Pharmacy Focus:
Amtagvi™ – A Novel Treatment for Metastatic Melanoma

Key Takeaways Regarding Amtagvi™

- There has been an unmet need for treatment options for those diagnosed with metastatic, inoperable melanoma that has progressed despite standards of care.
- Amtagvi is the first and only one-time individualized T-cell therapy approved for solid tumor cancer.
- Amtagvi was approved by the FDA February 16, 2024, under the designations of Orphan Drug, Regenerative Medicine Advanced Therapy, Fast Track, and Priority Review.
- The projected cost of Amtagvi is $618,000 for the drug (does not include ancillary costs).

Metastatic Melanoma Disease Overview[1-3]

Melanoma is a type of skin cancer that is caused by the uncontrollable growth of melanocytes, a type of skin cell responsible for producing melanin (pigment). Risk factors include age (diagnosis typically occurs around age 65), lighter skin, and blue or light-colored eyes. It is the fifth most common cancer in the United States. While melanoma only constitutes about 1% of skin cancers, it unfortunately leads to the majority of skin cancer-related deaths. In 2024, it is projected that there will be more than 100,000 new cases of melanoma diagnosed in the United States, with more than 8,000 deaths attributed to melanoma and representing approximately 1% of all cancer-related fatalities.

In the early stages, melanomas may not present with specific symptoms, making them challenging to detect. Self-monitoring and screening for early detection is highly encouraged. While most melanomas are diagnosed at an early stage that can be managed with surgical intervention, a portion of patients either present with metastatic disease at diagnosis or have future disease progression. About 15,000 patients are diagnosed annually with more advanced stages of melanoma. The anticipated overall five-year relative survival rate in localized disease is 93.5%, but the survival rate drops to only 35% for metastatic disease.

Current Treatment Options[3]

While there are several available treatment options on the market for melanoma, approximately 6,300 patients in the U.S. per year require second-line therapy, with about 4,800 progressing to third- and fourth-line therapy. Typically, once a patient has progressed while treated with a certain class of medications, there is little evidence that another drug in the same class will provide substantial benefit. Patients often progress through these therapies and are left with only chemotherapy as a last resort, which has limited efficacy, short durations of response, and significant side effects. There has been an unmet need for treatment options in this patient population until the approval of Amtagvi.

Continued...

Class	Drugs	Description	Price/Year (AWP)
Interleukin (IL-2)	Proleukin®	IV infusion; lymphocyte growth factor and immune system inducer	$373,000+ (weight-based)
BRAF Inhibitors	Braftovi®, Zelboraf®, Tafinlar®	Oral medications; targeted therapy that blocks processes responsible for stimulating tumor cell growth	$179,000 to $232,300
MEK Inhibitors	Mektovi®, Mekinist®, Cotellic®	Oral medications; targeted therapy that blocks processes responsible for stimulating tumor cell growth	$114,000 to $230,900
PDI-1 Blockers	Keytruda®, Opdivo®	IV infusion; immunotherapy that prevents immune system response blockade and increases T-cell activity	$192,740 and $194,610 (respectively)
PD-L1 Blocker	Tecentriq®	IV infusion; immunotherapy that prevents immune system response blockade and increases T-cell activity	$216,400
CTLA-4 Blocker	Yervoy®	IV infusion; immunotherapy that prevents immune system response blockade and increases T-cell activity	$170,650
LAG-3 + PD-1 Blocker	Opdualag™	IV infusion; immunotherapy that prevents immune system response blockade and increases T-cell activity	$348,800
Other – Gene Therapy	Imlygic®	Intralesional infusion; the exact mechanism of action is unknown, but produces an immune stimulatory protein that promotes an antitumor immune response	$798,370 (max of six months of treatment; can be used in multiple lesions)
Other – Cell Therapy	Amtagvi™	IV infusion; the specific mechanism of action is unknown, but provides targeted T-cells from the microenvironment of the solid tumor to kill tumor cells	$618,000 (one-time treatment)

Drug Overview – Amtagvi™ (lifileucel)[4-9]

Amtagvi™ (lifileucel), manufactured by Iovance Biotherapeutics, was approved February 16, 2024, and is the first and only one-time individualized T-cell therapy approved for solid tumor cancer. Amtagvi is a cell therapy, specifically described as a tumor-derived autologous T-cell therapy indicated for the treatment of adult patients with melanoma that cannot be removed surgically (unresectable) or has spread to other parts of the body (metastatic) and that has been treated unsuccessfully with other agents.

Amtagvi is approved for use as second-line after-treatment with a PD-1 antibody, like Keytruda®. If there is a specific genetic mutation present (BRAF V600 positive), Amtagvi is approved as a third-line after-treatment option with a PD-1 antibody and a BRAF inhibitor with or without a MEK inhibitor (e.g., Braftovi®/Mektovi®).

As a tumor-derived immunotherapy, Amtagvi is unique. Tumor-infiltrating lymphocyte (TIL) cells are collected from a patient's own tumor tissue, activated, and then infused back to the patient following a short course of chemotherapy. After the Amtagvi infusion, the patient receives a short course of six doses of interleukin-2 (IL-2) to stimulate and enhance the patient's immune response toward the cancer.

