Pharmacy Focus:
Adstiladrin® – A New Gene Therapy for a Specific Type of Bladder Cancer

Key Takeaways

- A gene therapy called Adstiladrin was approved December 16, 2022, for adult patients with a specific type of bladder cancer: high-risk bacillus Calmette-Guérin (BCG) unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.
- Adstiladrin is administered locally into the bladder once every three months.
- It is expected that Adstiladrin will be available in fall 2023.
- The estimated annual cost for Adstiladrin is $500,000 to $750,000 under medical benefits.

Non-Muscle Invasive Bladder Cancer Overview[1,2]

Bladder cancer occurs when cells that form the urinary bladder begin to grow without control. Common symptoms include hematuria (blood in the urine), as well as frequent urination, pain/burning during urination and frequent urination during the night. These symptoms can differ person to person. If the cancer has spread to other organs, symptoms can also include pain in the abdomen, bone pain/tenderness and unintended weight loss.

There are various types of bladder cancer. The most common is urothelial carcinoma, which is also known as transitional cell carcinoma (TCC). Bladder cancers can be described as invasive or noninvasive, which indicates how far the cancer has spread into the wall of the bladder. Noninvasive cancers are found in the inner layer of the bladder wall and have not penetrated deeper layers, a scenario that is referred to as carcinoma in situ (CIS) or stage 0 cancer. Clinically, whether the cancer has invaded the main muscle layer determines the course of treatment. If the cancer has not invaded the muscle layer, it is called superficial or non-muscle invasive bladder cancer (NMIBC), which can usually be cured.

The following relates to the prognosis:

- Success depends on the stage, type and patient's age/health.
- About half of all bladder cancers are detected when the cancer is noninvasive or in situ.
- Bladder cancer is the fourth most common cancer for men, but less common in women.
- It predominantly occurs in older people, with about 90 percent diagnosed over the age of 55.
- Average age of diagnosis is 73.
- Relative five-year survival rate (based on people diagnosed with bladder cancer between 2012 and 2018) is 96 percent for those with in situ bladder cancer and 70 percent for those with localized bladder cancer.

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Current Treatment Options[3,4]

Treatment for NMIBC often includes intravesical therapies, which means they are administered directly into the bladder. According to the National Comprehensive Cancer Network (NCCN) guidelines, recommended treatment for high-risk NMIBC is surgery to remove bladder tumors called TURBT, or transurethral resection of a bladder tumor. TURBT is typically followed by intravesical bacillus Calmette-Guérin (BCG) or a single-dose intravesical chemotherapy with chemotherapy agents gemcitabine or mitomycin.

Approximately 70 percent of patients will receive induction BCG therapy and experience a complete response; however, more than 50 percent of patients will experience tumor recurrence after therapy. Unfortunately, there are not many effective treatment options for patients who experience progression after BCG therapy.

Adstiladrin Overview[5,6]

Adstiladrin (nadofaragene firadenovec-vncg) is a new gene therapy produced by Ferring Pharmaceuticals A/S. It was approved December 16, 2022, for the treatment of adult patients with high-risk bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors. Adstiladrin should be avoided in immunodeficient or immunocompromised patients due to the risk of infection.

Additionally, those with the following scenarios – metastatic disease (cancer that has spread), prior adenovirus-based treatment, current systemic therapy for bladder cancer and recent intravesical therapy (except for cytotoxic agents given as a single instillation or previous intravesical BCG therapy) – are ineligible for Adstiladrin.

Patients with symptomatic urinary tract infection or bacterial cystitis and clinically significant or unexplained liver or renal function tests are also likely to be determined ineligible for Adstiladrin.

The goal of Adstiladrin is to increase the antitumor activity in NMIBC by incorporating the IFN alpha 2b gene into the patient's cellular DNA, ultimately producing large amounts of IFN alpha 2b protein. Clinical studies have shown that IFN alpha 2b protein can be measured in the urine of patients treated with Adstiladrin within 24 hours after dosing. Adstiladrin is instilled locally into the bladder once every three months. Participants in the clinical trial received Adstiladrin once every three months for up to 12 months. Although not yet available in the U.S. market, it is estimated that the annual cost will be $500,000 to $750,000 billed under medical benefits.

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 of 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**.

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Resources: [1]Bladder Cancer – Patient Version, National Cancer Institute, published 2019, https://www.cancer.gov/types/bladder, accessed May 15, 2023; [2]Bladder Cancer, American Cancer Society, https://www.cancer.org/cancer/types/bladder-cancer, accessed May 15, 2023; [3]High-risk Nonmuscle Invasive Bladder Cancer, Mayo Clinic, https://www.mayoclinic.org/medical-professionals/urology/news/high-risk-nonmuscle-invasive-bladder-cancer/mac-20507327, accessed May 15, 2023; [4]Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.2.2023. ©National Comprehensive Cancer Network, Inc. 2023 All rights reserved, accessed May 15, 2023, To view the most recent and complete version of the guideline, go online to NCCN.org; [5]ADSTILADRIN [package insert], Parsippany, NJ: Ferring Pharmaceuticals A/S, published December 16, 2022, https://www.fda.gov/media/164029/download, accessed May 15, 2023; [6]A Phase III, Open Label Study to Evaluate the Safety and Efficacy of INSTILADRIN® (rAd-IFN)/Syn3) Administered Intravesically to Patients With High Grade, BCG Unresponsive Non-Muscle Invasive Bladder Cancer (NMIBC), Ferring Pharmaceuticals, ClinicalTrials.gov, identifier: NCT02773849, updated December 5, 2022, https://clinicaltrials.gov/ct2/show/NCT02773849, accessed May 15, 2023.

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