CMS Proposal for New Oncology PET Tracers

On December 13 the Centers for Medicare & Medicaid Services (CMS) issued a proposed decision memo for PET (CAG-00065R2) that could make it easier for new oncology PET tracers to win reimbursement. However, the proposed change will not apply to tracers used for neurology and cardiology applications. CMS proposed that local Medicare Administrative Contractors determine coverage within their respective jurisdictions for oncologic PET imaging using radiopharmaceuticals for indications that are approved by the U.S. Food and Drug Administration (FDA).

This proposal would remove national noncoverage for uses of FDA-cleared PET radiopharmaceuticals that have not been determined nationally. The proposal would also cover hybrid modalities, such as PET/CT and PET/MR imaging. This proposal comes after a formal request regarding national noncoverage from the Medical Imaging and Technology Alliance, with the support of SNMMI, the American College of Radiology, the Council on Radionuclides and Radiopharmaceuticals, and the World Molecular Imaging Society.

In an official summary of the lengthy CMS document, the agency proposed "that local Medicare Administrative Contractors may determine coverage within their respective jurisdictions for PET using radiopharmaceuticals for their labeled indications for oncologic imaging that are approved by the U.S. Food and Drug Administration (FDA)." The summary added that "the effect of this decision, if finalized without change, would be to remove the national noncoverage for any of these identified uses of these radiopharmaceuticals that have not been more specifically determined nationally. Thus this change would not apply to any use of PET using radiopharmaceuticals FDG, NaF-1, ammonia N-13, or rubidium Rb-82. This would not prevent CMS from determining national coverage for any of these uses in the future, and if such determinations are made, a future determination would supersede local contractor determinations under §1862(a)(1)(A) of the Social Security Act." CMS also emphasized the following points: (1) Changing the "restrictive" language of prior PET decisions will not by itself suffice to expand Medicare coverage to new PET radiopharmaceuticals; (2) The scope of this change extends only to FDA-approved indications for oncologic uses of PET tracers; and (3) This change does not include screening uses of PET. The agency also added a reminder that local coverage cannot be in conflict with National Coverage Determinations (NCDs) or other national policies and that "future CMS NCDs, if any, regarding diagnostic PET imaging would not be precluded by this determination."

Public comment was requested through January. Full text of the Proposed Decision Memo can be accessed at www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=261.

Centers for Medicare & Medicaid Services
SNMMI

New Domestic ^{99m}Tc Generator Resource Planned

US Radiopharmaceuticals (USR) and the Australian Nuclear Science and Technology Organization (ANSTO) announced on November 24 an agreement that would enable USR to establish a ^{99m}Tc generator production facility in Denton, TX. The agreement allows USR to manufacture Australian-designed generators utilizing ^{99}Mo sourced from 100% low-enriched uranium (LEU) for distribution in the Americas. Under the terms of the agreement, USR will become the only U.S. generator manufacturer using LEU ^{99}Mo for 100% of their generators. USR has secured long-term supply contracts guaranteeing year-round availability of LEU ^{99}Mo from both the ANSTO Open Pool Australian Light Water reactor (Sydney) and the NTP SAFARI-1 reactor (Pelindaba, South Africa). The generator facility is scheduled to begin production in late 2013.

"USR understands the increasing importance of having a U.S. manufacturer dedicated to sourcing medical isotopes without the use of highly enriched uranium [HEU] and see this initiative as a major leap forward for the nuclear medicine community in the U.S.," said USR CEO Paul Crowe. "We anticipate our announcement today will go some way to alleviate the U.S. governments concerns associated with nonproliferation and also address recent technetium generator shortages in the U.S. nuclear medicine community."

The ANSTO generators have been used routinely in Australia and other countries for more than 30 y and are fully compatible with current usage practices in the United States. Customers will be able to take advantage of the recent announcement by the Centers for Medicare & Medicaid Services of higher reimbursement for technetium produced from LEU-based sources and will be unaffected by proposed federal tariffs on HEU-based, non-full-cost-recovery ^{99}Mo.

