

Mallinckrodt Institute of Radiology

April 14, 2009

Tamara Syrek Jensen, J.D.
Acting Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06
Baltimore, MD 21244

Re: Formal Request for Limited-Scope Reconsideration of National Coverage Determination (NCD) CAG-00181N as to Cervical Cancer

Dear Acting Director Jensen:

As the original requestor for a NCD for PET for cervical cancer and as co-chair of the National Oncologic PET Registry (NOPR) Working Group, we write jointly to request that the Centers for Medicare & Medicaid Services (CMS) open a limited-scope reconsideration of NCD CAG-00181N for the specific purpose of Medicare coverage of FDG-PET for staging of cervical cancer during the initial treatment strategy without participation in a clinical study under the Coverage with Evidence Development (CED) policy.

Given the extensive review of FDG-PET for cervical cancer over the past several years, we request that CMS expedite the NCD process by releasing its proposed decision memorandum at the same time that it opens the NCD (by posting the NCA tracking sheet on its website along with the proposed decision memorandum), and by foregoing the initial thirty-day comment period that generally occurs between the posting of the tracking sheet and the posting of the proposed decision memorandum.

I. Overview

Under the current NCD, Medicare covers medically necessary FDG PET imaging for the “subsequent treatment strategy” of cervical cancer. Coverage as part of the “initial treatment strategy” is divided into two parts. If conventional imaging was negative for extrapelvic metastasis, then FDG-PET imaging is covered during the initial phase of management. Other uses of FDG-PET during the “initial treatment strategy” are only covered under CED (§1862(a)(1)(E) of the Act).

We believe the intention of the original NCD (CAG-00181N) was primarily to exclude use of PET for cervical cancer under clinical circumstances where it would not be expected to guide patient management. Through NOPR and through other published studies in recent

years, significant clinical evidence supporting the inclusion of expanded PET coverage for cervical cancer has been developed; we have provided this evidence in several prior comments to CMS, and describe it again in the next section. We thus believe that the continuing exclusion of cervical cancer coverage of PET for this subset of patients with newly-diagnosed disease was likely unintentional, since the new NCD was designed to establish a consistent general coverage framework for similar cancers and similar clinical oncology decisions, and to obviate cancer-by-cancer coverage determinations across every family of related cancers.

CMS may find it appropriate to exclude coverage for ‘diagnosis’ of cervical cancer since this disorder is initially diagnosed by biopsy.

II. Rationale and Evidence

Both the existing literature and the University of Alberta technology assessment offer strong evidence for the utility of PET for initial staging of cervical cancer. Given the difference in sensitivity of PET versus CT or MRI alone, in almost all circumstances a patient with CT/MRI of the pelvis showing no extrapelvic metastatic disease will still require a subsequent PET to enable the treating physician to obtain the information necessary for comprehensive initial treatment planning, and this is acknowledged in the current coverage policy. Even if a CT or MRI study is considered “positive” for extrapelvic metastatic disease because it shows enlarged para-aortic lymph nodes, this is not the complete staging information needed to manage the patient. Additional nodal metastases, not seen by conventional imaging, are frequently detected by PET, and are now often treated to higher doses using intensity-modulated radiation therapy (IMRT) rather than with standard para-aortic treatment plans.

Moreover, PET would generally be needed as an additional test in order to enable the treating physician to assess the supraclavicular nodes. Patients with supraclavicular nodal disease or other distant metastasis have FIGO stage IVb disease and are treated differently than those with only para-aortic nodal metastasis. We have detected clinically occult supraclavicular nodal metastasis (which we have found to be a grave prognostic sign) in nearly 7% of our patients presenting for chemoradiation therapy of newly diagnosed cervical cancer).¹ Since the most commonly employed conventional imaging performed for initial staging of cervical cancer is CT of the abdomen and pelvis and chest radiography, there is no opportunity to detect these otherwise occult supraclavicular nodal metastases. Nearly all patients with supraclavicular metastasis have para-aortic nodal metastasis.² Additionally, relying on negative conventional imaging as the basis for performing PET ignores the fact that PET not only has greater sensitivity than CT or MRI, but also has about 20% greater specificity for detecting pelvic and para-aortic nodal metastasis.³ This principle, already well-established in the staging

¹ Grigsby PW. The contribution of new imaging techniques in staging cervical cancer. *Gynecol Oncol.* 2007;107(1, Supplement 1):S10-S12.

² Tran BN, Grigsby PW, Dehdashti F, Herzog TJ, Siegel BA. Occult supraclavicular lymph node metastasis identified by FDG-PET in patients with carcinoma of the uterine cervix. *Gynecol Oncol.* 2003/9 2003;90(3):572-576.

³ Grigsby PW, Siegel BA, Dehdashti F. Lymph node staging by positron emission tomography in patients with carcinoma of the cervix. *J Clin Oncol.* Sep 1 2001;19(17):3745-3749.

of other covered cancers, is a reflection of PET's much greater ability to discriminate nodal enlargement due to reactive hyperplasia from that due to metastasis. Cervical tumors often have significant necrotic components and thus reactive hyperplasia in regional nodes is quite common. The greater specificity afforded by PET is particularly important when PET data are used in planning treatment of para-aortic disease by IMRT and other highly conformal methods. Finally, the current sequencing of studies ignores the fact that the preponderant number of PET studies now performed in the United States are actually PET/CT studies. It is illogical to make most such patients undergo CT twice (for reasons of radiation exposure, patient convenience, and expense). Many gynecologic oncologists and radiation oncologists begin their imaging evaluation of the cervical cancer patient by performing PET/CT. We thus believe that coverage of PET in this subset of patients with cervical cancer is reasonable and necessary, as well as cost-efficient.

