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

יוני 2024

עדכון עלון לרופא ולצרכן לתכשיר:

Tecartus®

Cells dispersion for infusion

(brexucabtagene autoleucel)

ההתוויה הרשומה לתכשיר בישראל:

Tecartus is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after two or more lines of systemic therapy including a Bruton's tyrosine kinase (BTK) inhibitor unless ineligible to BTK inhibitor.

Limitation of use: Tecartus is not indicated for the treatment of patients with active central nervous system lymphoma.

Tecartus is indicated for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL).

רופאים ורוקחים נכבדים,

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

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:

4.8 Undesirable effects

Table 3 Adverse drug reactions identified with Tecartus

System Organ Class (SOC)	Frequency	Adverse reactions
Infections and infestations		
	Very common	Unspecified pathogen infections Bacterial infections Fungal infections Viral Infections
Blood and lymphatic system disorders		
	Very common	Leukopenia[a] Neutropenia[a] Lymphopenia[a] Thrombocytopenia[a] Anaemia[a] Febrile neutropenia
	Common	Coagulopathy
Immune system disorders		
	Very common	Cytokine Release Syndrome[b] Hypogammaglobulinaemia
	Common	Hypersensitivity Haemophagocytic lymphohistiocytosis
Metabolism and nutrition disorders		
	Very common	Hypophosphataemia[a] Decreased appetite Hypomagnesaemia Hyperglycaemia[a]
	Common	Hypoalbuminemia[a] Dehydration
Psychiatric disorders		
	Very common	Delirium Anxiety Insomnia
Nervous system disorders		
	Very common	Encephalopathy Tremor Headache Immune effector cell-associated neurotoxicity syndrome (ICANS[b, c]) Aphasia Dizziness Neuropathy
	Common	Seizure Ataxia Increased intracranial pressure
Cardiac disorders		
	Very common	Tachycardias Bradycardias
	Common	Non-ventricular arrhythmias
Vascular disorders		
	Very common	Hypotension

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System Organ Class (SOC)	Frequency	Adverse reactions
		Hypertension Haemorrhage
	Common	Thrombosis
Respiratory, thoracic and mediastinal disorders		
	Very common	Cough Dyspnoea Pleural effusion Hypoxia
	Common	Respiratory failure Pulmonary oedema
Gastrointestinal disorders		
	Very common	Nausea Diarrhoea Constipation Abdominal pain Vomiting Oral pain
	Common	Dry mouth Dysphagia
Skin and subcutaneous tissue disorders		
	Very common	Rash Skin disorder
Musculoskeletal and connective tissue disorders		
	Very common	Musculoskeletal pain Motor dysfunction
Renal and urinary disorders		
	Very common	Renal insufficiency
	Common	Urine output decreased
General disorders and administration site conditions		
	Very common	Oedema Fatigue Pyrexia Pain Chills
	Common	Infusion related reaction
Eye Disorders		
	Common	Visual impairment
Investigations		
	Very common	Alanine aminotransferase increased[a] Blood uric acid increased[a] Aspartate aminotransferase increased[a] Hypocalcaemia[a] Hyponatraemia[a] Direct bilirubin increased[a] Hypokalaemia[a]
	Common	Bilirubin increased[a]

Only cytopenias that resulted in (i) new or worsening clinical sequelae or (ii) that required therapy or (iii) adjustment in current therapy are included in Table 3.
[a] Frequency based on Grade 3 or higher laboratory parameter.
[b] See section Description of selected adverse reactions.
[c] The frequency of ICANS has been estimated from events reported in the post-marketing setting.
ZUMA-2 data cutoff: 24 July 2021; ZUMA-3 data cutoff: 23 July 2021

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Description of selected adverse reactions from ZUMA-2 and ZUMA-3 (n=182)

Cytokine release syndrome
CRS occurred in 91% of patients. Twenty percent (20%) of patients experienced Grade 3 or higher (severe or life-threatening) CRS. The median time to onset was 3 days (range: 1 to 13 days) and the median duration was 9 days (range: 1 to 63 days). Ninety-seven percent (97%) of patients recovered from CRS.

The most common signs or symptoms associated with CRS among the patients who experienced CRS included pyrexia (94%), hypotension (64%), hypoxia (32%), chills (31%), tachycardia (27%), sinus tachycardia (23%), headache (22%), fatigue (16%), and nausea (13%). Serious adverse reactions that may be associated with CRS included hypotension (22%), pyrexia (15%), hypoxia (9%), tachycardia (3%), dyspnoea (2%) and sinus tachycardia (2%). See section 4.4 for monitoring and management guidance.

Neurologic events and adverse reactions
Neurologic adverse reactions occurred in 69% of patients. Thirty-two percent (32%) of patients experienced Grade 3 or higher (severe or life-threatening) adverse reactions. The median time to onset was 7 days (range: 1 to 262 days). Neurologic events resolved for 113 out of 125 patients (90.4%) with a median duration of 12 days (range: 1 to 708 days). Three patients had ongoing neurologic events at the time of death, including one patient with the reported event of serious encephalopathy and another patient with the reported event of serious confusional state. The remaining unresolved neurologic events were Grade 2. Ninety-three percent of all treated patients experienced the first CRS or neurological event within the first 7 days after Tecartus infusion.

The most common neurologic adverse reactions including ICANS represented~~included~~ tremor (32%), confusional state (27%), encephalopathy (27%), aphasia (21%), and agitation (11%). Serious adverse reactions including encephalopathy (15%), aphasia (6%)~~ and~~, confusional state (5%) ~~have been reported in patients administered Tecartus. ICANS was reported as a serious adverse neurologic reaction at a low frequency (2%) in clinical trials. ICANS observed during clinical studies are represented under the adverse reaction encephalopathy. Serious~~and serious cases of cerebral oedema which may become fatal have occurred in patients treated with Tecartus. See section 4.4 for monitoring and management guidance.

~~ICANS was reported in the context of neurologic toxicity in the post marketing setting.~~

Febrile neutropenia and infections
Febrile neutropenia was observed in 12% of patients after Tecartus infusion. Infections occurred in 87 of the 182 patients treated with Tecartus in ZUMA-2 and ZUMA-3. Grade 3 or higher (severe, life-threatening or fatal) infections occurred in 30% of patients including unspecified pathogen, bacterial, fungal and viral infections in 23%, 8%, 2% and 4% of patients respectively. See section 4.4 for monitoring and management guidance.