US Radiopharmaceuticals
Australian Nuclear Science and Technology Organization

Einstein Researchers Receive Gates Grants

The Albert Einstein College of Medicine of Yeshiva University (Bronx, NY) announced on December 4 that 2 Grand Challenges Explorations (GCE) grants for innovative global health and development research projects from the Bill & Melinda Gates Foundation had been awarded to 3 Einstein scientists. Arturo Casadevall, MD, PhD, professor

and chair of microbiology and immunology and of medicine, will receive funding for his unconventional approach in antibody-based tuberculosis vaccines. Ekaterina Dadachova, PhD, a professor of radiology and of microbiology and immunology, and Joan Berman, PhD, a professor of pathology and of microbiology and immunology, received a Phase II GCE grant to study whether radioimmunotherapy (RIT) can kill the HIV virus in latently infected cells. All 3 awardees have worked together previously on RIT approaches in cancers and in infection, and both projects highlight the range of current radiolabeled agents in research with direct potential for wide clinical impacts.

Dadochova's project extends earlier GCE-funded research with Casadevall and is 1 of only 15 projects that advanced to the next level of funding in this series of awards. The team is working to develop a treatment strategy for HIV both systemically and in the central nervous system by targeting the gp41 viral antigen expressed on the surface of host HIV-infected cells. Dadachova and Berman will work in collaboration with Casadevall; Susan Zolla-Pazner, PhD, and Miroslaw Gorny, MD, PhD, from New York University (NY); and Alfred Morgenstern, PhD, and Frank Bruchertseifer, PhD, from the Institute of Transuranium Elements (Karlsruhe, Germany), who will supply radioisotopes for the project.

Albert Einstein College of Medicine of Yeshiva University

FDA Approves Cometriq in MTC

The U.S. Food and Drug Administration (FDA) announced on November 29 the approval of cabozantinib (Cometriq) to treat metastatic medullary thyroid cancer (MTC). The National Cancer Institute estimates that of the 56,460 individuals in the United States diagnosed with thyroid cancer in 2012, about 2,250 will have MTC.

"Cometriq is the second drug approved to treat MTC in the past 2 y and reflects FDA's commitment to the development and approval of drugs for treating rare diseases," said Richard Pazdur, MD, director of the Office of Hematology and Oncology Products in the FDA Center for Drug Evaluation and Research. "Prior to today's approval and the approval of Caprelsa in April 2011, patients with this rare and difficult-to-treat disease had limited therapeutic treatment options." Cometriq is marketed by Exelixis (San Francisco, CA).

The FDA completed review of Cometriq's application under the agency's priority review program. This program provides for an expedited 6-mo review for drugs that may offer major advances in treatment or that provide a treatment when no adequate therapy exists. Cometriq also received an orphan product designation from the FDA because it is intended to treat a rare disease or condition.

Cometriq is a kinase inhibitor that blocks abnormal kinase proteins involved in the development and growth of medullary cancer cells. Safety and effectiveness were established in a clinical study involving 330 patients with MTC. Treatment increased progression-free survival by 11.2 mo and achieved a response rate (reduction in tumor size) lasting an average of 15 mo in 27% of patients. Treatment with Cometriq, however, did not extend patients' lives.

U.S. Food and Drug Administration

New NIH BrIDGs Studies Funded

In a December 4 press release, the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH), described 3 studies targeted by 2012 funding from the Bridging Interventional Development Gaps (BrIDGs) program. The awarded studies will address therapeutics in cancer, spinal cord injury, and a rare disease that can lead to kidney failure. The 8-y-old BRIDGs program, previously known as NIH Rapid Access to Interventional Development, is supported by the NIH Common Fund. In addition, NIH institutes and centers at times contribute funding to support projects relevant to their missions.

Instead of directly funding successful applicants, BrIDGs enables NIH contractors to provide preclinical services—such as toxicology studies—for therapeutic projects that have demonstrated efficacy in a disease model. For the majority of projects, the goal is to enable submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA). To date, BrIDGs has generated data to support 12 INDs submitted to the FDA and 1 clinical trial application to Health Canada. Twelve of the 13 projects have been evaluated in clinical trials. Three BrIDGs-supported therapeutic agents have progressed as far as Phase II human clinical trials. Third-party investors have licensed 6 agents during or after development by BrIDGs.

BrIDGs selected the following new projects from its 2012 application solicitation: (1) Peritoneal cancers: tumor penetrating microparticles for peritoneal cancers, to Jessie Au, PharmD, PhD, and Optimum Therapeutics, LLC (San Diego, CA); (2) Lecithin-cholesterol acyltransferase (LCAT) deficiency syndrome: development of assays to detect antidrug antibodies against ACP-501 (recombinant human LCAT), to Brian Krause, PhD, and Alphacore Pharma, LLC (Ann Arbor, MI); and (3) Spinal cord injury: development of Nogo receptor decoy for the treatment of spinal cord injury, to George Maynard, PhD, and Axerion Therapeutics, Inc. (New Haven, CT).

