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Plan your strategy to engage eligible patients

5 minutes on ex vivo cell and gene therapies

Ex vivo cell and gene therapy refers to treatments that involve extracting a patient's cells, genetically modifying them ex vivo (outside of the body) and returning them back to the patient's body to help treat certain diseases. The FDA approval of CAR T-cell therapy in 2017 has brought significant advances in the treatment and cure of certain hematologic cancers. Beyond CAR T, other ex vivo cell and gene therapies have recently come to market to target solid tumors and treat genetic conditions (beta thalassemia and sickle cell anemia). For payers, these unfolding developments raise a key issue: **What is your strategy for managing these high-cost, clinically complex cases?**

How CAR T-cell therapy works

CAR T-cell therapy – chimeric antigen receptor T-cell therapy – reprograms a patient's own immune cells to recognize and eradicate malignant cells. Healthy T-cells, a type of disease-fighting white blood cell, are extracted from the patient's blood and engineered in a lab to produce chimeric antigen receptors through gene-transfer techniques. This enables the cells to target specific tumor proteins. The modified cells are then infused into the patient's blood where they can seek and attack the cancer cells.

Early success

Currently, each type of CAR T-cell therapy is intended to be a one-time treatment. These agents are approved for use when the underlying cancer has recurred or has not responded to more standard treatments, but the timing of treatment and the sequence of treatment with respect to the use of other agents is still being studied. While it's still too early to definitively assess the efficacy of CAR T-cell therapy, early clinical trials have been associated with response rates of over 80%.[1,2,3] Of course, as with any treatment, there may be negative side effects. Treatment with CAR T-cell therapy, for example, may cause cytokine release syndrome, brain swelling and neurological events, which require hospitalization and can be life-threatening.

High cost of treatment

Currently, ex vivo cell and gene therapies are one-time treatments targeted for a relatively small number of patients.[4] Even so, the cost is high. As of Sept. 30, 2024, the invoice prices in the U.S. are:

- Ex vivo cell therapy **$427K–$727K**
- Ex vivo gene therapy **$2.2M–$4.25M**

Additional costs

Besides manufacturing costs, therapy infusion expenses vary by facility and setting (inpatient or outpatient). The invoice price excludes other direct costs (hospital/facility charges, physician fees) and indirect costs (invoice markups, business development). Patients may also continue other treatments while preparing for ex vivo cell or gene therapy.

FDA-approved agents

Ex vivo cell therapies (CAR T, TIL and TCR T)

Agent name	Launch date	Indication	Invoice price
Kymriah®	Aug. 30, 2017	For patients up to age 25 who went into remission then relapsed or did not go into remission with other leukemia treatments	$543,827
		For patients with (1) large B-cell lymphoma that has worsened 2 or more earlier lines of therapy[5]; (2) relapsed or refractory follicular lymphoma[6]	$427,047
Yescarta®	Oct. 18, 2017	For adult patients with (1) certain types of large B-cell lymphoma who have not responded to other treatments or relapsed after treatment, second line of treatment[7]; (2) relapsed or refractory follicular lymphoma[8]	$462,000
Tecartus®	Jul. 24, 2020	For adult patients with (1) mantle cell lymphoma who have not responded to 2 or more previous lines of treatment; (2) relapsed or refractory B-cell precursor acute lymphoblastic leukemia[9]	$462,000
Breyanzi®	Feb. 5, 2021	For adult patients with (1) diffuse large B-cell lymphoma, second line of treatment; (2) relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma who have received at least 2 prior lines of therapy[10]	$487,447
Abecma®	Mar. 27, 2021	For adult patients with relapsed or refractory multiple myeloma who have received 2 to 3 prior lines of therapy[11]	$498,408
Carvykti™	Feb. 28, 2022	For patients with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy[12]	$522,056
Amtagvi™	Feb. 16, 2024	For patients with unresectable or metastatic melanoma previous treated with PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor[13]	$515,000
Tecelra™	Aug. 2, 2024	For adult patients with advanced MAGE-A4+ metastatic or unresectable synovial sarcoma of certain human leukocyte antigen types who have previously undergone chemotherapy[14]	$727,000

