Pharmacy Focus:
CAR T-Cell Therapy — 2025 Update

Key Takeaways Regarding CAR T-Cell Therapy

- Costs of CAR T-cell (CAR-T) treatment remain high (>$500,000 for the drug alone) and are expected to remain so in conjunction with the costs for the medical care associated with the available treatments (e.g., inpatient stay for administration, treatment of complications, etc.).
- Although still not considered a cure, CAR-T therapy shows continued promise for treatment-free durable responses and also demonstrates great potential as a treatment option outside of blood cancers (e.g., solid tumor cancers).
- CAR-T therapy also continues to face challenges, including costs, time to treatment, treatment hesitancy, etc., but viable solutions remain under development.

CAR T-Cell Treatment Overview[1-5]

T-cells are a part of the body's natural defense against disease, including the fight against cancer. By altering or reprogramming these immune cells, they can attack and destroy identified cells. Chimeric Antigen Receptor (CAR) T-cell therapy, generally referred to as CAR-T, is a process in which a patient's T-cells are genetically altered to combat all identified cells, including cancer cells.

CAR-T therapy is a multi-step process that starts with harvesting the patient's own immune cells and sending them to a manufacturer to be processed for the treatment. They are then administered back to the patient in their altered/reprogrammed form. When the treatment process is complete, patients are closely monitored for the development of common adverse events.

All CAR-T therapies currently approved by the FDA share common side effects that may occur immediately following the infusion or up to months and sometimes years after. Depending on severity, side effects may require inpatient care as well as additional treatments that can contribute to higher costs. For example, cytokine release syndrome (CRS), which can occur in 40% – 100% of patients, can cost $20,000 – $50,000 to manage depending on severity. Immune effector cell-associated neurotoxicity syndrome (ICANS) can occur in 20% – 70% of patients, bringing about additional costs exceeding $100,000 due to the more complex care needs associated with this diagnosis.

In January 2024, due to the risk of secondary T-cell malignancies, the FDA initiated labeling changes for all CAR-T therapies to include a boxed warning as well as updates to other label sections to highlight this risk. Although the incidence is small (4% – 6%), patients and clinical trial participants receiving treatment with these products are strongly recommended to have lifelong monitoring in place. As the number of patients that receive CAR-T treatment grows, so will further possible complications that can contribute to overall treatment costs.

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Current FDA Approved CAR-T Treatments, Indications, and Costs[6]

Even though the costs of CAR-T therapy seem to have stabilized, the costs of the total procedure are expected to remain high due to associated ancillary care that includes hospital stays and additional treatment for complications and side effects.

Name	Treatment	Indications	FDA Approval Date*	CPT Code/ HCPCS**	Cost (average wholesale price, med only)	Average Costs Observed by HM Insurance Group (2022 – 2024)
Abecma®	Multiple myeloma	**Adult** relapsed/refractory disease in the 3rd line	3/26/21 (04/04/2024)	Q2055	$598,090	$515,292
Carvykti®	Multiple myeloma	**Adult** relapsed/ refractory disease in 2nd+ line	2/28/22 (04/05/2024)	Q2056	$574,740	$674,293
Breyanzi®	• Large B-cell lymphoma • Chronic lymphocytic leukemia • Small lymphocytic lymphoma • Follicular lymphoma • Mantle cell lymphoma	**Adult** relapsed/ refractory disease - 2nd or 3rd line for LBCL - 3rd line for CLL, SLL, FL, and MCL	2/5/21 (06/24/2022, 05/30/2024)	Q2054	$584,973	$469,323
Yescarta®	• Follicular lymphoma • B-cell lymphoma	**Adult** relapsed/ refractory disease - 3rd line for FL - 2nd or 3rd line for BCL	10/18/17 (04/02/2021, 04/01/2022)	Q2041	$554,400	$557,208
Kymriah®	• B-cell acute lymphoblastic leukemia • Follicular lymphoma • B-cell lymphoma	• **Pediatric/young adult B-cell ALL** (<25 y/o), 3rd line (off-label in 2nd line) • **Adult**, 3rd line FL • **Adult**, 3rd line BCL	8/30/17 (05/01/2018, 05/27/2022)	Q2042	$652,593	$634,724
Tecartus™	• Mantle cell lymphoma • B-cell acute lymphoblastic leukemia	**Adult** relapsed/ refractory disease - 2nd line MCL - 2nd line B-cell ALL	7/24/20 (10/01/2021)	Q2053	$508,800	$651,134
Aucatzyl®	• B-cell acute lymphoblastic leukemia	**Adult** relapsed/refractory disease, 2nd+ line	11/8/24	C9399; J3590**	$630,000	n/a

