אוקטובר 2023

Gazyva® 1000mg/40ml
obinutuzumab
Concentrate for solution for infusion

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על מספר עדכונים שבוצעו בעלון לרופא של התכשיר גזייבה.

בהודעה זו מצוינים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויות הרשומות לתכשיר בישראל:

Chronic Lymphocytic Leukaemia (CLL)

Gazyva, in combination with chlorambucil is indicated for the treatment of patients with previously untreated chronic lymphocytic Leukaemia (CLL).

Follicular Lymphoma (FL)

Gazyva in combination with chemotherapy, followed by Gazyva maintenance therapy in patients achieving a response, is indicated for the treatment of patients with previously untreated advanced follicular lymphoma.

Gazyva in combination with bendamustine followed by Gazyva monotherapy is indicated for the treatment of patients with follicular lymphoma (FL) who did not respond or who progressed during or up to 6 months after treatment with a rituximab-containing regimen.

למידע נוסף יש לעיין בעלון לרופא כפי שנשלח למשרד הבריאות.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס ע"י פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079
טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

בתאור צפרי-חגג
מחלקת רישום

לביא עמי-עד
רוקח ממונה

עדכונים מהותיים בעלון לרופא

בסעיף 4.2 Posology and method of administration התווסף מידע הנוגע לאפשרות של קיצור משך מתן האינפוזיה בחולי לימפומה פוליקולרית.

Follicular lymphoma (FL)

Gazyva should be administered at the standard infusion rate in Cycle 1 (see Table 5). In patients who do not experience Grade ≥3 infusion related reactions (IRRs) during Cycle 1, Gazyva may be administered as a short (approximately 90 minutes) duration infusion (SDI) from Cycle 2 onwards (see Table 6).

[…]

Table 6 Follicular lymphoma: Short duration infusion rate and recommendations in case an IRR occurred with previous infusion

Cycle	Day of treatment	Rate of infusion For management of IRRs that occur during the infusion, refer to "Management of IRRs".
Cycles 2–6 or 2–8	Day 1 (1,000 mg)	If no IRR of Grade ≥3 occurred during Cycle 1: 100 mg/hr for 30 minutes, then 900 mg/hr for approximately 60 minutes. If an IRR of Grade 1-2 with ongoing symptoms or a Grade 3 IRR occurred during the previous SDI infusion, administer the next obinutuzumab infusion at the standard rate (see Table 5).
Maintenance	Every 2 months for 2 years or until disease progression (whichever occurs first)	

[…]

Management of IRRs occurring during SDI

- Grade 4 (life threatening): Infusion must be stopped and therapy must be permanently discontinued.
- Grade 3 (severe): Infusion must be temporarily stopped and symptoms treated. Upon resolution of symptoms, the infusion can be restarted at no more than half the previous rate (the rate being used at the time that the IRR occurred) and not greater than 400 mg/hr.
  If the patient experiences a second Grade 3 IRR after resuming the infusion, the infusion must be stopped and therapy must be permanently discontinued. If the patient is able to complete the infusion without further Grade 3 IRRs, the next infusion should be given at a rate not higher than the standard rate.
- Grade 1-2 (mild to moderate): The infusion rate must be reduced and symptoms treated. Infusion can be continued upon resolution of symptoms and, if the patient does not experience any IRR symptoms, the infusion rate escalation can resume at the increments and intervals as appropriate for the treatment dose (see Tables 5-6).

בסעיף 4.8 Undesirable effects, התווסף מידע בטיחותי הרלוונטי לקיצור משך מתן האינפוזיה:

Short Duration Infusion in patients with Follicular Lymphoma

In study MO40597 assessing the safety of SDI, a greater proportion of patients experienced any grade IRRs at Cycle 2 compared to the proportion who experienced IRRs after standard infusion at Cycle 2 in study BO21223 (10/99 [10.1%] vs. 23/529 [4.3%] respectively; IRRs attributed by the investigator to any component of study therapy). No patients experienced Grade ≥3 IRRs after SDI at Cycle 2 in MO40597; 3/529 (0.6%) experienced Grade ≥3 IRRs at Cycle 2 in study BO21223. IRR symptoms and signs were similar in both studies.
Infusion related reactions observed in Study MO40597/GAZELLE are summarized in Table 8.

Table 8Study MO40597/GAZELLE Short-Duration Infusion: Infusion Related Reactions[a] by Cycle (Safety-Evaluable Population)

CTCAE Grade	C1 Overall (standard infusion)	C1[b] by day				C2[C]	C3	C4	C5	C6	C7	Over all induction cycles
		Day 1	Day 2[d]	Day 8	Day 15							
All Grade	65/113 (57.5%)	57/113 (50.4%)	4/51 (7.8%)	6/112 (5.4%)	5/111 (4.5%)	13/110 (11.8%)	9/108 (8.3%)	7/108 (6.5%)	6/107 (5.6%)	5/105 (4.8%)	2/55 (3.6%)	71/113 (62.8%)
Grade ≥3	6/113 (5.3%)	5/113 (4.4%)	1/51 (2.0%)	0	0	0	0	0	1/107 (0.9%)	0	0	7/113 (6.2%)

C=cycle; CTCAE = Common Terminology Criteria for Adverse Events; IRR=infusion related reaction
[a] Infusion related reaction defined as any event that occurred during or within 24 hours from the end of study treatment infusion that were judged by the investigator to be related to any components of therapy.
[b] C1 comprised three infusions at the standard infusion rate, administered at weekly intervals
[c] Patients received short-duration infusion from C2 onward. The denominator at C2 and subsequent cycles represents the number of patients who received SDI at that cycle.
[d] Patients treated with bendamustine on Cycle 1 Day 2.

[…]

Short Duration Infusion in patients with Follicular Lymphoma

In study MO40597, assessing the safety of SDI, neutropenia was reported as an adverse event in a higher proportion of patients compared to study BO21223 in which patients receiving standard duration infusion 69/113 [61.1%] vs 247/595 [41.5%], respectively, throughout induction). The median and range of neutrophil count values were similar in both studies at each time point. Febrile neutropenia was reported in a similar proportion of patients in MO40597 and BO21223 (6/113 [5.3%] vs 31/595 [5.2%], respectively). Infection was reported less frequently in MO40597 than in BO21223 (45/113 [39.8%] vs 284/595 [47.7%], respectively).

[…]

Short Duration Infusion in patients with Follicular Lymphoma

In study MO40597, assessing the safety of SDI, thrombocytopenia was reported as an adverse event in a higher proportion of patients compared to study BO21223 in which patients received standard duration infusion (21/113 [28.6%] vs 63/595 [10.6%], respectively, throughout induction). The median and range of platelet count values were similar in both studies at each time point. No thrombocytopenia events reported in MO40597 were associated with bleeding.