Pharmacy Focus:
Beyond CAR-T — Advances in Cell Therapy

Key Takeaways

- The development of cell therapies still outpaces that of gene therapies, solidifying the valuable role cell therapies play in medicine today.
- Certain cell therapies offer unique treatment options for several disease states outside of blood cell cancers and cancers in general.
- Similar to CAR T-cell therapies, costs remain high for these cell therapies due to the complex and personalized manufacturing process involved, the research and development costs, and the limited patient base.

Cell Therapy Introduction[1-4]

The medical and scientific communities have long worked to capitalize on the human body's natural defense systems to develop effective treatment options. This approach has been used for centuries and continues to expand and adapt today from transfusions to transplants to adoptive cell and gene therapies. Cell therapies span multiple therapeutic areas, including regenerative medicine, immunotherapy, and cancer therapy.

Simply stated, cell therapy is the transfer of cellular material into a patient for medical purposes. Cellular material can be autologous (taken from an individual's own cells) or allogeneic (taken from a donor's cells). Specific cells are extracted, refined, concentrated, and administered according to their specialized functions. The therapies can be unicellular or multi-cellular and can consist of stem cells and non-stem cells. Stem cell therapies are of specific interest due to their ability to self-renew and differentiate into specialized cell types.

As of March 2025, there are 44 gene and cell therapy products that are approved by the Food and Drug Administration (FDA) and available on the market. This includes 15 gene therapies and 29 cell therapies. Of the cell therapies, there are seven CAR-T and 22 non-CAR-T products. The non-CAR-T products are comprised of nine hematopoietic progenitor cell (HPC) – stem cell – cord blood products and 13 unique cell therapies.

Adoptive Cell Therapy[5-12]

Adoptive Cell Therapy (ACT), which also is known as cellular immunotherapy, is a form of treatment that uses the cells of the immune system (e.g., T-cells) to eliminate cancer. ACT harnesses the special actions of immune cells that are essential for the identification and destruction of foreign cells, such as cancer or microbes, in the body. ACT includes Tumor-Infiltrating Lymphocyte (TIL) therapies, Engineered T-cell Receptor (TCR) therapies, Chimeric Antigen Receptor (CAR) T-cell therapies, and Natural Killer (NK) Cell therapies. CAR-T, TCR, and TIL therapies each harness the important actions of T-cells in their own unique way.

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Adoptive Cell Therapy T-Cell Origins and Modifications

Therapy	T-cell Origin	Modifications
CAR-T	Peripheral blood	Lab-modified with man-made receptors that target cell surface antigens
TCR	Peripheral blood	Genetically lab-modified to express specific tumor antigens within a cell
TIL	Tumor	Natural, expanded, and activated T-cells direct from a tumor

Costs remain high for ACT therapies due to the complex and personalized manufacturing process, research and development costs, and limited patient base. Each step of the process, which includes extracting a patient's own T-cells, genetically modifying them in a lab, and reinfusing them into the patient, requires specialized equipment, highly skilled labor, and strict regulatory compliance – all of which contribute to high production costs.

Product Focus

Cord Blood Products[1, 13-15]

Of the 22 FDA-approved non-CAR-T cell products, nine are classified as cord blood products. Cord blood, or the blood remaining in the umbilical cord and placenta after birth, contains red blood cells, white blood cells, platelets, plasma, and stem cells. Because of the stem cell content, cord blood is considered a regenerative medicine product, which is subject to FDA regulation.

Manufacturers of cord blood products are blood banks or medical institutions that are responsible for the collection, processing, testing, and distribution of blood components. Some manufacturers include Ducord, which is a Duke University of Medicine product, and Hemacord, which is the New York Blood Center's product. The FDA-approved cord blood products are used to treat blood disorders by providing blood-forming stem cells to aid in cell regeneration after chemotherapy, radiation, or other medical procedures.

Refined Specific Cell Products[1, 16-20]

Refined specific cell products comprise the bulk of the 12 unique non-CAR-T cell products. With this treatment option, specific cell types have been chosen and refined to replace damaged or missing cells, not unlike traditional transplantation. They can be autologously derived or created as "off the shelf" products using allogenic donor cells. Many of the products have been developed from structural cells like fibroblasts that produce connective tissue fibers, promoting healing or replacing damaged tissues. Newer products are being developed utilizing specific cells that are important for their physiological actions or properties.

Immune Cell Products[1, 5-6, 21-24]

Immune cell products are the most like CAR-T and are made up of unique adoptive cell therapies including TIL therapies, engineered TCR therapies, and NK cell therapies. The first two products in this category were approved in 2024.

Cancer Vaccines[1, 22-31]

Cancer vaccines are immunotherapies that are comprised of cellular products with unique and varying mechanisms. Unlike preventative vaccines that offer prophylaxis against cancer-causing agents prior to exposure (e.g., Gardasil for cervical cancer), therapeutic cancer vaccines are administered to patients already diagnosed with a disease. Therapeutic cancer vaccines exploit and enhance a patient's innate immune response to cancer cells, aiming to eradicate the disease. Amtagvi™, the TIL therapy previously discussed, can be considered a cancer vaccine since it involves the presentation of antigens isolated from a tumor to induce a targeted immune response.