**() denotes expanded indication approval date*
***Average of 1-2 years before a drug gets a unique HCPCS code after it comes to market*

CAR-T Therapy's Place in Treatment Options[7-9]

CAR-T therapy was previously reserved as third- or fourth-line therapy after other treatment options, such as a stem cell transplant or traditional chemotherapy regimens, were tried. Since the first approval of a CAR-T in 2017, five of the seven available products have been approved for use in the second line treatment space, allowing for treatment-free periods and extended life expectancy through the preservation of higher cost/ higher lines of therapy for cases of further relapse.

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Per updated study data, the complete response rates for CAR-T therapy (percentage of patients where all signs of cancer have been eliminated in the body) range from 50% – 90% or more depending on the type of blood cell cancer. Reporting has also demonstrated that although CAR-T is still not considered a curative treatment option, some therapies have shown durability of responses (time without need for active treatment) for up to five years.

The safety and effectiveness of a second CAR-T dose have not yet been established. Although still unapproved by the FDA and primarily only considered in the scope of clinical trials, second administrations are being approved by insurances through high-level appeal if the initial uptake of the cells was suboptimal. If traditional treatment options and the CAR-T therapy are ineffective, the patient may be considered for an additional stem cell transplant, high-cost fourth line therapies, or a clinical trial.

Non-CAR-T Therapy Competition[10,11]

There are several treatments available in the market that have complete response rates comparable to CAR-T therapies, including antigen-targeted monoclonal antibodies like Monjuvi® (tafasitamab-cxix) and bispecific T-cell engagers (BiTE therapies). There also are several possible competing classes of medications in the pipeline for the treatment of cancers including T-cell receptor-modified T-cells (TCRs), tumor-infiltrating lymphocytes (TILs), CAR-natural killer (CAR-NK) cells, and mRNA therapies.

BiTE therapies continue to gain approvals with favorable results and are currently the main CAR-T competitors. BiTE therapy is an immunotherapy that uses antibody-based connectors to link T-cells to cancer cells, enabling targeted destruction. These therapies have achieved response rates of 60% – 80% and have demonstrated up to 70% response rates in heavily pre-treated multiple myeloma, which ranged from only 20% – 30% previously. Costs and side effects are similar to CAR-T (e.g., Tecvayli®'s average annual AWP is $606,235). These treatments can continue until disease progression or toxicity, and they also are being investigated for use in solid tumors.

BiTE Therapies (bispecific T-cell engagers)*

Drug	Line of Therapy	Disease State	Average Costs (Average Wholesale Price)**
Epkinly™ (epcoritamab-bysp)	3rd/4th and later	Follicular lymphoma, non-Hodgkin lymphoma	$498,971
Lunsumio™ (mosunetuzumab-axgb)	3rd/4th and later	Follicular lymphoma	$242,358
Columvi™ (glofitamab-gxbm)	3rd/4th and later	Diffuse large B-cell lymphoma (large B-cell lymphoma from follicular)	$442,073 (12 cycles, 21-day cycles)
Blincyto® (blinatumomab)	1st and later	Acute lymphoblastic leukemia	$600,000+ *dose and costs are dependent on claimant weight and treatment protocol
Elrexfio™ (elranatamab-bcmm)	4th and later	Multiple myeloma	$587,100
Talvey® (talquetamab-tgvs)	4th and later	Multiple myeloma	$670,383
Tecvayli® (teclistamab-cqyv)	4th and later	Multiple myeloma	$606,235

**Table includes CAR-T competitors only*
***Average costs obtained through Advanced Medical Strategies (AMS) and IPD Analytics tools reflect one year of treatment unless otherwise specified*

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CAR-T Limitations, Solutions, and Advancements[12-19]