Iovance has indicated there are 30 authorized treatment centers (ATCs) ready to gather and ship tumor tissue from patients. Once cells are collected from patients, the manufacturing process takes an average of 34 days until the product is ready for infusion back into the patient. Regarding side effects, there is a boxed warning for risks that include treatment-related mortality; a prolonged, severe drop in blood counts; severe infection; and cardiac and renal issues. The more severe adverse reactions reported are mostly related to the short courses of chemotherapy and IL-2 required in the process of treatment.

Amtagvi approval came after the promising results of the Phase 2 C-144-01 trial were released. Of note, patients in the trial had been treated with about three prior lines of therapy, and a minimum of 1.5 cm of resectable tumor tissue was required to successfully generate the cell therapy. The primary efficacy outcome focused on a decrease in lesion size by at least 30% and the duration of that response to Amtagvi treatment. In a group consisting of 73 patients, 31.5% of people had either a partial (30% or greater) or complete response (disappearance of lesions) with a duration of response continuing beyond 18.6 months.

In a four-year post treatment group that included 153 patients, an average response duration of at least 12 months was noted in 43.5% of patients, and efficacy results were similar. Per the National Institutes of Health (NIH), more recent research on TIL therapy has demonstrated an upwards-of-56% response rate among patients, with 24% showing a complete disappearance of disease. Amtagvi continues to be studied for long-term efficacy as well as for use in earlier lines of treatment and in combination with Keytruda in the first-line setting for unresectable or metastatic melanoma.

The average wholesale price (AWP) for Amtagvi is $618,000 per patient for the one-time dose. This cost is for the medication only and does not include any costs for outpatient or inpatient care before, during, and after administration, which typically includes cell collection, a pre-infusion lymphodepleting regimen and post-infusion IL-2 treatment. The additional cost of the six doses of IL-2 will range, depending on claimant weight, between $60,000 and $100,000). Value-based contracting and outcomes-based agreements are being looked at for potential cost-savings strategies for first-line payers. While these options can be ideal for high-cost therapies, Amtagvi and TIL therapy pose several challenges to the implementation of these strategies, such as lesser response rates compared to other products.

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 preventing 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.

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**.

Resources: [1]Cancer Stat Facts: Melanoma of the Skin, https://seer.cancer.gov/statfacts/html/melan.html, accessed February 23, 2024; [2]Melanoma: Statistics, https://www.cancer.net/cancer-types/melanoma/statistics, accessed February 23, 2024; [3]Oncology: Melanoma, https://www.idpanalytics.com, accessed February 19, 2024; [4]"Emerging Therapy Solutions® (ETS) Announcement – BIG NEWS: Advanced Melanoma Cell Therapy Approved Today!" accessed February 16, 2024; [5]"Iovance's AMTAGVI™ (lifileucel) Receives U.S. FDA Accelerated Approval for Advanced Melanoma, Iovance Biotherapeutics, Inc., https://ir.iovance.com/news-releases/news-release-details/iovances-amtagvitm-lifileucel-receives-us-fda-accelerated?utm_campaign=Active%20Clients%20Campaign&utm_medium=email&_hsmi=294514382&_hsenc=p2ANqtz-91PWss1iW_HDQpNam-MLq12onFOyUsieG0QuG6GG220ulgDdHI56XtsiqugfrQjpVBzmiRWk90egKNkFo0QeN8omaCFMp-DLVJj9TONA_RAKoma6co&utm_content=294514382&utm_source=hs_emai, accessed February 19, 2024; [6]Amtagvi™ (lifileucel), Prescribing Information, Iovance Biotherapeutics Manufacturing, LLC (Philadelphia, PA), https://www.fda.gov/media/176417/download?attachment#:~:text=AMTAGVI%20is%20provided%20as%20a,72%20x%20109%20viable%20cells.&text=AMTAGVI%20is%20for%20autologous%20use%20only, accessed February 19, 2024; [7]"First Cancer TIL Therapy Gets FDA Approval for Advanced Melanoma," https://www.cancer.gov/news-events/cancer-currents-blog/2024/fda-amtagvi-til-therapymelanoma#:~:text=In%20an%20event%20more%20than,%2Dinfiltrating%20lymphocytes%2C%20or%20TILs, accessed March 6, 2024; [8]"A Watershed Moment for Cancer Therapies Has Arrived," https://www.axios.com/2024/02/21/til-cancer-treatment-cell-therapy-iovance-fda, accessed February 22, 2024; [9]"Long-term Efficacy and Safety of Lifileucel Tumor-Infiltrating Lymphocyte (TIL) Cell Therapy in Patients with Advanced Melanoma: A 4-year Analysis of the C-144-01 Study, Society for Immunotherapy of Cancer 38th Annual Meeting – November 3-5, 2023 in San Diego, CA," https://www.iovance.com/uploads/FINAL-SITC-2023_C-144-01-4-Year_Print-POS-2565-publication.pdf, accessed March 6, 2024.

MX3909350 (7/24)