Introduction

- **Brand name:** Yescarta
- **Generic name:** Axicabtagene ciloleucel
- **Pharmacological class:** CD19-directed genetically modified autologous T cell immunotherapy
- **Strength and Formulation:** may contain up to $2 \times 10^8$ CAR-positive viable T cells); per dose; susp for IV infusion; contains dimethyl sulfoxide (DMSO) and albumin (human)
- **Manufacturer:** Kite Pharma, Inc.
- **How supplied:** Infusion bag (approx. 68mL)—1
- **Legal Classification:** Rx
Indications

- Treatment of adults with **relapsed or refractory large B-cell lymphoma** after 2 or more lines of systemic therapy, including:
  - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
  - Primary mediastinal large B-cell lymphoma
  - High grade B-cell lymphoma
  - DLBCL arising from follicular lymphoma
Limitations of Use

- **Not** for treating primary CNS lymphoma
Dosage & Administration

- For autologous and IV use only; confirm patient identity prior to infusion
- Give lymphodepleting chemotherapy (cyclophosphamide 500mg/m² IV + fludarabine 30mg/m² IV on the 5th, 4th, and 3rd day prior to Yescarta infusion
Premedicate with APAP and diphenhydramine approx. 60mins prior to Yescarta infusion; avoid prophylactic corticosteroids

- Infuse contents of bag within 30mins
- **Target dose:** 2x10^6 CAR-positive viable T cells/kg; max 2x10^8 CAR-positive viable T cells
Considerations for Special Populations

- **Pediatric**: Not established
- **Pregnancy**: Not recommended; verify status prior to treatment start
- **Nursing mothers**: Consider mother’s clinical need with adverse effects on breastfed infant
- **Elderly**: Insufficient number of patients studied
Warnings/Precautions

- Increased risk of **cytokine release syndrome (CRS)**; do not give to patients with active infection and/or inflammatory disorders
- Have tocilizumab readily available
- Monitor at least daily for 7 days at healthcare facility following infusion for signs/symptoms of CRS and neurologic toxicities
Warnings/Precautions

- Continue to monitor for CRS for 4 weeks after infusion; at 1st sign, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated (see full labeling)

- Monitor for **neurologic toxicities** for 4 weeks after infusion and treat promptly (see full labeling)
Warnings/Precautions

- Monitor for infection, febrile neutropenia; evaluate, manage and treat appropriately
- Screen for HBV, HCV, and HIV prior to cell collection for manufacturing
- Monitor blood counts, immunoglobulin levels after treatment
Interactions

- **Concomitant live virus vaccines**: not recommended for at least 6 weeks prior to lymphodepleting chemotherapy, during Yescarta treatment, and until immune recovery
# Adverse Reactions

<table>
<thead>
<tr>
<th>CRS</th>
<th>Nausea</th>
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<tbody>
<tr>
<td>Fever</td>
<td>Hypoxia</td>
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<tr>
<td>Hypotension</td>
<td>Tremor</td>
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<tr>
<td>Encephalopathy</td>
<td>Cough</td>
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<tr>
<td>Tachycardia</td>
<td>Vomiting</td>
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<td>Fatigue</td>
<td>Dizziness</td>
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<td>Headache</td>
<td>Constipation</td>
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<tr>
<td>Decreased appetite</td>
<td>Arrhythmias</td>
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<tr>
<td>Chills</td>
<td>Hypersensitivity</td>
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<tr>
<td>Diarrhea</td>
<td>HBV reactivation</td>
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<tr>
<td>Febrile neutropenia</td>
<td>Others</td>
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<tr>
<td>Infections</td>
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</tbody>
</table>
Mechanism of Action

- Yescarta binds to CD19-expressing cancer and normal B cells, thereby activating downstream signaling cascades which lead to T cell activation, proliferation, acquisition of effector functions and secretion of inflammatory cytokines and chemokines, eventually leading to cell death.
Clinical Studies

- The efficacy of Yescarta was evaluated in a single-arm, open-label, multicenter trial involving 101 adults with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma.
- Patients received a single IV infusion of Yescarta following lymphodepleting chemotherapy.
Clinical Studies

- The **primary efficacy endpoint** was established based on the rate of complete remission (CR) and duration of response (DOR), as determined by an independent review committee.
Patients who were treated with Yescarta achieved a CR rate of 51% (95% CI: 41, 62)

The *median time to response* was 0.9 months (range: 0.8 to 6.2 months)

Response durations were longer in patients who achieved CR, as compared to patients with a best response of partial remission (PR)
Additionally, \textit{median time to improvement} in patients who achieved CR was 2.1 months (range: 1.6 to 5.3 months)

For more clinical trial data, see full labeling
New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/yescarta/drug/34786/