

CMS is committed to maintaining the highest quality and most effective medical care for its beneficiaries. Many organizations, including the National Quality Forum's National Priorities Partnership, Agency for Healthcare Research and Quality, the Institute of Medicine, the Dartmouth Atlas of Healthcare, and the Congressional Budget Office, have made statements about underuse and overuse of items and services used in patient care. Medicare may be paying for potentially ineffective or harmful items and services, and there may be potentially high value items and services that are being underutilized. While some topics may fall beyond the scope of the NCD authority, we believe that others may present opportunities to use Medicare coverage to help align program incentives with the best available clinical evidence.

In 2008, CMS published a list of potential NCD topics, giving the public an opportunity to comment on the items and services in the list. Since then, CMS has acted formally on several of these issues. Below are examples of our activities based on some items and services on the 2008 list:

- **Use of erythropoiesis stimulating agents (ESAs) for treatment of anemia in adults with chronic kidney disease (CKD).** We convened two MEDCAC meetings (Medicare Evidence Development & Coverage Advisory Committee - March 2010 and January 2011) and published an extensive national coverage analysis on the use of ESAs for CKD [i]. Though CMS did not ultimately implement an NCD, CMS' evidentiary review informed the revisions to the End-Stage Renal Disease Quality Incentive Program (ESRD QIP), the nation's first pay-for-performance incentive program [ii].
- **Bone morphogenetic protein (BMP):** BMP may be beneficial in the treatment of a variety of bone-related conditions including delayed union and non-union fractures. However, certain off-label uses in cervical spine fusion may be associated with life-threatening complications. We commissioned a technology assessment of BMP, and in September 2010, convened a MEDCAC meeting on this topic [iii].
- **Pharmacogenomic testing:** Pharmacogenomic tests are proliferating for DNA variants associated with response to therapeutic drugs. On February 25, 2009 we convened the MEDCAC to identify the desirable characteristics of evidence that could be used by CMS to determine whether genetic testing as a laboratory diagnostic service improves health outcomes. We published the, Pharmacogenomic Testing for Warfarin Response NCD on August 3, 2009. Because there was limited evidence of benefit to Medicare beneficiaries of this testing, we covered these tests only for eligible beneficiaries participating in approved randomized clinical trials under coverage with evidence development (CED) [iv].

Since the list was published in 2008, there have been significant developments in new technologies and changes to CMS authorities under statute. We believe that public input should inform a revised list. Rather than issuing a new list for public comment, we would like the public to provide us with a list of items and services.

CMS is inviting your input concerning any items and services you believe may be inappropriately used (i.e., underused, overused, or misused)--or provide minimal benefit --in hospitals, clinics, emergency departments, doctors' offices, or in other healthcare settings. We encourage you to be specific about items and services including surgical procedures, diagnostic tests or procedures, imaging or radiology services, lab tests, or durable medical equipment (such as wheelchairs); treatments for diseases such as cancer, heart disease, kidney disease or gastrointestinal disease; or procedures such as orthopedic or eye procedures.

CMS will review the comments based on:

- Relevance to the NCD authority under Part A and Part B; and
- Potential impact on the Medicare program and its beneficiaries.

The revised list will be published on our website.

[i] [https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=245&ver=14&NcaName=Erythropoiesis+Stimulating+Agents+\(ESAs\)+for+Treatment+of+Anemia+in+Adults+with+CKD+Including+Patients+on+Dialysis+and+Patients+not+on+Dialysis&bc=AAAAAAAAAAAA&](https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=245&ver=14&NcaName=Erythropoiesis+Stimulating+Agents+(ESAs)+for+Treatment+of+Anemia+in+Adults+with+CKD+Including+Patients+on+Dialysis+and+Patients+not+on+Dialysis&bc=AAAAAAAAAAAA&)

[ii] <https://www.cms.gov/ESRDQualityImproveInit/>

[iii] <https://www.cms.gov/medicare-coverage-database/details/medcac-meeting-details.aspx?MEDCACId=55&year=All&bc=AAAAAAAAAAAA&>

[iv] <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=333&ncdver=1&SearchType=Advanced&CoverageSelection=National&NCSelction=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&Keyword=warfarin&KeywordLookUp=Title&KeywordSearchType=Exact&kq=true&bc=IAAABAAAAAA&>

Commenter:

Bocchino, Carmella

Title:

EVP, Clinical Affairs and Strategic Planning

Organization:

America's Health Insurance Plans (AHIP)

Date:

11/22/2011

Comment:

November 23, 2011

Centers for Medicare and Medicaid Services

Mail Stop C1-09-06

7500 Security Boulevard

Baltimore, Maryland 21244-1850

To Whom It May Concern:

Thank you for the opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS's) Potential National Coverage Decision (NCD) Topics. America's Health Insurance Plans (AHIP) is the national association for the health insurance industry. Our members provide coverage to more than 200 million Americans, offering a broad range of health insurance products in the commercial market and demonstrating a strong commitment to participation in public programs.

General Comments

AHIP and our member health plans encourage CMS to ensure that all patients receive safe, effective and evidence-based treatments. The strength of the evidence and comparative information for existing therapies, drugs, interventions and patient criteria for each are key determinants in ensuring patient safety and meeting desired outcomes. Our industry recommends the following topics for further review, and we have grouped the topics by category:

- **High-Tech Imaging**
- **Cardiac-Related Procedures**
- **Invasive Back Procedures**
- **Prostate Cancer Screening and Treatment**
- **Genetic Testing Topics**
- **Other Topics**

Since the Institute of Medicine's landmark report, *Crossing the Quality of Chasm*, defined the problem of over- and inappropriate use more than 10 years ago, a growing body of evidence has emerged documenting that a portion of care that patients receive is redundant, unwarranted, and sometimes harmful.

High-Tech Imaging

Knee MRI for Likely Arthritic Condition

A recent study presented at the American Academy of Orthopedic Surgeons 2011 Annual Meeting showed that more than half of patients presenting to an orthopedic surgeon with acute knee pain have had a magnetic resonance imaging (MRI) scan at the request of their referring physician that was not necessary.^{lii} There has been concern regarding the overuse of MRI. AHIP recommends that CMS evaluate the current evidence to ensure that Medicare beneficiaries are provided services that have the most value and potential for health improvement.

Endoscopy for Gastroesophageal Reflux Disease (GERD)

There are a number of studies evaluating the relative safety and efficacy of endoscopic GERD treatments. While some have shown promising short-term results, long-term safety and efficacy remains unclear. CMS should evaluate the evidence on this treatment.

Radiation Exposure

Computed tomography (CT) pulmonary angiography for patients with suspected pulmonary embolism (PE) is an effective diagnostic tool, but this test can unnecessarily expose patients to high doses of radiation, which has been highlighted as an important patient safety issue. A recent study shows that CT technology is leading to the detection of clots that will not cause any harm, but sets off a cascade of potentially harmful drugs and treatments.^{liii}

A recent study showed that more than half of patients receiving abdominal CT scans did not need them, exposing them to excess radiation that could raise the long-term risk of cancer.^{liiii} Neuroimaging for headaches is another overused service, with research using data from the 2007 National Hospital Ambulatory Medical Care Survey (NHAMCS) suggesting that up to 4,000 future cancers may result from head CTs performed in 2007 alone.^{liiv}

Positron Emission Tomography (PET) Scan for Alzheimer's Disease

To date, there is no treatment available to slow or reverse the progression of Alzheimer's disease. Additionally, there remains a lack of direct evidence demonstrating the positive impact of PET scans on longer-term health outcomes in patients with Alzheimer's disease. CMS should continue to monitor the release of all new evidence and determine whether or not to update the NCD accordingly, with the most current information.

Cardiac-Related Procedures

Automatic Implantable Cardiac Defibrillators

Data from the National Cardiovascular Data Registry on implantable cardioverter-defibrillator (ICD) use showed that more than 20 percent of patients who had an ICD implanted fall outside the recommended eligibility guidelines for the procedure. Clinical trials have demonstrated the effectiveness of ICDs when used in patients with certain forms of heart failure, but the research fails to support a benefit for the device in people still recovering from a heart attack, coronary artery bypass surgery or those with a recent diagnosis of heart failure.

Percutaneous Transluminal Coronary Angioplasty (PTCA) and Stents

A 2011 study showed that one in eight U.S. patients who have non-emergency stenting procedures to clear blocked arteries in the heart are likely to see more harm than good

from the procedure.^[vi] The National Priorities Partnership has included these procedures as a target to reduce overuse.^[vii]

Nuclear Stress Tests for Cardiac Related Symptoms

A recent study showed that despite current guidelines, 12% of patients with a cardiac-related outpatient visit at least three months after revascularization underwent a stress test within 30 days of their visit; and that patients treated by practices who billed for the technical and professional fees were significantly more likely to order nuclear stress imaging after revascularization relative to those who did not directly bill for these tests^[viii].

Left Ventricular Assist Devices

Studies conducted on the cost-effectiveness of Left Ventricular Assist Devices for destination therapy found that LVADs were not cost effective.^[ix] Cost estimates have been quoted as high as \$200,000 to cover the cost of one LVAD, associated equipment, the surgery and hospital recovery time.^[x] Implementation of the device also comes with significant risks associated with any open heart surgery, including infection. Strokes are often common in patients with LVADs. While more recent studies report the cost-effectiveness associated with the use of LVADs for destination therapy has improved significantly, CMS should continue to evaluate the clinical effectiveness of LVADs including economic evaluations, quality of life, resources and costs before releasing a NCDs for LVADs.

Invasive Back Procedures

Back Surgery for Recurring Low Back Pain

Several studies have examined the issue of whether or not surgery for low back pain has better outcomes for patients, vs. less-invasive interventions. A recent study demonstrated that overly aggressive surgical treatment can result in severely adverse outcomes for the patient, including increased pain and loss of functionality.^[xi]

Facet Joint Injections

Clinical evidence about the very existence of facet joint syndrome is conflicting, and evidence from studies is inadequate regarding the superiority of periodic facet joint injections compared to placebo in relieving chronic spinal pain. The results of the Cochrane systematic review of the effects of injection therapy involving epidural, facet or local sites indicated that there was no strong evidence for or against the use of any type of injection therapy.^[xii] The authors concluded that there is insufficient evidence to support the use of injection therapy in subacute and chronic low back pain, but it cannot be ruled out that specific subgroups of patients may respond to a specific type of injection therapy.