Additional clinical evidence in support of our request comes from the data collected by the NOPR over the past two years. Based on 2004 data, the Centers for Disease Control and Prevention found that 37.2 percent of patients with cervical cancer were 65 years of age or older; the American Cancer Society estimates that there are 11,070 new cases of cervical cancer annually (2008 data). Thus, approximately 4,100 of the new cases of cervical cancer annually are in Medicare-age patients. As the initial results of the NOPR demonstrate, the two-year cohort examined therein contained only 341 patients who underwent initial staging of cervical cancer under NOPR (or about 170 per year), out of a total 40,863 cases with proven cancer included in the NOPR (for initial staging and restaging). We are unable to determine whether these patients were included in NOPR because they did not undergo antecedent CT or MRI, or because they did and were found to have evidence of extrapelvic metastatic disease. Notably, the NOPR data indicate that the percentage of these 341 cervical cancer patients who saw a "change in management" due to the use of PET was 36.1%, a similar percentage as the overall "change in management" percentage (39.8%) for all initial staging studies included in the NOPR.⁴ We also do not know the number of Medicare beneficiaries with cervical cancer, who underwent PET as a covered indication (i.e., after having had CT or MRI showing no evidence of extrapelvic metastatic disease), but this number is certainly greater than 170 per year. If the current restriction is lifted, we expect that many or most of these patients now having both CT or MRI and PET will undergo only PET/CT.

III. Request

On the basis of the evidence presented above, we formally request that CMS initiate a limited-scope reconsideration of NCD CAG-00181N for the specific purpose of providing PET coverage for staging of cervical cancer without restriction. We would propose the following manualization language for this request:

FDG PET is covered for the staging of cervical cancer in beneficiaries who have a histopathologic diagnosis of cervical cancer established by biopsy; and

⁴ Hillner BE, Siegel BA, Shields AF, et al. Relationship between cancer type and impact of PET and PET/CT on intended patient management: findings of the National Oncologic PET Registry. *J Nucl Med* 2008; 49:1928-1935.

FDG PET is not covered for the diagnosis of cervical cancer.

As stated above, we believe that an expedited approach is warranted under the specific circumstances present here. Much of the literature pertaining to the clinical value of PET in the staging of cervical cancer (described in detail above) was made available to CMS during the 2003 request for FDG-PET coverage for the staging and restaging of cervical cancer. Medicare coverage of PET for cervical cancer was summarized in the literature in 2006,⁵ and the clinical data were again made available in comment periods on both NCD CAG-00181N and CAG-00181R. Furthermore, the most recent data from the NOPR pertaining to cervical cancer were available during the comment period on the reconsideration of CAG-00181N. The public has thus had ample opportunity to comment on issues pertaining to these data, all of which support the extension of unrestricted PET coverage to cervical cancer for initial staging purposes. Notably, no public commenter has indicated either opposition to, or concern with, the extension of PET to cervical cancer for initial staging purposes. We therefore believe that it would be appropriate for CMS to release the proposed decision memorandum on the date it opens the reconsideration request, and to provide for a single public comment period following the posting of the proposed decision memorandum.

We would also note that CMS has the statutory authority to expedite the NCD process, and that there is precedent for exercising this authority. CMS has posted its proposed decision memorandum at the same time that it posted the tracking sheet in other NCAs, such as the reconsideration of the Clinical Trial Policy and, more recently, request for an NCD for home sleep testing devices for obstructive sleep apnea.⁶ In the case of the Clinical Trial Policy, CMS stated that it was expediting the process because there had been ample opportunity for public comment through a prior reconsideration of the policy, and because of the strong interest in an expeditious resolution of the policy given its broad applicability. We believe that the same rationale is applicable to this limited-scope reconsideration request, particularly as there has been ample opportunity for public comment on the matter, and where there is strong interest in the expeditious harmonization of the omnibus policy and the existing literature on the clinical value of PET for cervical cancer.⁷

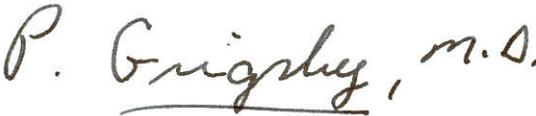
We look forward to working closely with CMS throughout this limited-scope reconsideration process, and to providing any additional information that CMS may require.

Sincerely,

⁵ Carey BP, Coleman RE, Grigsby PW, Siegel, BA. Medicare coverage of PET for cervical cancer. *J Am Coll Radiol*, 2006; 3(1):19-22.

⁶ See, e.g., NCA Tracking Sheet for Clinical Trial Policy (CAG-00071R2), in which the formal request was accepted and the review initiated on July 19, 2007, and the proposed decision memorandum was also released on July 19, 2007. At the beginning of this tracking sheet CMS explains its rationale for releasing the proposed decision memorandum on the same date that it opened the NCD. See also NCA Tracking Sheet for Sleep Testing for Obstructive Sleep Apnea (CAG-00405N).

⁷ As CMS is aware, there are no statutory or regulatory requirements that CMS open two consecutive thirty-day comment periods. Indeed, § 1862(l)(3) of the Social Security Act requires only a single thirty-day comment period after the posting of the proposed decision memorandum.

Handwritten signature of Perry W. Grigsby, M.D. in cursive script.

Perry W. Grigsby, MD, MBA
Professor of Radiation Oncology and Radiology

Handwritten signature of Barry A. Siegel, MD in cursive script.

Barry A. Siegel, MD
Professor of Radiology and Medicine
Director, Division of Nuclear Medicine
Co-chair, NOPR Working Group