Ex vivo gene therapies

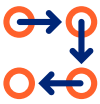
Agent name	Launch date	Indication	Invoice price
Zynteglo™	Aug. 19, 2022	For patients 12 years of age and older with transfusion-dependent beta thalassemia, a rare inherited blood disorder[15]	$2,800,000
Skysona™	Sept. 18, 2022	For boys 4–17 years of age with early, active cerebral adrenoleukodystrophy[16]	$3,000,000
Lyfgenia™	Dec. 8, 2023	For patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events[17]	$3,100,000
Casgevy™	Dec. 8, 2023	For patients 12 years of age and older with (1) beta thalassemia; (2) sickle cell disease with recurrent vaso-occlusive crises[18]	$2,200,000
Lenmeldy™	Mar. 18, 2024	For the treatment of children with pre-symptomatic late infantile, pre-symptomatic early juvenile or early symptomatic early juvenile metachromatic leukodystrophy[19]	$4,250,000

CAR T – chimeric antigen receptor T-cell therapy
TCR T – T-cell receptor T-cell therapy
TIL – tumor infiltrating lymphocyte
Price information as of Sept. 24, 2024.
Invoice price is equivalent to wholesale acquisition cost (WAC).

Considerations for payers

Payers may want to consider examining members who may be eligible for ex vivo cell and gene therapies.

Do you have access to clinical indications for ex vivo cell and gene therapies?



Is a prior authorization process in place that will flag the service as a cell or gene therapy case?

How will the therapy be reimbursed under the existing provider contracts?

How to analyze the total cost of care for patients treated with ex vivo cell and gene therapies?

Looking ahead: Broader impact

Novel therapies, like CAR T-cell therapy, are being driven by rapid advances in biotechnological research. As of 2024, more than 790 clinical trials for CAR T-cell therapy were recruiting, active or completed in the U.S. for a variety of conditions.[20] Looking ahead, ex vivo cell and gene therapy holds great promise as treatment solutions for more cancer diagnosis and perhaps for immune disease.

Visit optum.com/business/contact.html#sales to discuss your CAR T-cell therapy and other ex vivo gene therapy options with an account manager.

1. Wang D, Wang J, Hu G et al. A phase 1 study of a novel fully human BCMA-targeting CAR (CT103A) in patients with relapsed/ refractory multiple myeloma. *Blood.* 2021; 137(21):2890-2901.
2. Locke FL, Ghobadi A, Jacobson CA et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1–2 trial. *Lancet Oncol.* 2019; 20(1):31-42.
3. Zhao Y, Zhang J, Yang J et al. Long-term safety and efficacy of CD19 humanized selective CAR-T therapy in B-ALL patients who have previously received murine-based CD19 CAR-T therapy. *Front Oncol.* 2022; 12:884782.
4. Optum. Internal claims and pricing information. Oct., 2024.
5. US Food & Drug Administration. FDA approves tisagenlecleucel for adults with relapsed or refractory large B-cell lymphoma. May 3, 2018.
6. Novartis. FDA approves Novartis Kymriah® CAR-T cell therapy for adult patients with relapsed or refractory follicular lymphoma. May 28, 2022.
7. U.S. Food & Drug Administration. FDA approves axicabtagene ciloleucel for second-line treatment of large B-cell lymphoma. April 1, 2022.
8. Gilead. U.S. FDA approves Yescarta® for relapsed or refractory follicular lymphoma after two or more lines of systemic therapy. March 5, 2021.
9. U.S. Food & Drug Administration. Tecartus. June 13, 2024.
10. U.S. Food & Drug Administration. Breyanzi. June 13, 2024.
11. U.S. Food & Drug Administration. Abecma. June 12, 2024.
12. U.S. Food & Drug Administration. Carvykti. July 31, 2024.
13. U.S. Food & Drug Administration. Amtagvi. July 31, 2024.
14. U.S Food & Drug Administration. FDA approves first gene therapy to treat adults with metastatic synovial sarcoma. Aug. 2, 2024.
15. Fierce Pharma. FDA extends decision dates on bluebird bio's gene therapy drugs beti-cel and eli-cel by 3 months. Jan. 18, 2022.
16. U.S. Food & Drug Administration. Skysona. April 10, 2024.
17. U.S. Food & Drug Administration. Lyfgenia. July 10, 2024.
18. U.S. Food & Drug Administration. Casgevy. Feb. 21, 2024.
19. U.S. Food & Drug Administration. Lenmeldy. April 15, 2024.
20. National Institutes of Health. U.S. National Library of Medicine Clinical Trials search for "CAR T-cell therapy" in intervention/treatment. Accessed Oct. 16, 2024.

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