Vertebroplasty

Results from a recent multicenter, randomized, double-blind, placebo-controlled trial published in NEJM showed that a sham procedure was no more beneficial than vertebroplasty for certain patient populations.^[xiii] The Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) assessment demonstrated that the evidence was inconclusive as to whether or not vertebroplasty is effective.^[xiv]

Physical Therapy (PT) and Other Non-invasive Therapy for Back Pain

PT and non-invasive therapies for back pain may be an underused set of services, in contrast to many overused invasive procedures to treat back pain. Non-invasive therapies such as exercises and stretching have shown to be effective for certain patients. A recent study shows that people with chronic, nonspecific back pain may benefit from stretching exercises.^[xv]

Prostate Cancer Screening and Treatment

Prostate-Specific Antigen-Based (PSA) Screening

The U.S. Preventive Services Task Force recently published its draft recommendation against PSA **screening**, based on evidence that shows PSA screening results in small or no reduction in prostate cancer–specific mortality and is associated with harms related to subsequent evaluation and treatments, some of which may be unnecessary.^[xvi] This evidence suggests the need for CMS to re-evaluate its policy on PSA screening in asymptomatic men.

Surgery for Low Risk Prostate Cancers

A recent Johns Hopkins study is the largest and longest study of men initially diagnosed with a slow-growing, very nonaggressive form of prostate cancer to indicate that forgoing immediate surgery to remove the tumor or radiation poses no added risk of death. Results show delaying treatment is appropriate as long as the cancer’s progression and tumor growth are closely monitored through “active surveillance” and there is no dramatic worsening of the disease over time. The authors concluded that active surveillance may be a preferred course of action for many men in the Medicare beneficiary population.^[xvii]

Proton Beam Therapy

A recent study is the latest report to suggest that how men are treated for prostate cancer appears to be influenced by a variety of factors, including the technology and marketing goals, rather than scientific evidence on benefits and risks^[xviii]. The Agency for Healthcare Research and Quality’s 2008 report analyzed hundreds of studies to compare the effectiveness and risks of eight prostate cancer treatments, ranging from prostate removal to radioactive implants to no treatment at all. None of the studies provided definitive answers^[xviii]. CMS should evaluate the current evidence to ensure that Medicare beneficiaries are offered services that provide the most value and potential for health improvement.

Genetic Testing Topics

Genetic Testing and Local Coverage Decisions

CMS should consider a national coverage policy pertaining to decisions around genetic tests, rather than encourage local units to determine coverage, to ensure that appropriate evidence-based tests are covered for specific conditions. Cancer diagnostic tests that would benefit from further review include Oncotype DX for node positive breast cancer and colon cancer, which has not received support from the professional guidelines. In vitro chemoresponse assays have not been established as a standard of practice in the clinical setting, and data are insufficient to demonstrate an improvement of health outcomes with the use of these tests.

Whole Genome Profiling

The genetic components of most diseases are still largely unknown. According to the Centers for Disease Control and Prevention, many of the genome tests have been developed on the basis of limited scientific information, which may lead to the misuse of these tests and the potential for physical or psychological harms to the public it warns. CMS should further evaluate all available data and review recommendations of the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group of the CDC Office of Public Health Genomics prior to opening an NCD.^[xix]

Other Topics

Lap-band Surgery for Obesity

Before updating the existing NCD on bariatric surgery procedures, CMS should conduct a rigorous evidence review for each procedure, including patient selection criteria, short- and long-term safety and effectiveness, and comparative effective analysis between currently covered and emerging procedures.

Implantable Pain Stimulators

The use of pain stimulators are common in managing pain for terminal illness, but are also used to treat chronic non-malignant pain such as failed low back surgery syndrome. Implantable pain stimulators use electric currents or intrathecal and epidural subcutaneous devices, referred to as pumps to decrease pain. Chronic non-malignant pain can be complicated by physical, psychological, and behavioral factor. Successful treatment would include a multidimensional approach that takes into account multiple elements of a biopsychosocial model to successful treat or manage the pain. CMS should perform a review of the current evidence to ensure that other, more conservative treatments are attempted, and that implantable pain stimulators are used as a last resort for chronic non-malignant pain.

Lung Volume Reduction Surgery

Findings from the National Emphysema Treatment Trial (NETT) have added to our understanding of the impact of LVRS for patients with advanced emphysema. However, more studies need to be conducted. The randomized study conducted from 1996 – 2001 by the U.S. Department of Health and Human Services, National Institute of Health (NIH), Agency for Healthcare Research and Quality (AHRQ) and CMS, identified individuals who have an unacceptably high risk of mortality after surgery and little chance of functional benefit. Mortality rates for non-high-risk LVRS group were higher in the first three months after randomization than the non surgical group in the study. More participants who had received the LVRS required hospitalization or nursing home placement for the first eight months after treatment assignment than medical patients who participated in the study.^[xxi] Currently, CMS's ^[xxii]NCD for LVRS is in keeping with the findings of the study as released in 2001. CMS NCD allows coverage for patients with severe upper lobe predominant emphysema or severe non-upper lobe emphysema with low exercise capacity. Continued reviews of LVRS for patients with advanced emphysema should include additional and current research, an assessment of potential harms, a focus on patient selection criteria and how these tests will be able to influence clinical decision-making.

Negative Pressure Wound Therapy Devices (NPWT)

More than a dozen systematic evidence reviews produced by independent organizations have questioned the quality of the evidence supporting the use of NPWT, including systematic evidence reviews published by the Cochrane Collaboration and the Agency for Healthcare Research and Quality (AHRQ). AHRQ's 2009 Technology Assessment provides extensive evidence on the lack of well designed randomized controlled trials for NPWT^[xxiii]. The review also supports the lack of evidence for use of NPWT to attain complete wound closure. Data is needed to support length and value of use.

Thank you for the opportunity to comment on this important issue.

Sincerely,

/s/

Carmella Bocchino
Executive Vice President
Clinical Affairs and Strategic Planning

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<http://www.ahrq.gov/clinic/ta/negpresswtd/>

Commenter:**Douglas, Andrea**Organization:
PhRMADate:
11/23/2011

Comment:

Coverage and Analysis Group Centers for Medicare and Medicaid Services Mailstop: C1-12-28 7500 Security Boulevard Baltimore, MD 21244 Re: Potential NCD Topics Dear Sir or Madam; The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates this opportunity to comment on CMS' September 28 request for input in developing a list of potential national coverage determination (NCD) topics. PhRMA is a voluntary nonprofit organization representing the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to developing medicines that allow patients to lead longer, healthier, and more productive lives. We appreciate CMS taking this step to solicit input from the public on potential NCD topics. Maintaining an open, transparent process that ensures adequate input from patients, physicians and clinical experts, and other stakeholders will be essential to updating the agency's list of potential topics. PhRMA strongly supports CMS' goal of "maintaining the highest quality and most effective medical care for its beneficiaries." In addition to establishing a clear, transparent process for finalizing this list, PhRMA also is asking CMS to clarify some of the key terms used in its notice, explain how it will apply these terms in relation to existing NCD authority, and describe the factors it will use in updating the list. We address each of these topics in more detail below.

1. Clearly define terms and their application to national coverage policy CMS introduces several important new terms into the national coverage context in this notice, including "underuse," "overuse," "misuse," "potentially ineffective," "potentially high value," and "minimal benefit." In light of the potential role of these terms in the national coverage context, along with their considerable lack of precision, it is important for the agency to provide definitions of them and seek comment before using them to set policy. This will allow the public to provide relevant input and understand the terms' exact role in coverage policy. This is important for a number of reasons. First, these terms are used in various ways by researchers and policy-makers (reflecting a lack of specific, accepted definitions) and it will be important to ensure that a common set of definitions applies with respect to Medicare policymaking. Second, it is unclear how CMS' use of these terms relates to its basis for deciding what should be subject to a national coverage determination. In this regard, it will be important for CMS to ensure that use of these terms does not have the effect of creating a new evidence standard that differs from the "reasonable and necessary" standard that the agency operates under today. CMS also should describe the factors it will use in deciding whether to include a particular item or service on the list of potential NCDs, and should ensure that they align with the factors

described in CMS' April 11, 2006 guidance document "Factors CMS Considers in Opening a National Coverage Determination." The factors CMS defines will depend heavily on how the agency defines the key terms identified above and relates these terms to its NCD authority. It is unclear how NCD policy based on concepts such as appropriate use, "potentially high value," and "minimal benefit" align with current CMS guidance on factors the agency uses to initiate NCDs. For example, identifying "appropriate use" presumably will require a strong evidence base and clear consensus, whereas factors identified in CMS' April 2006 guidance include the existence of controversy (lack of consensus) about the evidence on an item or service. The importance of clearly defining criteria regarding CMS' NCD topics was highlighted in a 2010 report from the Center for Medical Technology Policy. In discussing the process used by CMS in 2007 and 2008 to develop its initial list of potential NCD topics, the report noted that the process "could have been improved with more explicit priority setting criteria and better overall direction to participants about how to select and define research questions". Expert opinion is essential to ensuring that research questions are appropriately defined and CMS should include consultation with external experts, as well as public comment, as part of its process for selecting and defining research questions. PhRMA appreciates CMS' recognition in the notice of the need to align terms in the Sept. 28 notice with existing statute and agency policy on coverage of items and services under Medicare Part A and Part B. In addition to defining key terms, CMS should briefly explain how it will apply them in the context of national coverage policy (for example, explaining how terms like "potentially high value" and "minimal benefit" relate to the statutory standard of covering items and services that are "reasonable and necessary"). Consistent with our comments on CMS' July 30, 2008 list of potential NCDs, PhRMA believes CMS should not use cost as a factor in deciding whether an item or service should be included on the list. This is particularly important in the context of appropriate use, since cost containment is often a major focus of efforts to address inappropriate use of health care items and services. For example, in testimony on "The Overuse, Underuse, and Misuse of Health Care" before the Senate Finance Committee in 2008, former Congressional Budget Office Director Peter Orszag suggested there are "substantial opportunities to reduce costs without harming health overall," and related inappropriate use to lack of evidence about "whether the benefits of more expensive therapies warrant their additional costs." CMS should clearly state that cost will not be a factor in creating the potential NCD list. This will ensure that policy on identifying potential NCDs aligns with CMS' April 2006 guidance, as well as provisions of the Patient Protection and Affordable Care Act. It also will ensure that coverage policy does not lead to access barriers to medically appropriate care for Medicare beneficiaries. The April 2006 guidance states: "Cost-effectiveness is not a factor CMS considers in making NCDs. In other words, the cost of a particular technology is not relevant in the determination of whether the technology improves health outcomes or should be covered for the Medicare population through an NCD." In addition, Sec. 1182(e) of the Patient Protection and Affordable Care Act states "The Secretary [of the Department of Health and Human Services] shall not utilize such an [cost-per] adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII." II. Potential NCD list should support existing regulatory and policy framework. Similar to our prior comments on CMS' list of potential NCDs, PhRMA believes CMS should ensure that its revised list does not include drugs and biologicals that have not yet been approved by FDA. FDA approval of new drug applications and biological license applications is based on a rigorous review of stringent evidence from randomized controlled trials demonstrating the safety and efficacy of the product. In general, these products should not be placed on a list of potential NCDs unless the manufacturer requests it. For example, the Medicare statute recognizes that any FDA-approved use of an anti-cancer medicine is considered a "medically accepted indication" under Medicare Part B. This policy reflects the rigor of the FDA premarket approval process for drugs and

