Alliance for Headache Disorders Advocacy

Alliance for Patient Access
American Academy of Neurology
American Headache Society
Association of Migraine Disorders
Clusterbusters
Headache Cooperative of New England
Headache Cooperative of the Pacific
Migraine Research Foundation
Miles for Migraine
National Headache Foundation
North Central Headache Society
Runnin' for Research
Southern Headache Society

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February 16, 2018

The Honorable Orrin Hatch, Chairman
The Honorable Ron Wyden, Ranking Member
United States Senate Committee on Finance
219 Dirksen Senate Office Building
Washington, DC 20510-6200

Dear Chairman Hatch and Ranking Member Wyden,

I am writing to you on behalf of the Alliance for Headache Disorders Advocacy (AHDA), a 501(c)(6) organization comprised of thirteen US not-for-profit organizations advocating on behalf of Americans with disabling headache disorders. We write in response to your open letter of February 2, 2018, requesting feedback to the Senate Committee on Finance on the following questions:

"*What barriers to non-pharmaceutical therapies for chronic pain exist in Medicare and Medicaid? How can those barriers be addressed to increase utilization of those non-pharmaceutical therapies when clinically appropriate?*"

In this regard, we request your urgent attention to reconsideration of the January 4, 2011, Centers for Medicare & Medicaid Services (CMS) Decision Memo for National Coverage Determination (NCD, CAG-00296R, attached) that denies coverage of home use of oxygen therapy for the acute treatment of cluster headache attacks by Medicare and Medicaid beneficiaries. The denial of this coverage places thousands of Americans at markedly increased and continued risk of recurrent attacks of excruciating pain, as well as increased risk of the adverse consequences of prescription opioid use disorders and overdose.

By way of background, cluster headache is widely recognized as one of the most severely painful disorders known. Approximately 500,000 people in the US may experience cluster headache, a disease with similar prevalence to multiple sclerosis. The pain of cluster headache occurs in abrupt and agonizing attacks that often reach extreme pain severity levels within seconds, last 15 minutes to 3 hours, and may occur up to eight times per day. Attacks typically occur in cyclical patterns of daily attacks that can last for weeks to months, though 15% percent of people with cluster headache experience attacks of excruciating pain every day.

High flow rate 100% oxygen therapy has been an undisputed first line agent for the acute treatment for cluster headache attacks, since it was first reported in 1952 (Horton, BT, *Lancet* 1952;72:92.). Oxygen therapy is usually effective within minutes, providing critical relief from the acute pain of cluster headache so that patients can regain quality of life. The speed of onset of oxygen is a crucial therapeutic benefit for a condition where recurrent individual attacks often reach extreme levels of pain within seconds.

Oxygen is the only widely reliable, safe, and effective acute therapy available for individuals living with cluster headache. This medical consensus is supported by broad clinical experience. It is also supported by controlled clinical trial research data that demonstrate its efficacy and safety, and with studies that specifically enrolled subjects up to 70 years of age (i.e. Medicare-eligible) (Cohen et al. *JAMA*. 2009;302:2451-2457, attached). Regarding the safety of oxygen for cluster headache, there are no published clinical trial reports or case reports, whatsoever, of any serious adverse events or serious side effects of its use among cluster headache patients of any age group.

As a consequence of the established clinical record of safety and efficacy of oxygen therapy, it is cited as the standard of care in the practice guidelines and texts for cluster headache therapy of the National Institutes of Health, Agency for Healthcare Research Quality, American Headache Society, American Academy of Neurology, Health Resources & Services Administration, European Federation of Neurological Societies, National Headache Foundation, and the Institute for Clinical Systems Improvement.

The Veterans Administration covers home oxygen therapy for its beneficiaries with cluster headache. Some private insurers also cover home use of oxygen for cluster headache (e.g. Anthem, Cigna, Aetna, Health Net), while other insurers cite the NCD as the basis for denial of such coverage (e.g. Minuteman Health).

As a result of the NCD denial of oxygen coverage, Medicare and Medicaid covered cluster headache patients often receive unnecessary, costly, and typically ineffective, emergency department services and hospital admissions. The duration of cluster headache attacks (mean approximately one hour) makes this treatment impractical in emergency departments; attacks

often end before patients can reach hospital-based oxygen treatment. Furthermore, the common nocturnal timing of attacks, and their high frequency in some patients, makes emergency department treatment infeasible.