Limitations

While CAR-T has afforded additional successful treatment options for many blood cancer patients, there are still challenges and barriers surrounding the CAR-T landscape for patients, providers, and payers including:

- **Length of procedure** – The entire CAR-T therapy process takes about three months to complete from the time an eligibility assessment is ordered by the physician to the completion of the 30-day observation period after the infusion.
- **Inpatient hospital stays** – The median length of inpatient stay associated with the procedure is about 14.5 days, which can lead to an increased risk for hospital-acquired infections due to the patient's depleted immune system (along with the additional health care costs associated).
- **Adverse events** – The common occurrence of adverse events with CAR-T is also a challenge that adds to increased costs.
- **Outcomes tracking** – There is no defined tracking process for claimants that have received CAR-T, which creates gaps in post-treatment care, reporting on adverse events/efficacy of treatments, and any value-based agreements contracted between sites of care and payers.

Solutions

However, there are several solutions to the noted limitations in process and development, including:

- **The investigation of "off the shelf" products** – There are currently clinical trials for products that seek to address the length of procedure concerns. These products use already existing donor cells instead of the auto stem cell collection procedure to cut down on total procedure time and decrease the patient invasive processes. There also are ongoing clinical studies to mitigate the possible complications (rejection, GVHD) associated with receiving allogenic/donor cells.
- **Shifting procedures from inpatient to outpatient** – Studies have found comparable outcomes in safety, efficacy, and quality of life with outpatient versus inpatient administration, and this approach also helps to reduce costs associated with health care resource utilization. For example, costs in the six-month post-infusion period reported from pooled trial data revealed a two to four times greater expense associated with the inpatient setting.
- **Advanced product design with more specific targeting** – The common adverse effects of treatments are being addressed through advancing product design that has more specific targeting. Aucatzyl, the newest approved CAR-T, was designed to mimic physiological T-cell receptor interactions, which, in turn, showed remarkably low levels of cytokine release syndrome in studies. There also are several other products being investigated under clinical trial that are designed to target proteins with little to no expression in normal immune cells, which would help to decrease the occurrence of hypogammaglobulinemia and cytopenias.

Advancements

Worldwide, there are 165 active (no longer recruiting) clinical trials involving CAR-T. Studies are being done to continue to move treatments up in line (first and second, prior to stem cell transplants), expand indications for blood cell cancers that currently have no CAR-T treatment option (e.g., acute myeloid leukemia, Hodgkin lymphoma, etc.), and for solid tumor and non-cancer related diagnoses (e.g., multiple sclerosis). The impact and success of CAR-T therapy is expected to continue and increase for years to come.

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Helpful Claims Review Codes

Disease Codes

Disease	ICD-10 Code Costs
Acute Lymphoblastic Leukemia (not having achieved remission; in relapse)	C91.0, C91.00, and C91.02
Diffuse Large B-Cell Lymphoma	C83 series
Other Unspecified Non-Hodgkin Lymphoma	C85 series
Multiple Myeloma	C90.0
Encounter for Antineoplastic Immunotherapy	Z51.12
Cytokine Release Syndrome	D89.83
Tumor Lysis Syndrome	E88.3

Additional Important Codes for Claims Identification

Current Procedural Technology (CPT) Codes	0537T, 0538T, 0539T, and 0540T
Procedure Codes	XW033C3 – Introduction of engineered autologous chimeric antigen receptor T-cell immunotherapy into peripheral vein, percutaneous approach, new technology group 3 XW043C3 – Introduction of engineered autologous chimeric antigen receptor T-cell immunotherapy into central vein, percutaneous approach, new technology group 3
Diagnosis Related Group (DRG) Code	0018
Revenue Codes	0871-0874, 0891

Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom line. The Pharmacy Operations (RxOps) team watches the market — and our book of business — to anticipate how current and future advancements will impact financial risk levels for HM's client base. Standard practices include reviewing, auditing, and collaborating on the content of current policies, monitoring trends, and implementing appropriate cost savings techniques. Additional practices include the prevention of stockpiling, working to ensure prescriptions are filled via in network pharmacies and assessing to determine if patients are properly dosed based on weight and lab values when appropriate. All these services are provided to HM's clients at no additional cost to them.

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Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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