biologics. In addition, current statute and CMS policy provide a sound basis for Medicare coverage of drugs and biologicals for medically appropriate, evidence based “off-label” uses (in which the physician prescribes a drug for an indication that is not included in the FDA-approved labeling). As recognized by the National Cancer Institute and many other experts and physicians, such off-label use often represents the standard of care. Specifically, the Medicare statute defines “medically accepted indications” for anti-cancer drugs to include off-label uses supported by certain compendia (or determined to be medically accepted by the contractor, based on articles in certain peer-reviewed journals). CMS guidance similarly provides that off-label uses of Part B drugs other than cancer drugs “may be covered if the carrier determines that use to be medically accepted taking in to consideration the major drug compendia, the authoritative medical literature and/or accepted standards of medical practice.” CMS coverage policy should support this framework to ensure timely beneficiary access to drugs and biologicals for medically appropriate, evidence-based off-label uses under Part B. Some data suggests that oncologists and hematologists face barriers to prescribing medically appropriate treatments because they are concerned that they will not be covered by local Medicare contractors. In a survey of oncologists and oncology practice managers conducted in 2008 by the Association of Community Cancer Centers, for example, oncology practices reported that “more than 60 percent of off-label uses are at least occasionally denied [coverage], despite being supported by compendia listing or peer-reviewed medical literature.” Although it likely is outside the scope of the CMS notice, the agency should consider potential steps to addressing these barriers. As CMS considers ways to address inappropriate use via national coverage policy, we urge the agency to ensure its policy preserves the ability of physicians to tailor care to the different needs of individual patients. Optimal care for the individual frequently diverges from average research results or broad practice recommendations. For beneficiaries with any disease or condition, the “most effective care” will vary substantially from one subgroup or individual to the next based on differences in clinical circumstances, genetic variation, and patient preferences. CMS should ensure its policies, NCD or otherwise, support doctors and patients in making use of best available evidence in choosing optimal care for the individual. This is particularly important in the area of national coverage policies, which define broad requirements that apply to the entire Medicare population and are less able to give physicians flexibility within those requirements. III. Develop priorities based on an open, transparent, clinically-driven process. To help ensure CMS policies are aligned with high-quality, patient-centered care, the agency should rely heavily on the input of practicing physicians, clinical experts, and patients in updating this list. The importance of providing opportunities for public input, and particularly input from patients, physicians, and clinical experts, was underscored in CMS’ work to establish the initial list of evidentiary priorities in 2007 and 2008. After releasing an initial draft list in October 2007, the agency sought input from a wide range of stakeholders, including experts in cardiovascular disease, diabetes, mental health, aging, cancer, arthritis and musculoskeletal conditions, among others. Obtaining similar input will be equally important now, particularly as CMS seeks to relate national coverage policy to inappropriate use. Identifying inappropriate use can be complex and controversial, as optimal care frequently deviates from established guidelines due to individual needs and preferences, and the agency should ensure a strong clinical consensus exists on the areas of inappropriate use that it identifies. For example, this is illustrated in the considerable amount of input and deliberation that goes into development of clinical consensus statements by the National Institutes of Health, reflecting the reality that the requisite breadth and depth of clinical expertise and perspectives do not reside in the NIH itself. In addition, similar to development of CMS’ initial list of evidentiary priorities, the agency should provide adequate opportunities for public input as it develops the new list of potential NCD topics. This should include providing an explanation of how the input received by the agency was taken into consideration and provide a rationale for items and

services included in the revised list. Because the 2008 list did not include this explanation (and because it was not clear if all the input received by CMS was publicly released) it was difficult to determine how CMS took commenters' input into consideration, and why specific items were included on the list. It is apparent that CMS did take into consideration the input received during the earlier NCD priority setting process, by making revisions to the final list that included modifying research questions and adding or deleting specific research topics. However, an analysis of CMS' list and the public comments and input available at the time indicated that almost one-third of the research topics included in the final list were not represented in the available public input. (It is possible that these items were identified in input that was not available to the public).

IV. Describe the process for finalizing the list and keeping it current We appreciate the publication of the September 28 notice as the first step in developing a revised list. When CMS develops an initial revised list, the agency should release it as a draft document and invite public input. In releasing a draft list, the agency should describe how it took public input into account by providing rationale that addresses the review criteria stated in the notice for comment for including or omitting items and services suggested. Describe the process for maintaining a current list As noted in our prior comments, PhRMA believes it will be important for CMS to keep the list of potential NCD topics current in order to provide predictability for public stakeholders. This will avoid situations in which the status of an item or service remains uncertain for an extended period of time because of its continued inclusion on the list. Such uncertainty would be detrimental to providers and patients who utilize the items or services, to patients with unmet medical needs awaiting approval and access to new tests and treatments, and to the companies that develop them. Consistent with our prior comments, PhRMA recommends that an item or service be kept on the list for a limited time period, for example, no more than 90 or 180 days, after which time CMS would either initiate a national coverage analysis or remove the item from the list. CMS should make this timetable explicit and describe the process it will use to add and remove items on the list.

V. Conclusion PhRMA appreciates the steps CMS has taken to improve the transparency and predictability of Medicare's national coverage decision-making process, and supports the public posting of a list of potential NCD topics. Consistent with the recommendations made above, we believe the list can further enhance transparency and predictability for patients, providers and medical product developers. We look forward to continuing working with CMS on this issue. Sincerely, Richard I Smith Executive Vice President, Policy Randy Burkholder Deputy Vice President, Policy

Commenter:**Guerra-Garcia, Patricia**

Date:

10/31/2011

Comment:

- Pain management (epidural, facet and transforaminal injections) and wound center debridement vs. active wound management. Frequent non-medically necessary debridements for very small wounds.
- Wound vacs (NPWT)
- Inappropriate, unnecessary PCI for chronic CAD cases (non meeting criteria for "appropriateness" of PCI/ACC/AHA)
- Power wheelchairs: some vendors misrepresenting the facts, unskilled physical therapists and physician lack of knowledge regarding criteria. Conflicting information from vendors and physical therapists evaluations (ex: ambulation status).
- Appeals on behalf of the members by DME companies and vendors, when there is conflict of interest.
- Misuse and overuse of non emergent ambulance transports:
 - o ER facilities .
 - o Also overuse transports for dialysis (they claim van transport is late, unreliable and member cannot transfer on to dialysis chair), morbid obesity (> 350 lbs) (when they claim the w/c van cannot accommodate member's weight)
- Misuse and overabuse of the hospital outpatient settings (SPU units) for iv infusions and injectables. . Physical/occupational/speech therapy in outpatient settings including long term care facilities.

Commenter:**Lynch, Ann-Marie**

Title:

Executive Vice President, Payment and Health Care

Organization:

Advanced Medical Technology Association (AdvaMed)

Date:

11/21/2011

Comment:

November 22,2011

Louis Jacques, MD

Director, Coverage and Analysis Group

Office of Clinical Standards and Quality

Centers for Medicare & Medicaid Services

Mail Stop S3-02-01

7500 Security Boulevard

Baltimore, MD 21244

Re: Solicitation on Potential National Coverage Determination (NCD) Topics

Dear Dr. Jacques:

On behalf of the Advanced Medical Technology Association (AdvaMed), we appreciate the opportunity to respond to the Centers for Medicare & Medicaid Services' (CMS') recent web site solicitation for input on potential Medicare National Coverage Determination (NCD) topics.¹ In the September 28, 2011, solicitation, CMS states that it seeks to update its current list of potential NCD topics after considering input from stakeholders regarding "potentially ineffective or harmful itCMS or services." CMS is requesting input concerning itCMS or services that may be "inappropriately used (i.e., underused, overused, or misused)" or that provide "minimal benefit" in certain health care settings. AdvaMed has a keen interest in Medicare's NCD process, and has provided comprehensive comments in the past on CMS documents and notices related to coverage and evidence issues.

As you know, AdvaMed's member companies produce the life-saving and life-enhancing medical devices, diagnostic products and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed members range from the largest to the smallest medical technology innovators and companies.

We have long supported efforts to make the Medicare coverage decision-making process more transparent and open, and we have worked for more opportunities for public

participation in the NeD process. While we appreciate the fact that CMS is asking the public to provide assistance in identifying topics for CMS to consider in the future with respect to national coverage, we note that the opportunity already exists for any member of the public to request a Medicare NeD. CMS makes this clear in its guidance document issued on April 11, 2006, which states that CMS may assist the requester if needed.²

In our experience, the generation and posting by CMS of listings of potential coverage topics suggested by the public is not sufficient, in itself, to provide the sort of transparency that is needed in the Medicare national coverage process. We recognize that CMS can receive advice from the public on potential coverage topics in various ways, including the submission of written requests and the suggestion of potential coverage topics. We also recognize that Medicare's contractors provide guidance on these topics, and that CMS has identified topics for which it is considering internally generating national coverage determinations. We believe that if CMS proceeds to post a listing of national coverage topics, it should list topics from all of these sources, along with an annotation stating its views on the topics identified.

In moving forward with this matter, we also urge CMS to proceed with caution with respect to itCMS and services identified by stakeholders as potentially providing "minimal benefit" in hospitals or other health care settings. In addition, we request CMS to provide an additional comment period on any revised list of potential NeD topics that emerges from this web site solicitation, in order to ensure an open and transparent process.

Our comments on these two recommendations are discussed in more detail below.

