October 23, 2016

eviCore Healthcare
Attn: Dr Greg Allen
400 Buckwalter Place Boulevard
Bluffton, SC 29910

RE: eviCore Draft Oncology Imaging Guidelines, v 19.0

Gentlepersons:

Prostate Cancer International is a not-for-profit 501(c)(3) founded in 2008. The mission of the organization is to “transform global understanding of the risks associated with prostate cancer and the strategies to manage those risks until prevention is possible and a cure can be found.”

We are primarily focused on providing high-quality informational and educational services for prostate cancer patients and their family members through The “New” Prostate Cancer InfoLink (see www.ProstateCancerInfoLink.net) and through an online social network with over 6,000 members. However, we also act as advocates for relevant research and for progress in the diagnosis and management of prostate cancer.

It has come to our attention that eviCore’s current draft Oncology Imaging Guidelines, tentatively scheduled for implementation on November 1, 2016, contain statements specific to the use of certain imaging agents and processes currently being used in the evaluation and work-up of patients suspected of having progressive or recurrent forms of prostate cancer which may not be identifiable with traditional imaging methods such as technetium-based bone scans. They also contain associated statements related to the management of prostate cancer itemized below.

Specifically, on page 12 of the current eviCore draft, we find the statement:

“PET imaging using isotopes other than $^{18}$F-FDG, including $^{18}$F NaF (PET bone scan), $^{11}$C-Choline, $^{68}$Ga-DOTATATE, and Fluciclovine F 18 is considered investigational at this time.”

Furthermore, on page 124 we find the following:

“Active surveillance describes the monitoring of disease progression in an individual with known diagnosis of prostate cancer. Current guidelines suggest the following protocol:

- PSA every 6 months;
- Digital Rectal Exam every 12 months and;
- Repeat prostate biopsy every 12 months.

“PET imaging (including $^{18}\text{F-FDG}$, $^{18}\text{F-NaF}$, and $^{11}\text{C-Choline}$) is considered investigational and experimental for all indications for prostate cancer at this time.

“Laser prostate ablation is considered investigational and experimental at this time, and advanced imaging for treatment planning and/or surveillance of laser prostate is not indicated.

“High intensity focused ultrasound prostate ablation is considered investigational and experimental at this time, and advanced imaging for treatment planning and/or surveillance of high intensity focused ultrasound prostate ablation is not indicated.

“MR Spectroscopy (CPT® 76390) is considered investigational and experimental in the evaluation of prostate cancer at this time.”

Prostate Cancer International is, frankly, puzzled and disturbed by some of these statements, which (in the opinion of this organization and others) clearly appear to be inaccurate, and we have grave concerns that the eviCore draft guidance, if implemented as currently written, will deprive numerous men who have been diagnosed with prostate cancer – as well as men who are suspected of being at high risk for prostate cancer despite a prior negative biopsy – of forms of care acknowledged by experts to be of high quality … and of forms of imaging that are clearly not “investigational” because they have been approved by the U.S. Food and Drug Administration (FDA) for use in the management of prostate cancer.

We note that on page 30 of the draft guidelines once can find the following definition:

"An experimental or investigational procedure is generally defined as the use of a service, supply, drug or device that is not recognized as standard medical care for the condition, disease, illness or injury being treated as determined by the health plan based on independent review of peer reviewed literature and scientific data."

This definition is, in and of itself, disturbing. It carefully and deliberately blurs the lines between a truly “experimental” technique, an “investigational procedure” (which has gone beyond the experimental level to be tested in significant numbers of patients), and an accepted and approved technique or procedure that has already been validated and endorsed by regulators and/or many opinion-leaders in the diagnosis and management of a specific disorder but that has only recently become widely available outside the centers in which it was originally developed and proven.

The use of such a definition actually guarantees the delay of access for patients to well-proven diagnostic and therapeutic procedures and techniques on grounds that have nothing to do with the
quality of the methodology. We understand that when such procedures and techniques are costly, it is reasonable for payers and health care insurance providers to ensure (through prior approval processes) that such procedures and techniques are going to be appropriately used among well-characterized patients who are likely to be benefit from their use. However, we would categorically disagree with your use of the definition as written. We certainly would not agree that “An experimental or investigational procedure is generally defined” in the above manner, and we suspect that the majority of the health care community would also dispute that definition.

Specifically, we would draw your attention to the items below.

(1) On September 12, 2012, production of $^{11}$Ccholine was approved by the FDA at the Mayo Clinic as “a Positron Emission Tomography (PET) imaging agent used to help detect recurrent prostate cancer.” In making this approval public, Charles Ganley, MD, then the director of the Office of Drug Evaluation IV in FDA’s Center for Drug Evaluation and Research, is quoted as saying, “Choline C 11 Injection provides an important imaging method to help detect the location of prostate cancer in patients whose blood tests suggest recurrent cancer when other imaging tests are negative” and “The FDA’s approval of Choline C 11 Injection at the Mayo Clinic provides assurance to patients and health care professionals they are using a product that is safe, effective, and produced according to current good manufacturing practices.” The use of $^{11}$Ccholine in this indication is therefore clearly not “investigational” by any reasonable definition of that term, and we respectfully request appropriate modification of your draft guideline to include this form of imaging as an approved practice. We acknowledge, however, that a payer may wish to put in place policies that require pre-approval for the use of this type of imaging test so that its use is limited to well-identified and appropriate patients.

