Gilead Sciences Israel Ltd.
4 HaHarash Street, Hod Hasharon
Tel: 972-8802050

ינואר 2026

עדכון עלון לרופא ולצרכן לתכשיר:

Yescarta®

Cells dispersion for intravenous infusion

(axicabtagene ciloleucel)

רופאים ורוקחים נכבדים,

חברת גיליאד סיאנסז ישראל בע"מ מבקשת להודיעכם על עדכון עלונים לתכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

Yescarta is indicated for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) that relapses within 12 months from completion of, or is refractory to, first-line chemoimmunotherapy.

Yescarta is indicated for the treatment of adult patients with relapsed or refractory (r/r) diffuse large B cell lymphoma (DLBCL) and primary mediastinal large B cell lymphoma (PMBCL), after two or more lines of systemic therapy .

Limitation of Use: Yescarta is not indicated for the treatment of patients with primary or secondary central nervous system lymphoma.

Yescarta is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

השינויים מסומנים בעלון המצורף כאשר הטקסט המודגש באדום הוסף לעלון ואילו הטקסט המחוק ~~בקו~~ ~~חוצה~~ נגרע ממנו. הסימונים בצהוב הינם החמרות במידע הבטיחותי.

העדכונים המשמעותיים ביותר מופיעים במכתב זה, קיימים עדכונים מינוריים נוספים.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות https://israeldrugs.health.gov.il/#!/byDrug/drugs/index.html.

כמו כן ,ניתן לקבלם מודפסים על ידי פנייה לבעל הרישום:

גיליאד סיאנסז ישראל בע"מ, רחוב החרש 4 ,ת.ד. 6090, פארק העסקים הוד השרון 4524075, ישראל

התכשיר זמין בכל קופות החולים.

בברכה,

מאיה מלל

רוקחת ממונה, גיליאד סיאנסז ישראל בע"מ

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העדכונים המהותיים בעלון לרופא:

4.4 Special warnings and precautions for use

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Cytokine release syndrome

Nearly all patients experienced some degree of CRS. Severe CRS, including life-threatening and fatal reactions, was very commonly observed with Yescarta with a time to onset of 1 to 12 days in ZUMA-1 and ZUMA-7, and 1 to 11 days in ZUMA-5 (see section 4.8). ~~CRS should be managed at the physician's discretion, based on the patient's clinical presentation and according to the CRS management algorithm provided in Table 1. Interleukin-6 (IL-6) receptor inhibitor based therapy such as tocilizumab has been administered for moderate or severe CRS associated with Yescarta.~~

Diagnosis of CRS requires excluding alternate causes of systemic inflammatory response, including infection.

Management of cytokine release syndrome associated with Yescarta
At least 1 dose per patient of tocilizumab , an interleukin 6 (IL 6) receptor inhibitor, must be on site and available for administration prior to Yescarta infusion. The qualified treatment centre must have access to an additional dose of tocilizumab within 8 hours of each previous dose.

Patients must be monitored daily for signs and symptoms of CRS for at least 10 days following infusion at the qualified clinical facility. After the first 10 days following infusion, the patient is to be monitored at the physician's discretion.

Patients are to be counselled to remain within proximity of a qualified clinical facility for at least 4 weeks following infusion and to seek immediate medical attention should signs or symptoms of CRS occur. Treatment algorithms have been developed to ameliorate some of the CRS symptoms experienced by patients on Yescarta. These include the use of tocilizumab or tocilizumab and corticosteroids for moderate, severe, or life-threatening CRS~~ as summarised in Table 1~~. ~~Patients who experience Grade 2 or higher CRS (e.g. hypotension, not responsive to fluids, or hypoxia requiring supplemental oxygenation) must be monitored with continuous cardiac telemetry and pulse oximetry. For patients experiencing severe CRS, consider performing an echocardiogram to assess cardiac function. For severe or life-threatening CRS, consider intensive care supportive therapy.~~

The management of patients should be conducted based on the patient's clinical presentation and in accordance with applicable local institutional and/or national or European/international clinical guidelines. Physicians are advised to exercise clinical judgment consistent with these standards.

Yescarta must not be administered to patients with active infections or inflammatory disease until these conditions have resolved.