I. Minimal Benefit

CMS has invited public comment regarding itCMS and services that may be inappropriately used or that provide "minimal benefit in hospitals, clinics, emergency departments, doctors' offices, or in other health care settings." We have concerns about this language and ask CMS carefully consider any national coverage determination activity that may grow out of public responses under this category. We would fully expect that CMS would only base any national coverage review on the statutory requirements for Medicare coverage and payment, i.e., that Medicare will condition payment on whether on that item or service:

- Falls within a Medicare benefit category;
- Is not specifically excluded from coverage; and
- Is "reasonable and necessary" for the "diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member."³

Therefore, while a stakeholder or commenter might provide input to CMS regarding itCMS or services the commenter feels are of limited or minimal benefit, CMS should only review that item or service in light of the statutory requirements for coverage, and avoid any attempt to establish a higher threshold for coverage based on some undefined degree of benefit.

In existing CMS guidance documents on the NCD process, the agency has detailed factors it may consider in opening an NCD. The Agency has stated that it may generate an NCD on an existing technology in circumstances where:

- Providers, patients or other members of the public have raised significant questions, that are supported by CMS' s initial review of available data, about the health benefits of currently covered itCMS or services, specifically regarding the Medicare population;

- Interpretation of new evidence or re-interpretation of previously available evidence indicates that changes may be warranted in current policies;
- Local coverage policies are inconsistent or conflict with each other to the detriment of Medicare beneficiaries. For instance, the noted variation is not related to local differences in the capabilities of health care providers to use the technology effectively which can be resolved over time, but rather is causing significant disparities in the care available to Medicare beneficiaries that are unlikely to be addressed effectively through provider training and education or through the local coverage process;
- Program integrity concerns have arisen under existing local or national policies; that is, there is significant evidence of wide variation in billing practices not related to variation in clinical need, or of potential for fraud under existing policies.⁴

Again, while CMS may take interest in comments it receives regarding potential NCD topics and may use this input to inform future NCD activity, the agency should base determinations about opening an NCD on the circumstances above, and not on some arbitrary determination about the level of benefit.

II. Additional Comment Period

CMS states in its solicitation notice that it intends to publish a revised list on the CMS website at some future date. We ask that CMS post on its web site the public comments received as a result of this solicitation, as is typically the case for a request for comments on coverage topics. We also urge CMS to provide another comment period when the revised list is posted, so that stakeholders may have the opportunity to provide substantive input on the actual proposed topics that result from this solicitation.

Our review of the recent solicitation notice raises a number of questions, detailed below.

- The notice does not identify the process CMS will use to generate and update the list of potential NCD topics. We suggest that CMS address this matter in its next web site posting.
- The notice does not address whether the revised list will include topics that are being considered for internally-generated NCDs, or topics suggested by contractors. We suggest that CMS include these itCMS, in addition to topics that come in through the public comment process.
- We suggest that CMS make public the identity of the requestor for each new topic that appears on the revised list as a result of the comments received.
- We suggest that CMS provide rationales for each of the topics included on the final list, as well as a prioritization of the listing.
- We suggest that CMS identify how the topics on the potential NCD topics list relate to other CMS efforts to establish Medicare evidence priorities (such as issues presented at MEDCAC meetings).

We believe that a CMS response to the matters we have raised above, along with an opportunity for comment on a draft list prior to a final decision would be consistent with the Agency's overall efforts to improve the openness and transparency of the Medicare national coverage decision-making process.

AdvaMed and its member companies have greatly appreciated CMS' open door policy with respect to the national coverage determination process and we look forward to working with CMS in the future. We are available to meet in person or via conference call at your convenience to discuss these and other issues.

Should you or your staff have any questions, please contact me or Chandra Branham, J.D. (cbranham@advamed.org or 202-434-7219).

Thank you for your attention to this letter.

Sincerely,

/s/

Ann-Marie Lynch

Executive Vice President, Payment and Health Care Delivery Policy

Cc: Patrick Conway, MD, CMS Chief Medical Officer

1 See Potential NCD Topics - Public Comment Period, posted 9/28/2011, [http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?](http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=8&McdName=CED+Public+Solicitation&mcotypename=Guidance+Documents&MCDInd)

2 CMS Guidance Document, "Factors CMS Considers in Opening a National Coverage Determination " (April 11 , 2006); see [http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?](http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=6&McdName=Factors+CMS+Considers+in+Opening+a+National+Coverage+Determinat)

3 Social Security Act § 1862(a)(1)(A); see also, Medicare Program; Revised Process for Making Medicare National Coverage Determinations, 68 Federal Register 55634 (September 26, 2003).

4 "Factors CMS Considers in Opening a National Coverage Determination" (April 11,2006); see FN2 above.

Commenter:**Ofman, MD, MSHS, Joshua**

Title:

Senior Vice President

Organization:

Amgen Inc. (Amgen)

Date:

11/22/2011

Comment:

November 23, 2011

Louis Jacques, MD, Director
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
Mailstop: S3-02-01
7500 Security Boulevard
Baltimore, MD 21244

Re: Amgen Inc. Response to Potential National Coverage Determination Topics

Dear Dr. Jacques:

Amgen Inc. (Amgen) is writing to comment on the process to revise the potential National Coverage Determination (NCD) topics list, which was posted on the website of the Centers for Medicare & Medicaid Services (CMS) on September 28, 2011.¹ As a science-based, patient-focused company committed to using science and innovation to dramatically improve people's lives, Amgen is vitally interested in helping to ensure appropriate access to innovative drugs and biologicals (collectively referred to in this letter as "drugs" following the agency's convention) for Medicare beneficiaries. The agency's NCD process is an important component in ensuring such access. Therefore, we are pleased to have this opportunity to submit a comment regarding the process for revising the list of potential NCD topics.

First, we would like to offer our support for the comments recently submitted by the Biotechnology Industry Organization (BIO) and the Pharmaceutical Research and Manufacturers of America (PhRMA) on the potential NCD topics list, including: use of existing standards (i.e., reasonable and necessary), clear definitions of terms, transparent processes for revising the potential NCD topics list. We believe the issues raised in those comments are important and ask the agency to consider them seriously as it again considers the list of potential NCD topics. We write separately to provide additional comments and recommendations in three specific areas:

- CMS should use the existing "reasonable and necessary" standard when making decisions relating to coverage, including whether to add a topic to the list of potential NCD topics.
- The agency should continue to provide for a comment period following the release of the revised list of potential NCD topics so the agency may have the benefit of public input on the topics.
- CMS should establish a process for removing topics from the list of potential NCD topics.

These recommendations are discussed in more detail below. The last recommendation is also supported by a Technical Appendix attached to this letter.

CMS Should Use the Existing "Reasonable and Necessary" Standard When Making Decisions Relating to Coverage.

By statute, Medicare payment for items and services is available when, among other things, the item or service is "reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member."² The purpose of a NCD is to make a determination with regard to when an item or service meets that standard.³ In general, in determining whether an item or service is reasonable and necessary, CMS has looked to whether the item or service improves health outcomes for beneficiaries.⁴ Specifically, CMS has said that: "For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality..."⁵ This makes the determination one about whether there is a benefit for individual Medicare beneficiaries in particular circumstances.

In the recently released potential NCD topics list, however, CMS seeks input on items and services that "may be inappropriately used (i.e., underused, overused, or misused) or provide a minimal benefit in hospitals, clinics, emergency departments, doctors' offices, or in other healthcare settings." These terms are not currently used by CMS with regard to its NCD process, and they do not appear in statute or in CMS guidance documents relating to NCDs or in any of the NCDs themselves. Importantly, they also are undefined. Amgen views the lack of definition as worrisome given that the terms are subject to variable interpretations and laden with value judgments. Even if consensus could be reached with regard to the meaning of these terms in the abstract, they often lack meaning at an individual patient level. For example, what may be perceived as a "minimal benefit" with regard to the average population at a study-level may nonetheless provide a substantial benefit to an individual Medicare beneficiary in need of care. Amgen is concerned that by seeking input on items and services that fall within these undefined phrases, the agency may create or imply a new evidence standard infused with judgments about when there is or is not enough of a clinical benefit for Medicare beneficiaries or appropriate uptake of a product that differs from the reasonable and necessary standard that the agency has discussed extensively in its guidance and NCDs and has relied on exclusively before now.

Current CMS standards for making coverage determinations are broad enough to accommodate the diverse medical needs of Medicare beneficiaries. The current standards also allow for incremental improvements in medical technologies by allowing for coverage of items and services that may improve health outcomes for some patients for whom the risks associated with the treatment are acceptable. The agency's request for comments regarding items and services that may provide a "minimal benefit," seems to undermine these existing standards by implying that CMS will now impose a minimum benefit threshold and deny coverage of a product unless some undefined level of clinical

improvement has been achieved. It also may inhibit access to covered items and services. Including an item or service on the list of potential NCD topics, especially if the basis for its inclusion is due to a belief that it may be "inappropriately used" or provide a "minimal benefit," may cause Medicare contractors or others to deny coverage, even where CMS has not considered the evidence or completed the NCD process.

For these reasons, we urge the agency to rely on the existing "reasonable and necessary" standard when making decisions related to coverage, including whether to add a topic to the list of potential NCD topics, and to withdraw its request for comments on items and services that might be "inappropriately used" or provide a "minimal benefit." We also urge the agency to take proactive steps to ensure that the patients, providers, and contractors do not infer that a topic's inclusion on the list of potential NCD topics means that CMS has determined that use of the product is inappropriate or provides only a minimal benefit to ensure continued patient access to items and services as appropriate where CMS has not actually evaluated the available evidence and published an NCD.

The Agency Should Provide for a Comment Period Following the Release of the Revised List of Potential NCD Topics

Amgen appreciates that CMS has given the public the opportunity to provide input to the agency on items and services that should be included in the list of potential NCD topics. Entities and individuals who are directly involved in developing and manufacturing drugs and devices, who use them to treat patients, and who receive them as prescribed can provide valuable feedback to CMS regarding the use and benefits of items and services across healthcare settings. Previously, the agency indicated that it would provide stakeholders with the opportunity to comment on potential NCD topics "to creat[e] a more transparent and predictable NCD process."⁶ The agency provided the opportunity for such public comment following the release of the first list of potential NCD topics in 2008.⁷ Allowing for such public comment can be helpful to the agency in a number of ways. First, unless and until a revised list of topics is released, stakeholders with relevant technical expertise may not submit comments to the agency. Without a public comment period, the agency may miss the opportunity to benefit from additional, substantive evidence and expertise that may help CMS take appropriate action. In addition, substantive inputs from technical experts in response to a particular topic also could provide the agency with different perspectives illuminating why the topic should not be included on the list, or should be framed differently. Consistent with its existing guidance and prior practice, CMS should provide the opportunity for public comment following the release of the revised list of potential NCD topics.

