CMS Proposes Coverage with Evidence Development for CAR T-Cell Therapy

The Centers for Medicare & Medicaid Services (CMS) on February 15 announced a proposal to cover Food and Drug Administration (FDA)–approved chimeric antigen receptor (CAR) T-cell therapy under Coverage with Evidence Development (CED). No national Medicare policy currently covers CAR T-cell therapy, and local Medicare Administrative Contractors have discretion over whether to reimburse for it. The proposed National Coverage Determination would require Medicare to cover the therapy nationwide when it is offered in a CMS-approved registry or clinical study in which patients are monitored for at least 2 years posttreatment. Evidence from the registries and studies would help CMS identify the types of patients who benefit from CAR T-cell therapy and support future decisions by the agency about the types of cases in which Medicare would cover treatment with no registry or trial requirement.

"CAR T-cell therapy was the first FDA-approved gene therapy, marking the beginning of an entirely new approach to treating serious and even life-threatening diseases," said CMS Administrator Seema Verma, MPH. "Today's proposed coverage decision would improve access to this therapy while deepening CMS's understanding of how patients in Medicare respond to it, so the agency can ensure that it is paying for CAR T-cell therapy for cases in which the benefits outweigh the risks."

A news release with the announcement indicated that "CMS proposes to leverage the FDA's requirements for postapproval studies for CAR-T to the fullest extent possible in reviewing studies for CMS approval." The agency issued its proposal in response to a formal request, and the proposal also was informed by a meeting of the Medicare Evidence Development & Coverage Advisory Committee on August 22, 2018. CMS requested public comments during the 30 days after proposing the CED initiative, and a final decision is expected by mid-May. The proposed decision is available at: https://www.cms.gov/medicare-coverage-database/details/nca-tracking-sheet.aspx?NCAId=291.

Centers for Medicare & Medicaid Services

Lutathera Approved as First PRRT in Canada

In a press release issued on February 7, Advanced Accelerator Applications (Saint-Genis-Pouilly, France) announced Health Canada approval for Lutathera (^{177}Lu-oxodotreotide) for treatment of unresectable or metastatic, well-differentiated, somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumors (GEP NETs) in adults with progressive disease. Barak Palatchi, Chief Commercial Officer for Advanced Accelerator Applications, said, "As the first ever approved peptide-receptor radionuclide therapy in Canada, Lutathera represents an innovative new treatment option for GEP NET patients. We believe nuclear medicine has the potential to offer many benefits to cancer patients and hope to bring further advances to Canada in the future as part of our commitment to reimagine medicine."

Lutathera was approved in the United States on January 26, 2018. The Canadian approval of Lutathera was based on many of the same results from the pivotal phase 3 NETTER-1 study, which was published in January 2017 in *The New England Journal of Medicine* (2017;376:125–135), and on supporting data from the ERASMUS trial, an investigator-sponsored phase I/II, open-label, single-arm clinical study. In its decision statement issued in January 2019, Health Canada noted that the primary efficacy endpoint as targeted in NETTER-1 was progression-free survival (PFS). With a median follow-up of 10.5 mo, the results of the PFS analysis indicated a 79% reduction in risk for a patient to progress or die under Lutathera compared to octreotide long-acting release (LAR) treatment. Key secondary endpoints were overall response rate as assessed by an independent review committee, duration of response, and overall survival. Among patients with independent response assessments the overall response rate and duration of response were substantially improved with Lutathera treatment. A prespecified interim analysis of overall survival found 17 (14.7%) deaths in the Lutathera arm and 31 (27.4%) in the octreotide LAR arm. The decision noted that the ERASMUS data were "supportive of the efficacy of Lutathera in patients with foregut, midgut, and hindgut GEP NETs, including bronchial and pancreatic tumors."

Simron Singh, MD, MPH, medical oncologist at the Odette Cancer Centre at Sunnybrook Health Sciences Centre (Toronto, Canada), said, "There are very few effective treatment choices for patients with advanced GEP NETs who are not eligible for surgery and whose disease has progressed on standard treatments. Having this therapy approved and available will offer physicians another alternative to help manage their patients' disease." Advanced Accelerator Applications is preparing notifications on timing and distribution of Lutathera in Canada.