(2) On May 27, 2016, $^{18}$Ffluclovine (also known as Axumin) was approved by the FDA for “positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated prostate specific antigen (PSA) levels following prior treatment.” In making this approval public, Libero Marzella, MD, PhD, then the director of the Division of Medical Imaging Products in the FDA’s Center for Drug Evaluation and Research, is quoted as saying that previously available imaging methods “are not able to determine the location of the recurrent prostate cancer when the PSA is at very low levels,” and that “Axumin is shown to provide another accurate imaging approach for these patients.” Again, the use of $^{18}$Ffluclovine in this indication is therefore clearly not “investigational” by any reasonable definition of that term, and we respectfully request appropriate modification of your draft guideline to include this form of imaging as an approved practice. We acknowledge, again, that a payer may wish to put in place policies that require pre-approval for the use of this type of imaging test so that its use is limited to well-identified and appropriate patients.

(3) It is unclear to us from what source you drew the statement about management of patients on active surveillance. We would bring to your attention that on February 16, 2016, the American Society of Clinical Oncology (ASCO) issued a set of formal guidelines about the management of
patients on active surveillance (see Chen et al. doi: 10.1200/JCO.2015.65.7759). In that set of guidelines, ASCO stated that

“3. The AS protocol should include the following tests:

- A PSA test every 3 to 6 months
- DRE at least every year
- At least a 12-core confirmatory transrectal ultrasound guided biopsy (including anterior directed cores) within 6 to 12 months, and then serial biopsy every 2 to 5 years thereafter or more frequently if clinically warranted. Men with limited life expectancy may transition to watchful waiting and avoid further biopsies.”

These guidelines also noted that the use of other tests, including the use of multiparametric MRI testing, was still considered to be “under investigation” at that time. We would request that eviCore amend its guidance about the management of patients on active surveillance to conform, at a minimum, to the guidance issued by ASCO. However, we would also advise you that Prostate Cancer International is highly supportive of the appropriate use of multiparametric MRI scans in the evaluation and management of men on active surveillance when used in conformity with the PI-RADS version 2 assessment and evaluation of such scans.

(4) We would also note that there is now extensive evidence of the value of multiparametric MRI scanning in the diagnosis and work-up of a broad range of men with early stage prostate cancer -- either post-diagnosis, in the determination of risk for spread of prostate cancer outside the prostate capsule (which can be of considerable value in the determination of the extent of extracapsular disease and therefore the planning of treatment) or in combination with transrectal ultrasound (TRUS) to ensure the accurate biopsying of areas of risk within the prostate. While it was arguable that this use of MRI scanning might have been “investigational” 2 to 3 years ago, we would argue strongly that this is no longer the case and that a large percentage of the urology community now carries out MRI/TRUS fusion biopsies with regularity in order to ensure the accurate biopsy of many men who have multiple signals risk for prostate cancer despite a negative systematic 12-core biopsy. Indeed, one review article published more than a year ago concluded as follows:

“... the benefits of targeted biopsy have been repeatedly shown in several studies. There is mounting evidence along with the recent literature suggesting that effectiveness of mp-MRI when used along with PSA, followed by targeted biopsy of the MRI-visible lesion, is a better alternative to systematic TRUS biopsy in the diagnostic pathway for prostate cancer detection and therefore benefits the diagnosis of cancer. The largest benefit may come from reduction of unnecessary biopsies (NPV of mp-MRI for clinically significant cancer), which could in turn prevent overdiagnosis and overtreatment. It also has the potential to decrease the number of missed clinically significant cancers and improves risk stratification; therefore, it provides a more accurate therapeutic option to
As we move toward personalized medicine, use of MRI to biopsy each man's prostate differently rather than based on a pre-defined 12 core seems to be supported in the recent literature.”

We would therefore disagree categorically with the statement in the draft guidelines that, “MR Spectroscopy (CPT® 76390) is considered investigational and experimental in the evaluation of prostate cancer at this time.”

We wish, respectfully, to suggest that eviCore Healthcare carefully reconsiders and amends its current draft guidelines on imaging in oncology with respect to the items above-listed. We believe that such amendments will lead to significant reductions in the costs of lengthy, expensive, and often inappropriate and unnecessary treatments for many patients with prostate cancer while simultaneously ensuring greater safety and accuracy of treatments for those men most in need of treatment.

Prostate Cancer International and the patients it represents appreciate your time and care in assessing the matters we have brought to your attention in this letter (which we will be sharing with other members of the prostate cancer advocacy community).

We would be pleased to discuss these comments with you further should this be of value.

Finally, as advocates for members of the prostate cancer community, it is only right and proper that we inform you that we can be expected to advise patients to appeal clinical decisions made by payers and health insurance companies that are based on several of the proposed eviCore guidelines as currently written, should these be finalized in their current form.

Sincerely

Mike Scott
E. Michael D. Scott
President and Co-Founder
mike@pcainternational.org
Tel: 215 446 8080

Jan Manarite
Executive Vice President
jmanarite@hotmail.com
Tel: 239 208 4400

Prostate Cancer International, Inc., PO Box 66355, Virginia Beach, VA 23466, USA