CMS Should Establish a Process to Remove Topics from the List of Potential NCD Topics

The agency has not indicated, either in the recently released document or otherwise, how it plans to remove topics from the list of potential NCD topics. We believe it is important for CMS to establish a transparent process to remove topics from the list and utilize that process to remove items from the current list. There are a number of reasons we believe CMS should establish a process for removing topics from the list of potential NCD topics, including when the reasons the topic was added to the list no longer apply. Having an item or service on the list creates uncertainty for all stakeholders: patients, their caregivers, and others, because of the characterizations made by CMS of the topic (e.g., unclear benefits in certain populations, questioning adequacy of evidence). Having statements like this in the public domain, particularly from CMS, can impede access to items and services because Medicare contractors and other payers may be influenced by them in their payment assessments. By removing items from the list in a timely manner particularly when the reasons that they were originally added to the list no longer apply,

CMS can remove the uncertainty associated with the listing of a topic and help ensure appropriate access to the item or service.

Establishing a process to remove topics from the list of potential NCD topics also would be consistent with the agency's efforts to implement Executive Order 13563, "Improving Regulations and Regulatory Review," as described recently in a Proposed Rule. 8 Although the list of potential NCD topics is not a regulation, revising it to remove topics when the reasons the topic was added to the list no longer apply would serve the same purpose as removing an obsolete regulation to ensure full access to care for beneficiaries, reduce burdens on providers of care, and make CMS a better business partner and would be consistent with the agency's approach to implementing the Executive Order.

For these reasons, Amgen urges CMS to establish a transparent process for removing items from the list of potential NCD topics. This process would apply both to the current topics, as well as topics that may be included on the list in future revisions. Through it, stakeholders would be able to submit information demonstrating that the reasons that a topic was initially included on the list are no longer applicable. Amgen anticipates that this might include scientific evidence developed after a topic is included on the list that demonstrates the health benefits of the item or service or otherwise addresses the concerns that CMS identified as pertinent to the item or service when initially including it on the list. CMS would review this evidence and remove a topic from the list when the reasons the topic was added to the list no longer apply.

An example of a topic that could be subject to this process and appropriately removed from the list is thrombopoiesis stimulating agents. This topic was included on the list of potential NCD topics released in 2008 when CMS indicated that such drugs "may elicit safety concerns," and "[l]ong term safety data are lacking." As explained more fully in the attached Technical Appendix, in the years since this topic was added to the list of potential NCD topics, additional data (including long-term safety data) on Nplate® (romiplostim), Amgen's thrombopoiesis stimulating agent, have emerged, lending support to the positive risk:benefit profile of Nplate®. We believe it would be appropriate for this topic to be removed from the list of potential NCD topics.

Amgen appreciates the opportunity to provide these comments and looks forward to working with you to ensure that the list of potential NCD topics is maintained in a manner that will assure appropriate access to innovative drugs for Medicare beneficiaries. Please contact Sarah Wells Kocsis by phone at (202) 585-9713 or by email at wellss@amgen.com to arrange a meeting or if you have any questions regarding our comments or the attached Technical Appendix. Thank you for your attention to this important matter.

Regards,

/s/

Joshua J. Ofman, MD, MSHS
Senior Vice President, Global Value & Access

Attachment 1 . Technical Appendix

cc: Patrick Conway, MD, Director, Office of Clinical Standards and Quality, and CMS Chief Medical Officer

TECHNICAL APPENDIX

Nplate® (romiplostim) is the first thrombopoietin (TPO) mimetic (also referred to as a thrombopoiesis stimulating agent) to market. Nplate® was approved by the U.S. Food and Drug Administration (FDA) in August 2008, shortly after release of the Centers for

Medicare & Medicaid Services (CMS) potential National Coverage Determination (NCD) topics list. CMS included thrombopoiesis stimulating agents on the 2008 potential NCD topics list, stating that such drugs "may elicit safety concerns," and "[l]ong term safety data are lacking."

In the years since this topic was added to the list of potential NCD topics, the safety data that Amgen has collected supports that the benefit:risk profile of Nplate® has remained favorable since product approval. We have an extensive clinical program to continue to monitor the longterm safety of Nplate®. Two large open-label studies have been published and presented in the years since the FDA approval of Nplate®.^{1,2} In addition, certain long-term safety data for Nplate® from commercial sales were collected from approximately 5,200 patients representing a cumulative patient exposure of 3,282.3 patient years as part of the Nplate® NEXUS (Network of EXperts Understanding and Supporting Nplate® and Patients) Program, an FDA-mandated Risk Evaluation and Mitigation Strategies (REMS) program described in more detail below.³ Based on this evidence, we respectfully propose that Nplate® be removed from the list of potential NCD topics.

Below we provide additional information in support of this recommendation, including:

- Description of immune thrombocytopenia (ITP) and the unmet medical need addressed by Nplate®;
- Long-term safety data for Nplate®;
- Clinical benefits associated with Nplate®; and
- Inclusion of TPO mimetics in treatment guidelines for ITP.

Nplate® was First Approved in August 2008, and Addressed an Important Unmet Medical Need for Patients with Chronic ITP.

Nplate® is a first-in-class drug for the TPO mimetic group and acts by stimulating platelet production to increase platelet counts rather than by modulating the immune system to decrease platelet destruction.⁴ Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate® is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than chronic ITP. Nplate® should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. Nplate® should not be used in an attempt to normalize platelet counts.

ITP is an orphan disease as defined by the Orphan Drug Act.⁵ Chronic ITP is estimated to affect about 64,000 adult patients in the US; approximately 18,000 adults are seeking treatment at any time.⁶⁻⁸ ITP is an autoimmune disorder characterized by isolated thrombocytopenia (defined as a platelet count of less than 100 x 10⁹/L) in the absence of any obvious initiating and/or underlying cause of the thrombocytopenia.^{9,10} As a result, ITP patients have a potential risk for serious, even fatal, bleeding when severe thrombocytopenia occurs which can be further confounded by other concurrent medical diagnoses or treatment needs.⁹⁻¹¹

Patients develop antibodies that target their platelets for an accelerated destruction. For this reason, traditional therapies (prior to the availability of TPO mimetics) were designed to interfere with platelet destruction through modulation of the immune system.^{9,11} These therapies, in general, cannot be used long-term, due to the potential for transient effectiveness and the potential for severe side effects such as immunosuppression and its increased risk for serious infections.^{9,10,12} Given these limitations, chronic ITP patients

generally require multiple therapies over the course of their care.⁹ In the last several years, data demonstrate that ITP patients also exhibit decreased platelet production in the bone marrow^{11,13} and that these patients also experience relative thrombopoietin deficiency,¹⁴ both contributing to thrombocytopenia seen in ITP. Nplate® is a therapy that acts like the natural TPO in the body to help drive platelet production and improve platelet counts. Nplate® addresses an important unmet clinical need in chronic ITP by elevating and sustaining platelet counts at hemostatic levels via a novel mechanism of action and by reducing the need for concurrent ITP and rescue medications.⁴

Long-term Safety Data for Nplate® Support That the Benefit:Risk Profile of Nplate® has Remained Favorable Since Product Approval.

Amgen is committed to understanding the safety of Nplate®. Since inception of the romiplostim development program, an estimated 1,493 subjects (1,739 subject-years) have been exposed to romiplostim in clinical trials.¹⁵ The clinical development program included two phase 3 pivotal placebo controlled clinical trials¹⁶, one phase 3 standard of care (SOC) controlled clinical study¹⁷ as well as two long-term open-label studies^{1,2}. Additionally, certain long-term safety data for Nplate® from commercial sales were collected from approximately 5,200 patients representing a cumulative patient exposure of 3,282.³ patient years as part of the Nplate® NEXUS Program, an FDA-mandated REMS program described in more detail below.³

As part of its development program, Amgen conducted phase 3 clinical studies of Nplate® versus placebo in adult patients with chronic ITP (defined as patients who had ITP for 6 months duration or more per definitions that predate the 2009 standardization guidelines¹⁰). Across both phase 3 pivotal clinical trials, the percentage of patients who experienced adverse events (AEs) was similar across Nplate® and placebo-treated patients.^{4,16} The majority of AEs were mild to moderate in severity.^{4,16} Almost all patients in the study experienced an AE.¹⁶ A slightly higher proportion of Nplate® patients experienced AEs compared with placebo patients, 100 percent versus 95 percent, respectively.¹⁶ Headache (35 percent for Nplate® patients versus 32 percent for placebo patients), fatigue (33 percent versus 29 percent), and epistaxis (32 percent versus 24 percent) were the most common AEs in both treatment groups.^{4,16}

In November 2010, Amgen published an additional randomized controlled phase 3 study comparing patients receiving either Nplate® treatment or SOC treatments and evaluating two co-primary endpoints, the incidence of treatment failure or the incidence of splenectomy.¹⁷ In this phase 3 trial, over 90 percent of patients in the two groups had at least one adverse event during the treatment period.¹⁷ However, as seen in the pivotal studies described above, the most common AEs were headache and fatigue.¹⁷

Amgen has an extensive clinical program to continue to monitor the long-term safety of Nplate®. Two large open-label studies have been published and publically presented in the years since the FDA approval of Nplate®.^{1,2} In the first study, 291 patients had been treated with Nplate® for up to 277 weeks with a median duration of 78 weeks and in some cases with 277 weeks of exposure.¹ In an interim analysis of the second study, 235 patients had received Nplate® for an average of 44.3 weeks.² The safety data from both of these studies are shown below.

Table 1. Long-term Safety Data, Nplate®

	Long-term Extension Study N = 291¹	Long-term Access Study N = 235²
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Serious AEs considered treatment-related, % (n)	8% (24)	3 % (8)
Thrombotic events, % (n)	9 % (25)	6% (14)
Bone marrow reticulिन present or increased, % (n)	4% (11)	1% (3)
Neutralizing antibodies to Nplate®, % (n)*	1% (2)	0
Neutralizing antibodies to TPO, % (n)	0	0
Deaths, n	16	9
Considered treatment-related	2 (unstable angina, myocardial infarction)	2 (hemolysis, aplastic anemia)

* In both cases neutralizing antibodies were absent on retesting after drug withdrawal
n = number of patients

At the time of FDA approval, Amgen worked with the FDA to develop a comprehensive REMS program to assure that Nplate® is used appropriately and safely. The goals of the Nplate® REMS program are as follows:

- To promote informed risk-benefit decisions before and during treatment to assure appropriate use of Nplate®.
- To establish the long-term safety and safe use of Nplate® through periodic monitoring of all patients who receive Nplate® for changes in bone marrow reticulिन formation and bone marrow fibrosis, worsened thrombocytopenia after cessation of Nplate®, thrombotic/thromboembolic complications, hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or MDS, and medication errors associated with serious outcomes.

