletal and connective tissue disorders**~~				
~~Musculoskeletal pain[a]~~	~~19~~	~~1~~	~~13~~	~~0~~
~~**Metabolism and nutrition**~~ **General disorders and administration site conditions**				
~~Tumor lysis syndrome~~ Fatigue[a]	22~~3~~	2~~3~~	~~1~~26	<1
[a]Includes multiple adverse reaction terms.				

Other clinically important adverse reactions (all grades) reported in ≥~~<~~10% of patients ~~in the~~ treated with VEN+R ~~arm in MURANO, and other important adverse reactions~~ are presented below:

Blood and~~&~~ lymphatic system disorders: ~~anemia (16%), thrombocytopenia (15%),~~ febrile neutropenia (4%)

Gastrointestinal disorders: ~~nausea (21%), constipation (14%), abdominal pain (13%), mucositis (10%),~~ vomiting (8%)

~~**Respiratory disorders:** cough (22%)~~

~~**General disorders and administration site conditions:** fatigue (22%), pyrexia (15%)~~

~~**Skin disorders:** rash (13%)~~

~~**Nervous system and psychiatric disorders:** headache (11%), insomnia (11%)~~

Infections and~~&~~ infestations: ~~pneumonia (10%),~~ sepsis (≤1%)

Metabolism and nutrition disorders: tumor lysis syndrome (3%)

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Table 12. ~~Common (≥10%)~~ New or Worsening Clinically Important Laboratory Abnormalities Occurring at ~~≥5% (Any Grade) or ≥2% (Grade 3 or 4) Higher Incidence~~ ≥10% (All Grades) in Patients Treated with VEN+R ~~Compared with B+R~~

Laboratory Abnormality	VENCLEXTA + Rituximab (N=194)		Bendamustine + Rituximab (N=188)	
~~Laboratory Abnormality~~	All Grades[a] (%)	Grade 3 or 4 (%)	All Grades[a] (%)	Grade 3 or 4 (%)
Hematology				
Leukopenia	89	46	81	35
Lymphopenia	87	56	79	55
Neutropenia	86	64	84	59
Anemia	50	12	63	15
Thrombocytopenia	49	15	60	20
Chemistry				
Blood creatinine increased	77	<1	78	1
Hypocalcemia	62	5	51	2
~~Hypophosphatemia~~	~~57~~	~~14~~	~~35~~	~~4~~
~~AST/SGOT increased~~	~~46~~	~~2~~	~~31~~	~~3~~
Hyperuricemia	36	36	33	33
~~Alkaline phosphatase increased~~	~~35~~	~~1~~	~~20~~	~~1~~

~~Hyperbilirubinemia~~	~~33~~	~~4~~	~~26~~	~~3~~
~~Hyponatremia~~	~~30~~	~~6~~	~~20~~	~~3~~
~~Hypokalemia~~	~~29~~	~~6~~	~~18~~	~~3~~
Hyperkalemia	24	3	19	2
~~Hypernatremia~~	~~24~~	~~1~~	~~13~~	~~0~~
~~Hypoglycemia~~	~~16~~	~~2~~	~~7~~	~~0~~
[a]Includes laboratory abnormalities that were new or worsening, or with worsening from baseline unknown.				

8.1 Pregnancy

Risk Summary

There are no available data on VENCLEXTA use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. Based on toxicity observed in mice, VENCLEXTA may cause fetal harm when administered to pregnant women. In mice, venetoclax was fetotoxic at exposures 1.2 times the human clinical exposure based on AUC at a human dose of 400 mg daily. ~~If~~ Advise ~~VENCLEXTA is used during pregnancy or if the patient becomes~~ pregnant women ~~while taking VENCLEXTA, the patient should be apprised~~ of the potential risk to a fetus.

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13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

~~Carcinogenicity studies have not been conducted with venetoclax~~. Neither venetoclax nor M27, a major human metabolite, were carcinogenic in a 6-month transgenic (Tg.rasH2) mouse study at oral doses up to 400 mg/kg/day of venetoclax, and at a single oral dose level of 250 mg/kg/day of M27.

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העלון לצרכן עודכן בסעיפים הבאים:

4. תופעות לוואי

ספר לרופא אם אתה מבחין באחת מתופעות הלוואי הבאות:

בחולי CLL או SLL

שכיחות מאוד (עלולות להשפיע על יותר מ- 1 מתוך 10 אנשים)

- ~~חוסר שינה~~

בנוסף, ניתן לראות בבדיקות דם:

- עלייה ברמות מלחי גוף (אלקטרוליטים) הכוללים פוספאט או~~,~~אשלגן ~~או נתרן~~
- ירידה ברמות מלחי ~~ה~~גוף (אלקטרוליטים) הכוללים פוספאט, ~~אשלגן,~~סידן או נתרן
- ~~רמות גבוהות של אנזימי כבד הנקראים פוספטאזה בסיסית (alkaline phosphatase [ALP])~~
- ~~רמות נמוכות של סוכר בדם~~
- ~~רמות גבוהות של חלבון הנקרא בילירובין~~

שכיחות (עלולות להשפיע על עד 1 מתוך 10 אנשים)

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בנוסף, ניתן לראות בבדיקות דם:

- ירידה ברמת מלח גוף (אלקטרוליט) הנקרא אשלגן
- רמות נמוכות של סוכר בדם

העלונים המעודכנים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, AbbVie Biopharmaceuticals Ltd, רחוב החרש 4, הוד השרון או בטלפון 7909600 – 09.

בברכה,
אינה רגצקי - רוקחת ממונה