Immunological Cellular Therapies and Gene Therapies

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member, including care that may be both medically reasonable and necessary.

The Medicare Advantage medical policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and Centers of Medicare and Medicaid Services (CMS) policies and manuals, along with general CMS rules and regulations. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of a specific CMS coverage determination for a requested service, item or procedure, the health plan may apply CMS regulations, as well as their Medical Policy Manual or other applicable utilization management vendor criteria developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Some services or items may appear to be medically indicated for an individual, but may be a direct exclusion of Medicare or the member's benefit plan. Medicare and member EOCs exclude from coverage, among other things, services or procedures considered to be investigational (experimental) or cosmetic, as well as services or items considered not medically reasonable and necessary under Title XVIII of the Social Security Act, §1862(a)(1)(A). In some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services. Members, their appointed representative, or a treating provider can request coverage of a service or item by submitting a pre-service organization determination prior to services being rendered.

DESCRIPTION

Immunological cellular and gene therapies are methods of treating cancer and other diseases. The theory is that a patient's immune system can delay tumor progression and, on rare occasions, eliminate tumors altogether.

Adoptive cellular therapy is a method of treatment used to help the immune system fight diseases, such as cancer and infections with certain viruses. T-cells are collected from the patient, processed, and returned to the patient. Autologous lymphocytes used as part of cellular immunotherapy may be harvested in a pheresis procedure or may be isolated from resected tumor tissue.

Gene therapy is proposed to treat or prevent certain diseases by inserting foreign genetic information into a person's cells, to either change, replace, or suppress disease-causing genes.

MEDICARE ADVANTAGE POLICY CRITERIA

Note:

- Allogeneic stem cell transplantation following nonmyeloablative conditioning of the recipient (known as reduced-intensity conditioning [RIC]) also may be referred to as "adoptive immunotherapy" in literature. However, RIC conditioning cell transplantation relies on a donor-versus-malignancy effect of donor lymphocytes. In contrast, the adoptive immunotherapy techniques described in this evidence review enhance autoimmune effects primarily. Please see Cross References below.
- This policy does **not** address the following therapies. Please see the Medication Policy Manual noted in Cross References below:
    - Non-cellular based immunotherapies, including but not limited to IL-2 monotherapy or in combination with other cytokines.
    - sipuleucel-T (Provenge®)
    - voretigene neparvovec-rzyl (LUXTURNA™)
    - Onasemnogene abeparvovec-axgt (Zolgensma®)
    - Chimeric antigen receptor (CAR) T-cells, including but not limited to the following:
        - axicabtagene ciloleucel (axi-cel; Yescarta™)
        - tisagenlecleucel (KYMRIAH™)
        - brexucabtagene autoleucel (Tecartus™)
        - lisocabtagene maraleucel (Breyanzi®)
        - idecabtagene vicleucel (ABECMA®)

CMS Coverage Manuals*	None
National Coverage Determinations (NCDs)*	None Medicare has several NCDs for related procedures; however, these NCDs are not applicable to adoptive immunotherapy. Below are the NCDs and the rationale for why they are not applicable: • NCD for apheresis (110.14)[1]: This NCD includes leukapheresis as a treatment for leukemia. However, this NCD is specific to the removal of blood components with the remaining components re-transfused into the patient. This is different from adoptive immunotherapy. • NCD for autologous cellular immunotherapy treatment (110.22)[2]: This NCD is specific to the use of Sipuleucel-T (Provenge®) for the treatment of prostate

	cancer, which is a different type of treatment from adoptive immunotherapy. • NCD for cellular therapy (30.8)[3]: This NCD also describes a different type of treatment from adoptive immunotherapy. • NCD for chimeric antigen receptor (CAR) T-cell therapy (110.24)[4]: This NCD addresses services that are outside the scope of this medical policy (see the Medication Policy Manual in Cross References below).
Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles (LCAs)*	None
Medical Policy Manual	*Medicare coverage guidance is not available for immunological cellular therapies or gene therapies. Therefore, the health plan's medical policy is applicable.* For the following services, use Immunological Cellular Therapies and Gene Therapies, Medicine, Policy No. 42 *(see "NOTE" below)* • Adoptive cellular therapy for the administration of cytotoxic T lymphocytes; • Cytokine-induced killer cells; • Tumor-infiltrating lymphocytes; • Antigen-loaded autologous dendritic cells; • Genetically engineered T-cells

NOTE: If a procedure or device lacks scientific evidence regarding safety and efficacy because it is investigational or experimental, the service is noncovered as not reasonable and necessary to treat illness or injury. (*Medicare IOM Pub. No. 100-04, Ch. 23, §30 A*). According to Title XVIII of the Social Security Act, §1862(a)(1)(A), only medically reasonable and necessary services are covered by Medicare. In the absence of a NCD, LCD, or other coverage guideline, CMS guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an ***objective, evidence-based process, based on authoritative evidence***. (*Medicare IOM Pub. No. 100-16, Ch. 4, §90.5*). The Medicare Advantage Medical Policy - Medicine Policy No. M-149 - provides further details regarding the plan's evidence-assessment process (see Cross References).

POLICY GUIDELINES

REGULATORY STATUS

Several immunological cellular therapies and gene therapies have received U.S. Food and Drug Administration approval (see Cross References for specific therapies).

CROSS REFERENCES

Investigational (Experimental) Services, New and Emerging Medical Technologies and Procedures, and Other Non-Covered Services, Medicine, Policy No. M-149

Stem Cell and Bone Marrow Transplants, Transplant, Policy No. M-45

Medication Policy Manual; *NOTE: Select the applicable state, if prompted, On the "Pre-Authorization" page, do a "find" (Ctrl+F) and enter drug name in the find bar to locate the appropriate policy.*

REFERENCES

1. NCD for *Apheresis (Therapeutic Pheresis)* (110.14)
2. NCD for *Autologous Cellular Immunotherapy Treatment* (110.22)
3. NCD for *Cellular Therapy* (30.8)
4. NCD for *Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers* (110.24) [Last cited 05/10/2023]

CODING

NOTE: HCPCS code S2107 is a Medicare Status "I" code, and therefore, is not valid for Medicare or Medicare Advantage use.

Codes	Number	Description
CPT	36511	Therapeutic apheresis; for white blood cells
	37799	Unlisted procedure, vascular surgery (therapeutic leukapheresis)
	96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to one hour
HCPCS	S2107	Adoptive immunotherapy i.e. development of specific anti-tumor reactivity (e.g., tumor-infiltrating lymphocyte therapy) per course of treatment *(Not valid for Medicare purposes)*

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.*