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Non-CAR-T Cell Products

Product	Source/Type of Cells	Indications	Cost
Refined Specific Cell Products			
Gintuit™ approved March 12, 2012	Allogeneic cultured keratinocytes and fibroblasts in collagen	Scaffold product indicated for topical application over a surgically created oral wound bed	Withdrawn from U.S. market
LaViv™ (Azficel-T) approved June 21, 2011	Autologous dermal fibroblasts	Improvement of the appearance of moderate to severe wrinkles in adults	Withdrawn from U.S. market
Maci® approved December 13, 2016	Autologous chondrocytes and collagen	Scaffold product for the repair of cartilage defects of the knee with or without bone involvement in adults	Procedure costs are between $38,000 and $45,000
Omisirge® (omidubicel-onlv) approved April 17, 2023	Allogenic HPCs from cord blood enriched with nicotinamide (NAM)	Adults and pediatric patients 12 years and older with blood cancers who are planned for cord blood transplantation to reduce infection risk	Average wholesale price of $405,600
Stratagraft® approved June 15, 2021	Allogeneic keratinocytes and dermal fibroblasts in collagen	Promote durable wound closure and regenerative healing in the treatment of adult patients with debrided thermal burns	$4,800 per film
Symvess™ approved December 19, 2024	Acellular tissue engineered vessel composed of organized extracellular matrix (ECM) proteins	Use in adults as a vascular conduit for extremity arterial injury when urgent revascularization is needed	$29,500 per unit/graft
Lantidra® (donislecel) approved June 28, 2023	Allogeneic pancreatic islet cellular therapy	Treatment of adults with "brittle" Type 1 diabetes (T1D)	Still TBD; estimated at $300,000 (product alone) or $1,500,000 (with admin costs, etc.)
Ryoncil® (remestemcel-L-rknd) approved December 28, 2024	Allogeneic bone marrow-derived mesenchymal stromal cell (MSC)	Treatment of steroid-refractory acute graft versus host disease (SR-aGvHD) in pediatric patients two months of age and older	Estimated wholesale acquisition cost of $194,000 per infusion with typically 8 infusions per course, resulting in $1,552,000 for a full course
Encelto™ (revakinagene taroretcel-lwey) approved March 5, 2025	Allogeneic encapsulated retinal pigment epithelial (RPE) cell-based gene therapy	Indicated for the treatment of adults with idiopathic macular 13 telangiectasia type 2 (MacTel)	Estimated costs of $600,000 to $1,000,000 for 2 implants
Immune Cell Products			
Amtagvi™ (lifıcleucel) approved February 16, 2024	Autologous TIL therapy	Treatment of adult patients with previously treated unresectable or metastatic melanoma	Estimated wholesale acquisition cost of $562,000
Tecelra® (afamitresgene autoleucel) approved August 2, 2024	Autologous TCR therapy	Treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy	Estimated wholesale acquisition cost of $727,000

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Product	Source/Type of Cells	Indications	Cost
Cancer Vaccines			
Provenge® (sipuleucel-T) approved April 29, 2010	Cellular gene therapy product comprised of autologous peripheral blood cells, including activated antigen presenting cells (APCs)	Treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer	Wholesale acquisition cost of $187,808 for 3 total doses
Imlygic® (talimogene laherparepvec) approved October 27, 2015	Oncolytic virus therapy modified to replicate within tumors and to produce immune stimulatory protein	Treatment of advanced unresectable melanoma	Wholesale acquisition cost of $698,579

The Future of Cell Therapies[32-41]

There are numerous on-going studies involving specific cell type products. One example is Daramiocel (CAP-1002), an "off the shelf" treatment for Duchenne Muscular Dystrophy (DMD)-associated cardiomyopathy. This product utilizes cells harvested from donor heart tissue that are responsible for releasing signaling molecules that aid in reducing inflammation, preventing cell death, and promoting the regeneration of damaged tissues. Positive three-year results in the HOPE-2 trial showed improvement in skeletal muscle function tests and in multiple cardiac measures of cardiac function in males ages 10 and older. Deramiocel can be incorporated into existing DMD treatment regimens. Based upon the target cost estimate shared by Capricor Therapeutics, the cost for a full year of treatment (four doses) is expected to be around $600,000. Daramiocel currently has a PDUFA date of August 31, 2025.

Currently there are numerous on-going clinical trials for TCR therapies, TIL therapies, and NK cell therapies. Ebvallo® (tabelecleucel; Tab-cel; ATA129), an "off the shelf" T-cell immunotherapy already approved in Europe, was set for approval in the United States on January 1, 2025; however, a complete response letter (CRL) was received from the FDA citing manufacturing questions. A resubmission and approval are anticipated for later in 2025 considering Ebvallo's approval in Europe and the prevalence of the EBV positive post-transplant lymphoproliferative disorder (PTLD) complication after transplant, which occurs 50% to 80% of the time. Treatment is likely to be approved as second line after failure of the standard of care treatment with rituximab, and costs are anticipated to reach $900,000 after two to three treatment courses.

There are at least 150 on-going clinical trials in the cancer vaccine space, offering promising future treatments for advanced cancers with minimal available options (lung cancers, brain cancers, female reproductive cancers, etc). Vigil (gemogenovatucel-T) is being studied for multiple diagnoses, including Ewing's sarcoma (Phase III) and ovarian cancer (Phase II). Vigil is a personalized autologous tumor cell vaccine that capitalizes on a patient's unique tumor neoantigens (new proteins that form in cancer cells due to DNA mutations). Annual wholesale acquisition cost is estimated to be between $500,000 to $750,000.

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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