Opioid medications are typically ineffective for reducing the pain of cluster headache, but nonetheless carry established risks of dependency, abuse, and addiction. Lack of availability of home oxygen therapy has led to increased prescription of opioids for cluster headache patients. In a recent study, 41% of a cluster headache cohort population was actively prescribed opioids for cluster headache; this cohort was associated with a 3-fold higher incidence of drug dependence compared to a matched control population (Choong et al. *Headache* 2017;57,S3:181).

Unfortunately, there is no safe and effective alternative to oxygen therapy for many Medicare-eligible cluster headache patients. Other available acute therapy options carry clear and serious risks. For example, 6mg subcutaneous sumatriptan is an FDA-approved acute treatment for cluster headache attacks, however it is not approved or proven safe for use more than twice per day, or used daily for weeks on end, which is a common pattern of cluster headache attacks. CMS also limits availability of sumatriptan, to no more than 10 treatments per month. Moreover, Sumatriptan is also contraindicated in the setting of significant risks of cardiovascular ischemia or stroke, which are prevalent among Medicare-eligible patients. Finally, comparative cost analyses indicate that the estimated annual costs of oxygen treatments for cluster headache are typically significantly less than those for sumatriptan (O'Brien et al, *Headache* 2017;57:1416).

The lack of availability of home oxygen for relief from excruciating cluster headache attacks may also lead to patient self-harm; cluster headache is associated with a 20 fold increased risk of suicide. Finally, further financial hardship may fall to low-income Medicare or Medicaid beneficiaries if they have been prescribed home oxygen for cluster headache, but must pay for this out of pocket due to the NCD.

The NCD justifies the denial of coverage of home use of oxygen for cluster headache on the grounds of hypothetical safety risks that are simply not relevant in this setting. Specifically, the NCD cites a "risk of suppression of the hypoxic drive to breathe" in unsupervised COPD patients receiving oxygen therapy. However, such potential physiological effects are only associated with prolonged oxygen exposures not seen with cluster headache treatment. Oxygen therapy when delivered, as indicated, for cluster headache attacks is only deployed intermittently as needed for a maximum of 20 minutes at a time, typically once or twice daily, but up to a maximum of 8 times per day. Whereas, according to a publication cited in the NCD, "100% oxygen at atmospheric pressure is safe if given for less than six hours" (Park JH, et al, *Heart* 2010;96:533.). In other words, the medical literature specifically referenced in the NCD

undermines concerns for a significant safety risk of suppression of hypoxic drive to breath by oxygen therapy when used for cluster headache attacks, as appropriately clinically indicated.

The NCD also cites oxygen therapy as leading to risks of significant tissue damage, such as "blindness and pulmonary fibrosis", that do not apply in this clinical setting. The NCD again cites publications that undermine assertions in the NCD. For example, NCD-cited publications state that "the first signs of toxicity appear after 10 hours of oxygen at 1 ATA [atmosphere]" (Tinits, P, *Ann Emerg Med*. 1983;12:321) and that "100% oxygen can be tolerated at sea level for about 24-48 hours without any serious tissue damage" (Patel et al, *Journal Indian Academy of Clinical Medicine*, 2003; 4:234). This latter publication further mentions toxicity risks from prolonged oxygen that are certainly irrelevant to the situations of Medicare beneficiaries, such as blindness from retrolental fibroplasia (reported almost exclusively in premature infants) or deafness from dysbaric osteonecrosis (reported almost exclusively in astronauts in space). These remote risks of oxygen therapy cited in the NCD should not weigh against the manifest relief from recurrent excruciating pain afforded by the therapy.

Ironically, current CMS Guidelines for Home Oxygen Therapy (ICN 908804; October 2016) actually appear to already cover home use of oxygen for cluster headache, though this is not recognized by CMS. That is, CMS covers home use of oxygen in the setting of "morning headaches", if these symptoms are deemed to be "hypoxia-related". This clinical indication is directly comparable to cluster headache. That is, cluster headache attacks often occur with nocturnal timing, awakening patients from sleep (i.e. "morning headaches"). Cluster headache is also strongly linked to hypoxic mechanisms. Apart from cluster headache attacks being relieved by high-flow 100% oxygen, sleep apnea is associated with hypoxia and has a greater than 8 fold higher prevalence among cluster headache patients.