Health Canada
Advanced Accelerator Applications

FDA Warns Companies About AD Treatment Claims

The U.S. Food and Drug Administration (FDA) on February 11 posted 12 warning letters and 5 online advisory letters to foreign and domestic companies that are illegally selling more than 58 unapproved new drugs and/or misbranded drugs that claim to prevent, treat, or cure Alzheimer disease (AD) and a number of other serious diseases and health conditions. These products, which are often sold on websites and social media platforms, have not been reviewed by the FDA and are not proven safe and effective to treat the diseases and health conditions they claim to

address. These products may be ineffective, unsafe, and/or could prevent individuals from seeking appropriate diagnoses and treatments.

"Science and evidence are the cornerstone of the FDA's review process and are imperative to demonstrating medical benefit, especially when a product is marketed to treat serious and complex diseases like Alzheimer's. Alzheimer's is a challenging disease that, unfortunately, has no cure. Any products making unproven drug claims could mislead consumers to believe that such therapies exist and keep them from accessing therapies that are known to help support the symptoms of the disease, or worse––as some fraudulent treatments can cause serious or even fatal injuries," said FDA Commissioner Scott Gottlieb, MD. Gottlieb also outlined several important new actions and policy priorities the agency will take in the coming months to improve the safety of dietary supplements, including efforts to more rapidly communicate potential safety issues to the public, establishing a flexible regulatory framework that promotes innovation and upholds product safety, and other steps the FDA could consider to better ensure product safety and integrity.

The products cited in the warning and online advisory letters have been sold in violation of the Federal Food, Drug, and Cosmetic Act. The products include a variety of types, such as tablets, capsules, and oils. The companies were asked to respond to the FDA within 15 days of receipt of the letters with information on how the violations will be corrected. Failure to correct the violations promptly may result in legal action, including product seizure and/or injunction. The FDA has issued more than 40 warning letters in the past 5 years to companies illegally marketing more than 80 products making AD-related claims on websites, social media, and in stores.

A list of the companies warned is available by link at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm631064.htm.

U.S. Food and Drug Administration

DOE Selects 4 Companies for ^{99}Mo Production

The Department of Energy National Nuclear Security Administration (DOE/NNSA) announced on February 20 that it had completed its evaluation of applications submitted in response to a funding opportunity for production of ^{99}Mo without the use of highly enriched uranium (HEU). Based on evaluations and recommendations from an independent technical review panel, DOE/NNSA selected 4 U.S. companies to begin negotiations for potential new cooperative agreement awards. The companies are NorthStar Medical Radioisotopes, LLC (Beloit, WA), SHINE Medical Technologies (Janesville, WI), Northwest Medical Isotopes (Corvallis, OR), and Niowave, Inc. (Lansing, MI). The U.S. Congress has appropriated funds that would allow DOE/NNSA to create cooperative agreements up to $15 million for each company. The industry partners will match any awarded funding amount.

DOE/NNSA is supporting the establishment of a redundant, reliable domestic supply of non-HEU ^{99}Mo. The effort's goal is to support the companies in achieving the objective of supplying ~3,000 6-day curies of ^{99}Mo each week. In addition to these cooperative agreements, DOE/NNSA also funds the DOE National Laboratories to advance industry efforts to produce non-HEU ^{99}Mo within the country.

^{99}Mo is used in more than 40,000 medical procedures in the United States every day. In the last decade, supplies have been challenged by the move toward non-HEU ^{99}Mo and by frequent production challenges at reactors outside the country. The American Medical Isotopes Production Act of 2012 directed DOE/NNSA to implement a technology-neutral program (i.e., open to any method of ^{99}Mo production that does not use HEU) in cooperation with nonfederal entities. "^{99}Mo is such a critical tool in health care. Doctors count on it every day," said U.S. Secretary of Energy Rick Perry. "This industry outreach helps to develop a reliable domestic supply of a vital medical isotope, reduce dependence on foreign imports, and bring new opportunity to the heartland."

For more information on DOE/NNSA efforts to establish a reliable supply of ^{99}Mo without the use of HEU, see https://www.energy.gov/nnsa/nnsa-s-molybdenum-99-program-establishing-reliable-supply-mo-99-produced-without-highly.