CRS has been known to be associated with end organ dysfunction (e.g., hepatic, renal, cardiac, and pulmonary). In addition worsening of underlying organ pathologies can occur in the setting of CRS. Patients with medically significant cardiac dysfunction must be managed by standards of critical care and measures such as echocardiography are to be considered.

Evaluation for haemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) is to be considered in patients with severe or unresponsive CRS. HLH/MAS should be managed per local institutional and/or national or European/international clinical guidelines.

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Yescarta continues to expand and persist following administration of tocilizumab and corticosteroids. Tumour necrosis factor (TNF) antagonists are not recommended for management of Yescarta-associated CRS.

Table 1: CRS grading and management guidance

CRS Grade[a]	Tocilizumab	Corticosteroids
Grade 1 Symptoms require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgia, malaise).	If not improving after 24 hours, manage as Grade 2.	N/A
Grade 2 Symptoms require and respond to moderate intervention. Oxygen requirement less than 40% FiO_2 or hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicity[b].	Administer tocilizumab[c] 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24 hour period; maximum total of 4 doses if no clinical improvement in the signs and symptoms of CRS, or if no response to second or subsequent doses of tocilizumab, consider alternate measures for treatment of CRS.	Manage per Grade 3 if no improvement within 24 hours after starting tocilizumab.
Grade 3 Symptoms require and respond to aggressive intervention. Oxygen requirement greater than or equal to 40% FiO_2 or hypotension requiring high dose or multiple vasopressors or Grade 3 organ toxicity or Grade 4 transaminitis.	Per Grade 2	Administer methylprednisolone 1 mg/kg intravenously twice daily or equivalent dexamethasone (e.g., 10 mg intravenously every 6 hours). Continue corticosteroids use until the event is Grade 1 or less, then taper. If not improving, manage as Grade 4 (below).
Grade 4 Life-threatening symptoms. Requirements for ventilator support or continuous veno-venous haemodialysis or Grade 4 organ toxicity (excluding transaminitis).	Per Grade 2	Administer methylprednisolone 1 000 mg intravenously per day for 3 days; if improves, then manage as above. Consider alternate immunosuppressants if no improvement or if condition worsens.

N/A = not available/not applicable
(a) Lee et al 2014.
(b) Refer to Table 2 for management of neurologic adverse reactions.
(c) Refer to tocilizumab summary of product characteristics for details.

Neurologic adverse reactions

Severe neurologic adverse reactions, also known as immune effector cell-associated neurotoxicity syndrome (ICANS), have been very commonly observed in patients treated with Yescarta, which could be life-threatening or fatal. The median time to onset was 6 days (range: 1 to 133 days) in ZUMA-1 and

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ZUMA-7, and 7 days (range: 1 to 177 days) in ZUMA-5 following Yescarta infusion (see section 4.8). Patients with a history of CNS disorders such as seizures or cerebrovascular ischaemia may be at increased risk. Fatal and serious cases of cerebral oedema have been reported in patients treated with Yescarta. Patients must be monitored for signs and symptoms of neurologic adverse reactions ~~(Table 2)~~. Patients must be monitored at least daily for 10 days at the qualified clinical facility following infusion for signs and symptoms of neurologic toxicity/ICANS. After the first 10 days following the infusion, the patient is to be monitored at the physician's discretion. Patients are to be counselled to remain within proximity of a qualified clinical facility for at least 4 weeks following infusion and to seek immediate medical attention should signs or symptoms of neurologic toxicity/ICANS occur. Vital signs and organ functions must be monitored depending on the severity of the reaction.

~~Patients who experience Grade 2 or higher neurologic toxicities /ICANS must be monitored with continuous cardiac telemetry and pulse oximetry. Intensive care supportive therapy must be provided for severe or life-threatening neurologic toxicities/ICANS. Non-sedating, anti-seizure medicines are to be considered as clinically indicated for Grade 2 or higher adverse reactions. Treatment algorithms have been developed to ameliorate the neurologic adverse reactions experienced by patients on Yescarta. These include the use of tocilizumab (if concurrent CRS) and/or corticosteroids for moderate, severe, or life-threatening neurologic adverse reactions as summarised in Table 2.~~
The management of patients should be conducted based on the patient's clinical presentation and in accordance with applicable local institutional and/or national or European/international clinical guidelines. Physicians are advised to exercise clinical judgment consistent with these standards.