As a condition of reconsideration of the NCD and instating CMS coverage of home oxygen for cluster headache, the NCD mandated that an approved prospective clinical study be performed to prove the safety of this therapy in a cohort of Medicare eligible patients (Coverage with Study Participation (CSP) form of Coverage with Evidence Development (CED)). This demand presents multiple, almost certainly insurmountable, challenges. Prevalence estimates indicate that fewer than 50,000 Americans with cluster headache are 65 years or older (i.e. Medicare-eligible). That is, cluster headache in the elderly is effectively an "orphan disease". The NCD also mandates that adequate safety assessments be performed in particular patient subgroups of that elderly population that include racial, sex, sexual orientation, ethnic, and socio-economic demographics. Further, for validity, study subjects would likely be excluded from the trial if they had previously received oxygen therapy for cluster headache. A valid trial would also exclude subjects that had significant cardiovascular risks (common among Medicare-eligible patients) since this would contra-indicate the use of subcutaneous sumatriptan, either as rescue therapy

or as a positive treatment control arm. It would be unethical to include a placebo arm in the proposed trial given the availability of a therapy with proven efficacy (i.e. sumatriptan) for these severely painful attacks. Moreover, subjects in this study would need to live sufficiently close to investigator study sites for appropriate study follow-up visits, either scheduled or possibly emergent. This proposed large, diverse, elderly study cohort would then need to be followed longitudinally, for possibly ten years of participation, to generate meaningful long-term safety results. In other words, it would be essentially impossible to identify, recruit, and retain study subjects in sufficient quantity and for sufficient duration for the required study to be successfully executed. Finally, such a safety trial would also likely be exorbitantly expensive to undertake, with no obvious funding mechanism in sight. Did CMS require a similar prospective safety trial before coverage of home oxygen was granted to Medicare beneficiaries with "hypoxia-related" "morning headaches"?

Since 2010, leaders of the American Headache Society, the American Academy of Neurology, AHDA (attached letter), and Clusterbusters (the national cluster headache patient advocacy organization) have appealed to CMS on multiple occasions to instate coverage of home oxygen use for cluster headache. These appeals were uniformly denied.

In May 2014, a number of your US congressional colleagues (Senators Coons, Johaans, Inhofe, Durbin, Fischer, Tester, Ayotte, Warren, Markey, Merkley, Manchin, Pryor, Casey, Carper, Shaheen, and Representative Eshoo) also wrote to then CMS Administrator Marilyn Tavenner to appeal the NCD (letters attached). Administrator Tavenner's response letter to them (6/24/14, attached) indicated that the non-coverage policy of the NCD would continue, with her explanation limited to stating that "no clinical trials involving the home use of oxygen to treat CH have been approved by the Centers for Medicare & Medicaid Services".

On June 1, 2017, Mr. Bryan Shuy, Deputy Chief of Staff for Representative Andy Harris, MD, spoke directly with Dr. James Rollins (Director, Division of Items and Devices, Coverage and Analysis Group, CMS), who was one of the principal authors of the NCD. At that time, Dr. Rollins re-iterated the CMS requirement for new trial safety data, prior to considering reversal of the NCD. We believe that this insistence is contrary to the specific CMS standard for "reasonable and necessary" coverage that Dr. Rollins, himself, has asserted and articulated: "… *a clinically meaningful outcome from the patient's perspective*… [such as a]… *significant improvement in symptoms*". [https://www.youtube.com/watch?v=pDV9ZpVPfak]

Subsequent to Mr. Shuy's (6/1/17) conversation with Dr. Rollins, new clinical data have, in fact, emerged that strongly support reversal of the NCD. Dr. Larry Schor and colleagues at the University of West Georgia are currently preparing data for publication from a retrospective survey of patients diagnosed with cluster headache. Among 61 cluster headache patients aged 65 or older (mean age 70 years old, range 65 to 98 years old) who had used oxygen therapy for

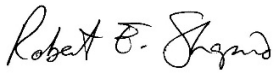
cluster headache attacks (mean 2503 oxygen treatments per respondent lifetime), none had ever experienced any severe psychological, emotional, physical, or medical complications of oxygen therapy. Moreover, 64% of these respondents reported oxygen to be either very or completely effective for acute treatment of cluster headache attacks. While Dr. Schor anticipates submission of these data to a peer-reviewed publication soon, we do not believe that reversal of the NCD should be delayed until publication of this study.

In summary, it is the uniform consensus medical opinion that home use of oxygen for cluster headache is very safe and highly effective. This is beyond dispute. The value of this therapy is not in clinical equipoise. It is therefore unethical for CMS to continue to withhold coverage of this treatment from Medicare and Medicaid patients and place them at continued risk of excruciating pain and risk of the adverse consequences of opioid use.

We respectfully request your urgent review and reversal of the harmful and wholly unjustified NCD that denies coverage of home use of oxygen to treat cluster headache attacks among Medicare and Medicaid beneficiaries.

We would greatly appreciate your careful and timely attention to this request.

Sincerely,



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