"The success of BrIDGs demonstrates there is a vital need in the research community for the services offered through the program and speaks to the quality of the projects it supports," said John McKew, PhD, chief of the NCATS Therapeutics Development Branch. "While not all projects will make it as treatments, the support gained through BrIDGs provides each with a shot at success."

More information about BrIDGs is available at www.ncats.nih.gov/research/rare-diseases/bridgs/bridgs.html.

National Center for Advancing Translational Sciences

FDA and MDIC

The U.S. Food and Drug Administration (FDA) reported on December 3 that it is part of the first public–private partnership to promote medical device regulatory science with a focus on speeding the development, assessment, and review of new medical devices. The new Medical Device Innovation Consortium (MDIC) is an independent, nonprofit corporation, created by Life-Science Alley, a biomedical science trade association. The MDIC will receive input from industry, government, and other nonprofit organizations. MDIC will prioritize the regulatory science needs of the medical device community and fund projects to help simplify the process of medical device design and pathways to market for these innovations.

The FDA noted that the MDIC will "bolster the country's investment in regulatory science research by pooling people, funding, resources, and ideas to develop new tools, models, and methods that may be utilized to better and more efficiently evaluate new devices." FDA staff may collaborate with the consortium on MDIC-supported research and other projects. "By sharing and leveraging resources, MDIC may help industry to be better equipped to bring safe and effective medical devices to market more quickly and at a lower cost," said Jeffrey Shuren, MD, JD, director of the FDA Center for Devices and Radiological Health.

MDIC lists its strategies to advance medical device regulatory sciences as: (1) creating a forum for collaboration and dialogue, working within a flexible governance structure to encourage broad participation from medical device industry stakeholders, including nonprofits, industry, and government; (2) making strategic investments in regulatory science, utilizing working groups to identify and prioritize key issues and to request, evaluate, and implement project proposals that support MDIC's mission; and (3) providing tools to drive cost-effective innovation, emphasizing education and the development of new methods and approaches with well-documented data and details to enable implementation. The MDIC Web site is available at www.deviceconsortium.org/.

U.S. Food and Drug Administration

NIH and Future Biomedical Research

The National Institutes of Health (NIH) announced on December 7 that it is seeking to launch multiple initiatives designed to help strengthen the biomedical research enterprise and sustain the global competitiveness of the U.S. scientific community well into the future. Faced with significant challenges affecting the biomedical research workforce and the storage and use of large biomedical datasets, NIH Director Francis S. Collins, MD, PhD, earlier charged the Advisory Committee to the Director (ACD) with developing recommendations. The ACD used 3 specialized committee working groups, focusing on diversity in the biomedical research workforce, the future of the biomedical research workforce, and data and informatics.

The ACD presented its recommendations to the NIH director in June 2012. NIH leadership further deliberated on the recommendations and presented an implementation plan at the 105th meeting of the ACD on December 6 and 7. Among the workforce diversity actions announced are: (1) The launch of a new NIH program called Building Infrastructure Leading to Diversity (BUILD), intended to provide rigorous mentored research experiences for undergraduates at participating schools, financial support to pursue biomedical research careers, faculty support for training highly effective mentors, and innovation space to develop new approaches for increasing diversity in the PhD training pathway. (2) Establishment of a National Research Mentoring Network to connect students, postdoctoral fellows, and faculty with experienced mentors; develop standards of good mentorship in biomedical research; and provide workshops and training opportunities in grants, among other goals; (3) Promotion of fairness in peer review through interventions, including implicit bias and diversity awareness training for both scientific review officers and members of review panels, and piloting a program that would make grant applications completely anonymous; and (4) establishing various initiatives to increase engagement of NIH leadership. Actions targeted at the future workforce include: (1) efforts to enhance training of graduate students and postdoctoral researchers; (2) exploration of increased support for training mechanisms to accelerate the development of independent research careers; and (3) identification and tracking of NIH-supported graduate students and postdoctoral researchers to better assess future needs. Actions in data and informatics include: (1) creation of a new Big Data to Knowledge initiative that would enhance training for biomedical big data, improve data and software sharing policies and analysis methods, and create new centers of excellence; and (2) launch of the new NIH InfrastructurePlus adaptive environment to advance high-performance computing, agile hosting and storage approaches, and modernization of the network.