~~Table 2: Neurologic adverse reaction/ICANS grading and management guidance~~

<table>
<tr><th>~~Grading assessment~~</th><th>~~Concurrent CRS~~</th><th>~~No concurrent CRS~~</th></tr>
<tr><td rowspan="2">~~Grade 2~~</td><td>~~Administer tocilizumab per Table 1 for management of Grade 2 CRS.
If no improvement within 24 hours after starting tocilizumab, administer dexamethasone 10 mg intravenously every 6 hours if not already taking other corticosteroids. Continue dexamethasone use until the event is Grade 1 or less, then taper.~~</td><td>~~Administer dexamethasone 10 mg intravenously every 6 hours.
Continue dexamethasone use until the event is Grade 1 or less, then taper.~~</td></tr>
<tr><td colspan="2">~~Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.~~</td></tr>
<tr><td rowspan="2">~~Grade 3~~</td><td>~~Administer tocilizumab per Table 1 for management of Grade 2 CRS.
In addition, administer dexamethasone 10 mg intravenously with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper.~~</td><td>~~Administer dexamethasone 10 mg intravenously every 6 hours.
Continue dexamethasone use until the event is Grade 1 or less, then taper.~~</td></tr>
<tr><td colspan="2">~~Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.~~</td></tr>
</table>

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~~Grading assessment~~	~~Concurrent CRS~~	~~No concurrent CRS~~
~~Grade 4~~	~~Administer tocilizumab per Table 1 for management of Grade 2 CRS.~~ ~~Administer methylprednisolone 1 000 mg intravenously per day with first dose of tocilizumab and continue methylprednisolone 1 000 mg intravenously per day for 2 more days; if improves, then manage as above.~~ ~~If not improving, consider 1 000 mg of methylprednisolone intravenously 3 times a day or alternate therapy.[a]~~	~~Administer methylprednisolone 1 000 mg intravenously per day for 3 days; if improves, then manage as above.~~ ~~If not improving, consider 1 000 mg of methylprednisolone intravenously 3 times a day or alternate therapy.[a]~~
	~~Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.~~	

~~*a. Alternate therapy includes (but is not limited to): anakinra, siltuximab, ruxolitinib, cyclophosphamide, IVIG and ATG.*~~

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6.4 Special precautions for storage

Yescarta must be stored in the vapour phase of liquid nitrogen (≤ -150˚C) and must remain frozen until the patient is ready for treatment to ensure viable live autologous cells are available for patient administration.

Yescarta may be stored a single time at -80 °C (± 10 °C), for up to 90 days. After storage at -80 °C ± 10 °C, the product must be used within the 90-day period or the labelled expiration date, whichever comes first. After these dates, the product must not be used and must be discarded.

Thawed medicinal product should not be refrozen.

For storage conditions after thawing of the medicinal product, see section 6.3.

העדכונים המהותיים בעלון לצרכן:

5. כיצד לאחסן את התכשיר?

המידע הבא מיועד לרופאים בלבד.

מנע הרעלה! אחסן תרופה זו וכל תרופה אחרת מחוץ לטווח ראייתם והישג ידם של ילדים ו/או תינוקות ועל ידי כך תמנע הרעלה. אל תגרום להקאה ללא הוראה מפורשת מהרופא.

אל תשתמש בתרופה לאחר שעבר תאריך התפוגה שלה. תאריך התפוגה מצוין על תווית המיכל ועל שקית העירוי לאחר "EXP".

תנאי אחסון:

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אחסן קפוא באדי חנקן נוזלי בטמפרטורה של ≤ 150°C- עד להפשרה לשימוש.

ניתן לאחסן יסקרטה באופן חד פעמי בטמפרטורה של (± 10°C) 80°C-, עד 90 יום. לאחר האחסון ב - 80°C ± 10°C, יש להשתמש תוך 90 יום או עד סיום חיי המדף, התאריך המוקדם מבין השניים. לאחר התאריכים הללו יש להשמיד את התכשיר.

אין להקפיא מחדש.

היציבות של יסקרטה לאחר הפשרה היא עד 3 שעות בטמפרטורת החדר (20°C עד 25°C). אולם, יש להתחיל את העירוי ביסקרטה תוך 30 דקות מסיום ההפשרה ומשך זמן העירוי הכולל של יסקרטה לא יעלה על 30 דקות.