Under the current REMS, Nplate® is available only through a restricted distribution program called the Nplate® NEXUS Program. Under this program, only health care providers and patients registered with the program are able to prescribe and receive Nplate®. All physicians prescribing Nplate® must be enrolled in the Nplate® NEXUS program to ensure that appropriate education is delivered on the risks and benefits of the drug, and all patients receiving Nplate® must be enrolled in the Nplate® NEXUS patient education and long-term safety registry program (U.S. Nplate® Safety Registry). Adverse event information are continuously monitored and actively solicited twice a year for all Nplate® patients. As of Jan 2011, over 3,282.3 cumulative years of patient exposure data has been collected.³

Amgen and the FDA are currently in discussions to determine whether certain elements of the REMS program, including the restricted distribution and further collection of safety-data, should be modified. A decision is expected in the near future.

Nplate® Sustains a Hemostatic Platelet Count in Adults with Chronic ITP.

In phase 3 pivotal placebo controlled clinical trials of Nplate® versus placebo, the overall proportion of patients who achieved a durable platelet response was significantly higher

in the Nplate® groups versus in the placebo groups.^{4,16} Durable platelet response is defined as at least six weekly platelet responses ($\geq 50 \times 10^9/L$) during the last eight weeks of treatment without the use of rescue medications.^{4,16}

- 38 percent of splenectomized subjects in the Nplate® group and no subjects in the placebo group achieved a durable platelet response ($P = 0.0013$).
- 61 percent of non-splenectomized subjects in the Nplate® group and 5 percent of subjects in the placebo group achieved a durable platelet response ($P < 0.0001$).
- For both phase 3 studies combined (splenectomized and non-splenectomized patients), the overall proportion of patients who achieved a durable platelet response was 49 percent in the Nplate® groups and 2 percent in the placebo groups ($P < 0.05$).

In these studies, patients in the Nplate® arm also experienced higher overall platelet responses, defined as the total of durable platelet response and transient platelet response (at least four weekly platelet responses) without the use of rescue medications, compared with the placebo arm.^{4,16} For both phase 3 studies combined (splenectomized and non-splenectomized patients), 83 percent of patients in the Nplate® group compared to 7 percent in the placebo group ($P < 0.0001$) achieved an overall platelet response.¹⁶

In the Nplate® or SOC study, 11 percent (18/157) of patients receiving Nplate® experienced a treatment failure compared with 30 percent (23/77) of patients in the SOC arm ($P < 0.001$).¹⁷ Treatment failure was defined as a platelet count of $20 \times 10^9/L$ or lower for four consecutive weeks at the highest recommended dose, a major bleeding event, or requirement for a change in therapy (including splenectomy) because of an adverse event or bleeding symptoms.¹⁷ In addition, the time to treatment failure was significantly longer in the Nplate® group than in the SOC group ($P = 0.02$).¹⁷ The incidence of splenectomy (as defined by the protocol) was significantly lower among patients receiving Nplate® (14 of 157 [9 percent]) than among those in the SOC arm (28 of 77 [36 percent], $P < 0.001$).¹⁷ The time to splenectomy was also significantly longer in the Nplate® group than in the SOC group ($P < 0.001$).¹⁷

In the open-label extension study of patients who had previously completed a prior ITP Nplate® trial, a platelet response to Nplate® (defined as a platelet count at a scheduled weekly visit that was $\geq 50 \times 10^9/L$ outside an eight week window of rescue therapy) was demonstrated in 94.5 percent of patients and after the first week median platelet counts remained within the target range (50 to $200 \times 10^9/L$) for the duration of the study while maintain a stable dose over the duration of the study.¹

Patients Treated with Nplate® Have Statistically and Clinically Lower Rates of Moderate or More Severe Bleeding Events Relative to Placebo.

Patients who received Nplate® in phase 3 clinical trials experienced fewer grade 2 (moderate) and above bleeding events and as well as fewer grade 3 and above (severe, life-threatening, or fatal) bleeding events than patients receiving placebo.^{4,18} Clinically significant bleeding AEs (severity grade 2 or higher) were noted in 15 percent of Nplate® and 34 percent of placebo-treated patients ($P = 0.018$).¹⁸ The percentage of patients experiencing bleeding AEs of grade 3 severity was 7 percent and 12 percent in the Nplate® and placebo groups, respectively ($P = 0.36$).¹⁸ Furthermore, in phase 3 clinical trials, there was a 55 percent reduction in the rate of bleeding related episodes, a composite endpoint developed to examine the number of bleeding events together with the use of rescue medications to prevent imminent bleeding events, in patients receiving Nplate® compared with those receiving placebo.¹⁹

In the more recently completed Nplate® or SOC trial, the Nplate® group had significantly lower adjusted incidences of overall bleeding events ($P = 0.001$) and bleeding events of grade 3 or higher ($P = 0.02$) as compared with the SOC group.¹⁷ No significant differences between the two groups were noted with respect to bleeding or grade 2 or higher ($P = 0.17$).¹⁷ Furthermore, 41 blood transfusions were administered to 12 of 154 patients (8 percent) receiving Nplate®, and 76 blood transfusions were administered to 13 of 75 patients (17 percent) receiving SOC.¹⁷ The duration adjusted rate of bleeding related episodes in Nplate®-treated patients was 3.1 per 100 patient-weeks compared with a duration adjusted rate of 9.4 per 100 patient-weeks in the SOC arm.²⁰

During the open-label extension study the patient incidence of bleeding events of moderate or greater severity (. Grade 2) and of severe or higher (. Grade 3) did not increase over time.¹

Nplate® Results in a Reduction or Discontinuation in the Use of Concurrent Oral Immunosuppressive Therapies (Corticosteroids, Azathioprine, or Danazol).

Among patients in phase 3 clinical trials who were receiving concurrent ITP medications at baseline, all splenectomized patients who received Nplate® were able to reduce dosage of concurrent ITP medication by more than 25 percent or discontinue concurrent ITP therapies during the first 12 weeks of treatment.^{4,16} This compares with 17 percent of splenectomized patients who received placebo.^{4,16} Similarly, among non-splenectomized phase 3 trial participants, 73 percent of patients who received Nplate® were able to reduce dosage of concurrent ITP medication by more than 25 percent or discontinue concurrent ITP therapies during the first 12 weeks of treatment.^{4,16} This compares with 50 percent of non-splenectomized patients who received placebo.^{4,16}

In the open-label extension study, 81 percent (30/37) of patients receiving concurrent therapy at baseline were able to discontinue or reduce by 25 percent their concurrent therapy.¹

Nplate® is Associated with a Reduction in Rescue Therapy Use, Including a Significant Reduction in Use of Immunoglobulins.

In both phase 3 clinical trials, rescue therapies (i.e., corticosteroids, Intravenous immunoglobulin (IVIG), platelet transfusions, and anti-D immunoglobulin) were permitted for bleeding, wet purpura, or if the patient was at immediate risk for hemorrhage.⁴ The percentage of splenectomized patients who required rescue therapy was more than 50 percent lower for Nplate® patients when compared to placebo patients (26 percent vs. 57 percent, respectively; $P < 0.0175$).^{4,16} Only 20 percent of non-splenectomized patients who received Nplate® required rescue therapy; this compares with 62 percent for patients who received placebo ($P < 0.0004$).^{4,16}

In the 24-week period for both phase 3 studies combined (splenectomized and nonsplenectomized patients), there were 19 immunoglobulin administrations among 83 Nplate® patients and 68 immunoglobulin administrations among 42 placebo patients.²¹ Differences in the proportions of patients requiring immunoglobulin were statistically significant at all 4-week intervals, ranging from 17 percent in Week 1 to 4 (19 percent of placebo and 2 percent of Nplate®) to 37 percent in Week 12 to 12 (37 percent for placebo and 1 percent for Nplate®).²¹ The cumulative probability (standard error [SE]) of immunoglobulin use in 24 weeks was 0.51 (0.08) for the placebo arm and 0.13 (0.04) for the Nplate® arm, with a hazard ratio of 5.3 (95 percent CI: 2.6 to 11.1, $P < 0.001$).²¹

Both US Guidelines and an International Consensus Report Identify TPO Mimetics as a Treatment Option for ITP Patients.

Clinical practice guidelines for ITP are used by hematologists in their treatment decisions for this orphan disease. The 2011 guidelines by the American Society of Hematology (ASH) and the 2010 International Consensus Report provide updated recommendations for the diagnosis and management of ITP.^{9,11} The reports were authored by two distinct panels of experts in ITP including prominent US experts. These reports include TPO mimetics, such as Nplate®, as a second-line medical therapy choice for ITP patients who have not had a splenectomy and as a first-line therapy choice for ITP patients who have had a splenectomy but have ITP that is refractory or relapsed.

9,11

Guidance documents (Guidelines from American Society of Hematology and International Consensus Report) maintain that recommendations are intended as guides only and should not supersede physician's judgment when making treatment decisions based on the patient's specific needs, characteristics, or preference.^{9,11}

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1 Centers for Medicare and Medicaid Services. Potential NCD Topics.

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3 Id. ~ 1862(l)(1)

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7 Id.. Note, "In 2008, CMS published a list of potential NCD topics, giving the public an opportunity to comment on the items and services in the list."

8 76 Fed. Reg. 65909.

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Date:

11/23/2011

Comment:

November 23, 2011

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Director, Coverage and Analysis Group

Office of Clinical Standards and Quality

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Re: Solicitation on Potential National Coverage Determination (NCD) Topics

Dear Dr. Jacques:

Boston Scientific Corporation (Boston Scientific) appreciates the opportunity to provide comments in response to the Centers for Medicare & Medicaid Services' (CMS) recent web site solicitation for input on potential Medicare National Coverage Determination (NCD) topics.

As the world's largest company focused on the development, manufacturing, and marketing of less-invasive medicine, Boston Scientific supplies medical devices and technologies used by the following medical specialty areas, all of which provide beneficiary care in the hospital inpatient setting:

- Cardiac Rhythm Management;
- Gastroenterology;
- Interventional Bronchoscopy;
- Interventional Cardiology;
- Interventional Radiology;
- Oncology;
- Neuromodulation;
- Urology; and
- Women's Health.