National Institutes of Health

FDA OIR

On December 17 the U.S. Food and Drug Administration (FDA) posted additional information about the Office of In Vitro Diagnostics and Radiological Health (OIR), 1 of the 8 FDA Center for Devices and Radiological Health offices that cover the product lifecycle of regulated medical devices and radiation-emitting products. Previously called the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), OIR consolidates all regulatory activities for IVDs and radiologic medical devices, along with electronic product radiation control responsibilities and leadership of the

Mammography Quality Program. OIR combines pre- and postmarket responsibilities into a single multidisciplinary office and also administers the Clinical Laboratory Improvement Amendments.

The OIR includes 6 divisions: Chemistry and Toxicology Devices, Immunology and Hematology Devices, Microbiology Devices, Radiological Health, Mammography and Quality Standards, and Program Operations and Management. Additional information is available at: www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/ucm115904.htm.

U.S. Food and Drug Administration

New Molecular Imaging Journal

On December 10 Springer (part of Springer Science + Business Media) announced the 2013 launch of a new bimonthly journal, *Clinical and Translational Imaging: Reviews in Nuclear Medicine and Molecular Imaging*, which will be the official publication of the Italian Association of Nuclear Medicine and Molecular Imaging (AIMN) as of 2013. Giovanni Lucignani, MD, editor-in-chief of the new journal and president of AIMN, said, "AIMN has long been committed to consistently raising the standard and impact of its scientific publications, and we now feel that the time has come to launch our own official journal."

Targeting nuclear medicine practitioners and other professionals involved in molecular imaging and therapy, this international peer-reviewed journal will publish timely and updated reviews, collected in single-themed issues, on clinical practice and translational research. It will also present clinical applications of approved and experimental radiopharmaceuticals for diagnostic and therapeutic purposes. Advanced preclinical evidence in the fields of physics, dosimetry, radiation biology, and radiopharmacy with relevance to clinical applications will also be included.

Springer Science + Business Media

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

CHOP and RIT in Follicular NHL

Members of the Southwest Oncology Group (SWOG) and the Cancer and Leukemia Group B, both National Cancer Institute–sponsored clinical research networks, reported on December 10 ahead of print in the *Journal of Clinical Oncology* on results of a phase III randomized intergroup trial of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy plus rituximab compared with CHOP chemotherapy plus ^{131}I-tositumomab for previously untreated follicular non-Hodgkin lymphoma. The lead author was Oliver W. Press, MD, PhD, from the University of Washington Medical Center (Seattle). The study (SWOG S0016) included 554 patients with previously untreated, advanced-stage (bulky stage II, III, or IV) follicular lymphoma of any grade. One group of patients received 6 CHOP cycles at 3-wk intervals, with 6 doses of rituximab (CHOP-R). Another group received the 6 cycles of CHOP followed by consolidation therapy with tositumomab/^{131}I-tositumomab radioimmunotherapy (CHOP-RIT). Over a median follow-up of 4.9 y, 2-y estimates of progression-free survival rates were similar for the CHOP-R and CHOP-RIT groups (76% and 80%, respectively), with 2-y estimates of overall survival also similar (97% and 93%, respectively). The authors concluded that the study had found "no evidence of a significant improvement in progression-free survival comparing CHOP-RIT with CHOP-R," but that both progression-free and overall survival were "outstanding on both arms of the study." They called for future studies to determine the potential benefits of combining CHOP-R induction chemotherapy with RIT consolidation and/or extended rituximab maintenance therapy.

Journal of Clinical Oncology

PET/CT in Recurrent Sarcoma

In an article e-published on December 11 ahead of print in *Cancer*, Al-Ibraheem et al. from the Technische Universität München (Germany) and the King Hussein Cancer Center (Amman, Jordan) reported on the results of a clinical study of the diagnostic accuracy and incremental value of ^{18}F-FDG PET/CT in patients with a history of sarcoma and clinically suspected disease recurrence. The study included 43 patients with histories of bone or soft tissue sarcoma and complete remission. All underwent ^{18}F-FDG PET/CT imaging. The 43 ^{18}F-FDG PET images; 30 contrast-enhanced spiral CT images; and 43 combined PET/CT images were separately analyzed, with imaging findings rated