As a result, we are interested in the CMS NCD process and topic areas that affect less invasive and innovative technologies. We support the current CMS NCD identification and review process as defined in the current CMS Guidance document, Factors CMS Considers in Opening NCDs(1). Boston Scientific believes that is critical to ensure that beneficiaries have access to the most appropriate and safe medical devices and careful attention should be given to effectiveness of CMS services. As a result, we are pleased to provide input on the CMS public solicitation of NCD topics in areas where CMS services may be ineffective and overused or services that may be underused, but effective (2).

Our comments will focus on two areas: First, our overarching considerations on the NCD process, and second we offer comments on the most recent NCD request process as the agency solicits and prioritizes input from the public.

General Comments on Coverage Policy

Boston Scientific understands that the Medicare program spends more than \$500 billion annually for more than 46 million senior and disabled beneficiaries (3). Per the Federal statutory requirement, CMS pays for medical services that are “reasonable and necessary” for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member (4). CMS’s interpretation of “reasonable and necessary” as evolved over the years, and it is clear from CMS guidance, that the standard of “reasonable and necessary” is a flexible one in which little evidence is available. Recent efforts by the program have focused on trying to improve the individual experience of care, improve the health of populations and reduce per capita costs for populations (5).

Coverage policies are required to help ensure that the optimal Medical diagnostics and treatments are available for appropriate populations. *We agree with CMS that optimal and impactful Medical intervention should be available to help the most appropriate patients, resulting in better patient care experiences, and improvement of general health.* Thus, coverage policy involves much more than reviewing evidentiary tables and design methodology, but balances evidence available, potential benefits and risks to patients, resources required, and determines under what conditions where coverage is appropriate (6).

In 2008, CMS’ published a list of 20 topics in which uncertainty around benefits and risks existed, prompting CMS to consider a NCD review of these areas (7). The NCD reviews did not occur and the list has not been updated officially. Currently, CMS has solicited comments from the public for potential NCD topics.

Specific Comments on Most Recent NCD Process

We remain very supportive of the existing CMS criteria when choosing to initiate a new NCD or NCD for existing technology (8). CMS Guidance states that the reasons for initiating a new NCD or for existing technology include:

- There are significant questions about the health benefits of currently covered items or services, specifically regarding the Medicare population;
- Interpretation of new evidence or re-interpretation of previously available evidence indicates that changes may be warranted in current policies;
- Local coverage policies are inconsistent or conflict with each other to the detriment of Medicare beneficiaries.
- Program integrity concerns have arisen under existing local or national policies;
- The health technology represents a substantial clinical advance and is likely to result in a significant health benefit if it diffuses more rapidly to all patients for whom it is indicated.

- More rapid diffusion of the technology is likely to have a significant programmatic impact on Medicare and on other Medicare-related public policies (e.g., reduction in health inequalities).
- Significant uncertainty exists concerning the health benefits, patient selection, or appropriate facility and staffing requirements for the new technology.

All of above criteria are important consideration for NCD identification and assessment. For the most recent public request for NCD topics we will focus our specific NCD comments on: 1) Request for Potential NCD Topics and Process, 2) Transparency in Request for Potential NCD Topics and Process, and 3) Maintenance in Criteria for Potential NCD Topics and Process.

Comment 1: Request for Potential NCD Topics Process

Although there is an existing mechanism for the public to solicit Medicare NCD requests, CMS has asked the public for new topic areas for potential NCD reviews (9). In the CMS solicitation, the Agency has stated that there currently may be areas of both overuse of CMS services that may be ineffective or underuse of services that may be effective (10). CMS has also requested comments for NCD topics that may or may not provide minimal clinical benefit.

Instituting a new and undefined threshold, such as minimal benefit, is challenging and we *would encourage CMS to adhere to the established CMS Guidance on rationale and questions around evidence needs when considering the **clinical benefit** of any new NCD for evaluation of a coverage decision (11).*

Comment 2: Transparency in Request for Potential NCD Topics Process

While we appreciate the need to identify areas of ineffective and effective use of CMS services we *encourage CMS to continue to make the current NCD topics request transparent*. For each potential NCD, topic information (**Submitter, Rationale for Inclusion, and Ranked Priority**) should be made available in tabular format at the CMS website, with appropriate time for public comment for each proposed NCD.

Comment 3: Maintenance of Current NCD Rationale in Request from Public for Potential NCD Topics Process

We encourage CMS to maintain similar NCD rationale as described in its initial Guidance when it reviews comments from the public. Specifically,

CMS NCD Guidance – “There are significant questions about the health benefits of currently covered items or services, specifically regarding the Medicare population.”

In assessing public comments, and prioritizing potential NCD topics, we encourage close review by CMS to determine if the standard practice of Medicine for each potential NCD topics actually deviates from existing evidence, and whether existing evidence supports the “reasonable and necessary” threshold.

In addition to changes in significant effectiveness data related to CMS services as rationale for a NCD, we believe that NCDs are ideally opened if new information emerges indicating a serious or potentially serious safety issue for Medicare patients. Generally, safety issues should be viewed within the context of treatment alternatives, and consideration of NCD should take into account the varying clinical outcomes often associated with treating patients of varying complexity and co-morbidities.

CMS NCD Guidance – “Local coverage policies are inconsistent or conflict with each other to the detriment of Medicare beneficiaries”

We believe that NCDs are also best suited for situations in which local coverage determinations (LCDs) diverge and the misalignment of these LCDs leads to significant variability in treatments among similarly situated Medicare patients.

CMS NCD Guidance – “Interpretation of new evidence or re-interpretation of previously available evidence indicates that changes may be warranted in current policies.”

We support reconsiderations of negative NCDs when new clinical outcomes data is available that suggests improved health outcomes resulting from the non-covered item or service. The prospect of expanding and contracting coverage based on the latest evidence is appropriate and ensures that Medicare patients obtain care reflecting up-to-date practice, specialty consensus and clinical evidence.

In closing, Boston Scientific applauds CMS efforts to be open and transparent in this process. We support the CMS goal to ensure that patients receive the optimal Medical therapy to improve their care and general health through the NCD process.

We believe that CMS should use existing NCD determination criteria to assess public comments on potential NCD topics.

We appreciate the opportunity to comment on this important topic, and your consideration of our overall perspectives. If you or your staff has questions, please do not hesitate to contact Michael Ferguson, PhD (Director Health Economics, 508-6652-5234; michael.ferguson@bsci.com) or Kristen Hedstrom, MPH (Director Healthcare Policy, 202-637-8021; kristen.hedstrom@bsci.com).

Sincerely,

Parashar B. Patel
Global Vice President, Health Economics & Reimbursement
Boston Scientific Corporation

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- 9 See Potential NCD Topics – Public Comment Period, posted 9/28/2011,

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[MCDId=19&McdName=Potential+NCD+Topics&mcctypename=Potential+National+Coverage+D\(NCD\)+Topics&MCDIndexType=2&bc=AgAEAAAAAAAA&](https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=19&McdName=Potential+NCD+Topics&mcctypename=Potential+National+Coverage+D(NCD)+Topics&MCDIndexType=2&bc=AgAEAAAAAAAA&)

10 Ibid.

11 Ibid

Commenter:**Todd, Laurel L.**

Title:

Managing Director, Reimbursement and Health Policy

Organization:

Biotechnology Industry Organization

Date:

11/22/2011

Comment:

November 23, 2011

VIA ELECTRONIC SUBMISSION

Donald Berwick, MD

Administrator

Centers for Medicare and Medicaid Services

Department of Health and Human Services

Hubert H. Humphrey Building

200 Independence Ave. SW

Washington, DC 20201

Re: Potential NCD Topics

Dear Administrator Berwick:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) Medicare Coverage document entitled "Potential NCD Topics."¹ BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the world. BIO represents more than 1,100 biotechnology centers, academic institutions, state biotechnology centers, and related organizations in the United States and in more than 30 other nations. BIO members are involved in the research and development of health care, agricultural, industrial and environmental biotechnology products.

BIO represents an industry that is devoted to discovering and ensuring patient access to new and innovative therapies. Medicare coverage of these therapies is vital to ensuring the health and wellness of many Medicare beneficiaries, and a predictable and transparent Medicare coverage process is essential to providing timely access to appropriate treatment options.

In general, BIO supports CMS's efforts to improve the transparency of the national coverage determination (NCD) process by seeking input on potential NCD topics. We are very concerned, however, that CMS's request for NCD topics refers to a new "minimal

benefit” standard for determining whether to issue an NCD that not only is contrary to federal law and the agency’s own guidance, but also threatens to restrict beneficiary access to much needed medical therapies. Instead, we urge CMS to follow the “reasonable and necessary” standard set forth under federal law and the agency’s own guidance interpreting that standard when seeking potential NCD topics. Furthermore, we urge CMS to seek public comment on any new list of NCD topics that it publishes and consider removing items from the list of potential NCD topics.

I. CMS Should Use Existing Standards When Identifying Potential Topics for NCDs

In the request for potential NCD topics, CMS invites input concerning items and services that “may be inappropriately used (i.e., underused, overused, or misused) or provide minimal benefit in hospitals, clinics, emergency departments, doctors’ offices, or in other healthcare settings.”² These criteria for identifying potential NCD topics are different from the criteria established by statute and CMS guidance. In particular, the “minimal benefit” standard is new, undefined, and conflicts with longstanding guidance on interpretation of the statutory “reasonable and necessary” requirement for coverage.

Under the federal Medicare statute, Medicare payment for most items or services is contingent upon the determination that the item or service falls within a benefit category, is not specifically excluded from coverage, and is “reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member.”³ CMS has the authority to implement NCDs that identify the circumstances under which items and services are considered to be “reasonable and necessary,” as well as to develop guidance documents that explain the factors considered in making NCDs.⁴

We could find no instance in CMS’s guidance documents or its coverage decisions where “minimal benefit” has been used or defined as a criterion for developing an NCD for an item or service. Although CMS has not defined “reasonable and necessary” in regulation, in numerous NCDs and CMS’s own guidance documents on the development of NCDs, CMS has identified “improved health benefit” as a key standard for determining whether an item or service is “reasonable and necessary.”⁵ In addition, in statements to the medical community, CMS has said that it uses the following definition for “reasonable and necessary:” “adequate evidence to conclude that the item or service improves clinically meaningful health outcomes for the Medicare population.”⁶

In addition, CMS’s guidance on the factors it considers when deciding whether to open a national coverage analysis (NCA) do not refer to “minimal benefit” as a criterion for coverage. This notice provides a comprehensive outline of the agency’s policies with respect to the NCD process developed after a period of notice and comment. In this guidance, CMS set forth the necessary aspects of a request for an NCD, including:

- A rationale for how the evidence selected demonstrates the medical benefits for the target Medicare population;
- Information that examines the magnitude of the medical benefit; and
- Reasoning for how coverage of the item or service will help improve the medical benefit to the target population.

CMS asks the party seeking an NCD to describe the “magnitude of the medical benefit” of the item or service at issue, but CMS does not define the magnitude necessary to support coverage. The recent request for potential NCD topics diverges from the 2003 notice by suggesting that items and services with only “minimal benefit” might not be covered by Medicare.

CMS provided additional guidance on the criteria that could prompt the opening of an NCA in its April 11, 2006 guidance document, “Factors CMS Considers in Opening a National Coverage Determination,” issued on April 11, 2006. This guidance identified the following criteria for an existing technology that already is in use:

- Providers, patients or other members of the public have raised significant questions, that are supported by CMS’s initial review of available data, about the health benefits of currently covered items or services, specifically regarding the Medicare population;
- Interpretation of new evidence or re-interpretation of previously available evidence indicates that changes may be warranted in current policies;
- Local coverage policies are inconsistent or conflict with each other to the detriment of Medicare beneficiaries. For instance, the noted variation is not related to local differences in the capabilities of health care providers to use the technology effectively which can be resolved over time, but rather is causing significant disparities in the care available to Medicare beneficiaries that are unlikely to be addressed effectively through provider training and education or through the local coverage process;
- Program integrity concerns have arisen under existing local or national policies; that is, there is significant evidence of wide variation in billing practices not related to variation in clinical need, or of potential for fraud under existing policies.⁷

In addition, CMS identified the following criteria for generating an NCD for “a new item or service, an existing item or service that has been substantially modified, or for a proposed new use of a covered product.”

- The health technology represents a substantial clinical advance and is likely to result in a significant health benefit if it diffuses more rapidly to all patients for whom it is indicated.
- More rapid diffusion of the technology is likely to have a significant programmatic impact on Medicare and on other Medicare-related public policies (e.g., reduction in health inequalities).
- Significant uncertainty exists concerning the health benefits, patient selection, or appropriate facility and staffing requirements for the new technology. The presence of significant uncertainty about benefits and risks is of particular concern when rapid diffusion of the item or service is likely when:
 - Use of the new item or service likely conflicts with existing NCDs.
 - Available evidence suggests that local variation is not warranted.⁸

CMS also specified:

Cost effectiveness is not a factor CMS considers in making NCDs. In other words, the cost of a particular technology is not relevant in the determination of whether the technology improves health outcomes or should be covered for the Medicare population through an NCD.⁹

These criteria recognize that an item or service might be a good subject for an NCD if there are questions about its benefits, but unlike the “minimal benefit” standard mentioned in the request for potential NCD topics, they do not suggest that there is a threshold level of benefit needed for coverage. Similar to the 2003 Federal Register Notice, the guidance document requires that requests for NCDs provide information “that measures the medical benefits of the item or service,”¹⁰ but CMS has not established a particular

amount of benefit that is necessary to support coverage. Under the published criteria for consideration of potential NCD topics and the “improved health outcome” standard, it only is necessary to demonstrate that an item or service has a potential clinical benefit to some Medicare beneficiaries in order for CMS to consider issuing an NCD.

If CMS wishes to collect suggestions for topics for NCDs, we ask that it use these criteria, which have been shared with the public and developed after public notice and comment, to identify items and services for which an NCD might be appropriate. By seeking to identify items and services that provide “minimal benefit” as candidates for NCDs, CMS appears to establish a new standard for coverage analysis that is inconsistent with CMS’s longstanding interpretation of the Medicare statute’s “reasonable and necessary” standard because it suggests that some items and services that improve health outcomes could be denied coverage because they fail to achieve an undefined level of improvement.

Beyond being inconsistent CMS’s interpretation of “reasonable and necessary,” the “minimal benefit” standard also threatens to hinder beneficiary access to medically necessary items and services. First, it is not clear that the “minimal benefit” standard takes into consideration the needs of specific patient sub-populations. As CMS is aware, the medical needs of Medicare beneficiaries are varied and diverse. An item or service could be beneficial for one patient population but not for another. CMS’s longstanding interpretation of the Medicare statute’s “reasonable and necessary” standard is able to accommodate this diversity by covering items and services for even the smallest subset of beneficiaries to the extent that such care improves health outcomes for them. The “improved health outcome” criterion also recognizes that the size of an item or service’s effect on a patient’s health outcomes may vary depending on the patient’s unique condition, and that patients and their physicians are best suited to judge whether the benefits of a particular therapy justify any associated risks. For beneficiaries with few treatment options, a therapy that provides even a small benefit could be worth pursuing. In addition, the “improved health outcome” criterion recognizes that improvements in medical technologies often are incremental, and it allows Medicare to cover items and services that help to improve health outcomes without attempting to establish a minimum threshold for improvement for any patient population that is necessary for coverage. As a result, this criterion permits Medicare to cover items and services that can improve a patient’s health outcomes to any degree, and patients and physicians can determine whether the potential benefit for each patient justifies use of that technology. The same cannot be said for the “minimal benefit” standard. This standard suggests that an item or service must show not only that it is beneficial, but also that it exceeds a currently undefined threshold of benefit that is necessary for coverage.

Second, merely publishing a list of technologies that CMS suspects provide “minimal benefit” will have negative implications for access to care. In particular, by posting a list of items and services believed to be of “minimal benefit,” CMS may encourage Medicare contractors to cease coverage for these items and services given the negative connotations of this designation, even though CMS has not considered the available evidence or completed the NCD process. Thus, even if CMS ultimately decides to cover an item or service on the list, beneficiaries will not have had access to that benefit in the interim. We believe that this is a serious concern given that that our members have experienced contractors’ denials of coverage for their therapies during development of an NCD. BIO urges CMS to provide clear guidance to local carriers instructing them to continue coverage while an NCD is open.

In light of the foregoing, we urge CMS to withdraw the request for comments on items and services that provide “minimal benefit” from the September 28 Coverage Document. Instead, we urge CMS to rely on the Medicare statute’s “reasonable and necessary”

standard and the clinical benefit standards articulated in the agency's 2003 and 2006 guidance in deciding whether to open an NCD.

II. CMS Should Explain the Basis for Adding to the List of Potential NCD Topics

If CMS develops a list of potential NCD topics based on the September 28, 2011 request for comments, we ask CMS to seek public comment on that list before it is finalized. In addition, BIO requests that CMS identify the origin of each topic recommendation (i.e. CMS headquarters, medical specialty society, patient group etc). In 2008, when CMS published a list of potential NCD topics, it provided a brief description of each topic on the list, but often did not describe the clinical basis for proposing an NCD, cite publications, or discuss the evidence considered by CMS when it placed the item or service on the list. As a result, some of the topics may not have reflected the most recent evidence on the item or service. BIO urges CMS to clarify why a topic may be under consideration for an NCD. Stakeholders may be able to provide comments to CMS on a draft list of topics that could respond to questions about the technology or the clinical evidence that could help CMS refine the list or remove items from the list without expending the resources to open an NCA.

In addition, we ask CMS to consider removing an item or service from the list of potential NCD topics, or to revise the description of an item or service on that list, after the initial comment period has ended. As the evidence develops, CMS may find that it does not need to dedicate time and resources to develop an NCD on a topic. Removing topics from the list in these circumstances helps to clarify CMS's intentions and resolve any confusion among stakeholders about potential changes in coverage for that item or service. BIO asks CMS to develop a clear and realistic timeline for updating the list and to consider removing topics from the potential NCD list without requiring initiation of an NCA.

Lastly, after the list has been created, we ask CMS to ensure that it has the specific internal expertise that is necessary to conduct accurate assessments of each topic. Given the complexity of these issues, it is crucial that CMS enlist the assistance of trained, current, technical experts to ensure that accurate determinations are made in the best interest of patients. As we noted in our comments on the parallel review process, Medicare coverage of most drugs and biologicals is determined appropriately by local contractors. CMS's policies allow contractors to cover both approved and off-label uses of other drugs that are approved by the FDA and are "reasonable and necessary for diagnosis or treatment of an illness or injury."¹¹ In practice, contractors make coverage determinations for drugs and biologicals in an appropriate and timely manner. Thus, we ask that CMS ensure the same level of expertise in its review of items and services at the national level as it does at the local level.

III. Conclusion

BIO appreciates the opportunity to comment on Potential NCD Topics. We look forward to continuing to work with CMS to address this and other issues in the future. Please feel free to contact me at 202-962-9220 if you have any questions or need any additional information. Thank you for your attention to this very important matter.

Sincerely,

/s/

Laurel L. Todd
Managing Director
Reimbursement and Health Policy

1 CMS, Potential NCD Topics (Sept. 28, 2011), available at <http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx>?

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2 Id. (emphasis added). This definition requires only that the item or service improve health outcomes; it does not attempt to establish a minimum level of improvement necessary for coverage.

3 Social Security Act (SSA) § 1862(a)(1)(A). Coverage of certain other services, such as certain preventive services, is provided under other subparagraphs of § 1862(a)(1) or other specific provisions of the SSA.

4 SSA § 1862(l)(1).

5 CMS, Factors CMS Considers in Opening a National Coverage Determination (Apr. 11, 2006), available at: http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=6; CMS, National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development (July 12, 2006), available at: <https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?>

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24+Coverage+with+Evidence+Development&mcdtypename=Guidance+Documents&MCDIndex
see also, e.g. Decision Memo for Magnetic Resonance Imaging (MRI) (CAG-00399R3), July 7, 2011; Decision Memo for Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (CAG-00422N), June 30, 2011; and Decision Memo for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (CAG-00415N), August 4, 2010.

6 See, e.g., Barry M. Straube, MD, CER, Personalized Medicine & Coverage, October 20, 2010, at 7,

http://conferences.thehillgroup.com/CERandPMconference/presentations/Day%202/Day%202_Straube.pdf; Tamara Syrek Jensen, Medicare Coverage, November 14, 2008, at 11, http://www.npcnow.org/App_Themes/Public/pdf/events/2008_event/syrekjensen.pdf.

7 CMS, Factors CMS Considers in Opening a National Coverage Determination (Apr. 11, 2006), available at http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=6.

8 Id.

9 Id.

10 Id.

11 Medicare Benefit Policy Manual, ch. 15, §§ 50.4.1-50.4.3.

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