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January 3, 2018

Commissioner Scott Gottlieb, MD
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Citizens Petition to Ban Ultra-high Dose Opiates, FDA-2017-P-5396

Dear Commissioner Gottlieb:

The National Comprehensive Cancer Network® (NCCN®), an alliance of 27 leading academic cancer centers in the United States, is dedicated to improving the quality, effectiveness, and efficiency of care provided to patients with cancer. NCCN Clinical Practice Guidelines in Oncology ([NCCN Guidelines®](#)) are the recognized standard for clinical policy in cancer care and are the most thorough and frequently updated clinical practice guidelines available in any area of medicine. As a leading developer of authoritative information regarding cancer prevention, screening, diagnosis, treatment, and supportive care, including the [NCCN Guidelines®](#) for Adult Cancer Pain and Palliative Care, we write today with concern about the recent Citizen Petition to Ban Ultra-high Dose Unit Opioid Analgesics Ultra-high Dose Opiates. We agree with the petitioners that the opioid epidemic is a serious public health issue and must be addressed through comprehensive prevention strategies and treatment access. However, NCCN is concerned that the policy proposed by the Citizen Petition does not include an exemption for patients with cancer and/or patients receiving palliative or hospice care.

The NCCN Guidelines are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. NCCN Guidelines and their derivatives help ensure access to appropriate care, clinical decision-making, and assessment of quality improvement initiatives. Since 2008, CMS has recognized the NCCN Drugs & Biologics Compendium ([NCCN Compendium®](#)) as a mandated reference for establishment of coverage policy and coverage decisions regarding the use of drugs and biologics in cancer care.

The NCCN Guidelines for Adult Cancer Pain and Palliative Care are each developed by a panel of interdisciplinary representatives from 27 leading academic cancer centers in the United States that treat hundreds of thousands of patients with cancer annually. The Guidelines Panel for Adult Cancer Pain identifies principles and best practices in assessing and managing pain in adults with cancer. The NCCN Guidelines Panel for Palliative Care helps ensure that each patient with cancer experiences the best quality of life possible throughout the illness trajectory. The Citizen Petition requests a complete

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Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center

Duke Cancer Institute

Fox Chase Cancer Center

Huntsman Cancer Institute
at the University of Utah

Fred Hutchinson Cancer
Research Center/
Seattle Cancer Care Alliance

The Sidney Kimmel
Comprehensive Cancer
Center at Johns Hopkins

Robert H. Lurie Comprehensive
Cancer Center of Northwestern
University

Mayo Clinic Cancer Center

Memorial Sloan Kettering
Cancer Center

Moffitt Cancer Center

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute

Roswell Park Cancer Institute

Siteman Cancer Center
at Barnes-Jewish Hospital
and Washington University
School of Medicine

St. Jude Children's
Research Hospital/
The University of Tennessee
Health Science Center

Stanford Cancer Institute

University of Alabama at
Birmingham Comprehensive
Cancer Center

UC San Diego
Moores Cancer Center

UCSF Helen Diller Family
Comprehensive Cancer Center

University of Colorado
Cancer Center

University of Michigan
Comprehensive Cancer Center

The University of Texas
MD Anderson Cancer Center

University of Wisconsin
Carbone Cancer Center

Vanderbilt-Ingram
Cancer Center

Yale Cancer Center/
Smilow Cancer Hospital

ban of certain opioid products from the market, which we believe is not in concordance with the NCCN Guidelines for Adult Cancer Pain and Palliative Care and could have substantial and negative quality-of-life implications for patients with cancer and patients receiving palliative or hospice care.

There is increasing evidence in oncology that survival is linked to symptom control and that pain management contributes to broad quality-of-life improvement.¹ Banning these opioids from the market entirely, without creating an exemption for patients with cancer or receiving palliative or hospice care, will create unreasonable hardship for a vulnerable population of patients.

The unique needs of patients with cancer have been recognized in previous opiate restriction policies by both private and public entities. A recent policy to restrict opiate access implemented by CVS Caremark, CVS' pharmaceutical benefit manager, creates an exemption for patients with cancer, in hospice, or palliative care. Additionally, CMS' recent *2019 Policy and Technical Changes to the Medicare Advantage, Medicare Cost Plan, Medicare Fee-for-Service, the Medicare Prescription Drug Benefit Programs, and the PACE Program Proposed Rule* includes a provision to allow Part D sponsors to implement a drug management program to restrict access to opioids. Within this proposal CMS explicitly exempts patients with cancer, in hospice, or in long term care from this requirement. The Center for Disease Control (CDC) recently published *Guidelines for Prescribing Opioids for Chronic Pain* and specifically exempted patients in active cancer treatment, palliative care, or end-of-life care from their guidelines.² These policies spanning the public and private sectors set an important precedent for the exemption of patients with cancer or those receiving palliative or hospice care from policies which would otherwise create barriers to needed supportive care.

Pain Management Needs of Adult Cancer Patients

The NCCN Guidelines for Adult Cancer Pain recommend prescribing patients the lowest possible dose to minimize pain and maximize functioning, while differentiating recommended prescribing between opioid-naïve and opioid-tolerant patients. Opioid-tolerant patients, including patients at end of life, may require opioid dosing that is a hundred-fold or even thousand-fold higher than dosing for an opioid-naïve patient, in order to appropriately manage their pain. For these patients, opioids, which may be considered high-dose to some, are actually a therapeutic and appropriate dose. These

¹National Comprehensive Cancer Network. Adult Cancer Pain Guidelines (Version 2.2017). 2017 Nov-https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf

² Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49. DOI: <http://dx.doi.org/10.15585/mmwr.rr6501e1>

products help to improve their quality of life and comfort at end of life. Moreover, removing products from the market could restrict the tools available to physicians to help patients adequately manage pain as outlined in the NCCN Guidelines.

Patients living with cancer pain already face a number of barriers to accessing appropriate pain management medications. Increasingly, patients may face shortages of opiate medication at pharmacies as they reduce the number of opiates they keep in stock, may be forced to wait several business days as insurance companies require prior authorizations, and may face difficulty traveling to refill their prescription with new laws and regulations in some states limiting treatment duration.

A complete ban on opioids that are a therapeutic dose for opioid-tolerant cancer patients would exacerbate the challenges described above. The additional pills required to replace these products may result in a more regular need for refills due to limits on the number of pills that can be dispensed, increased co-pays and financial burden, and increased prior authorizations and paperwork required by payers. More frequent refills would pose particular challenges for cancer patients in rural areas as pharmacy retailers may not be accessible within a reasonable distance and are less likely to offer a delivery service than in urban and suburban areas. Additionally, studies have found compliance with medication regimens decreases as dosing per day increases, with very little compliance at a greater than four times per day dosing requirement.³ Increased dosing may also interfere with a patient's sleep schedule, further impeding their quality of life. Removing ultra-high dose unit opioids from the market will result in patients having to swallow more pills, leading to a decreased quality of life and decreased compliance with needed pain management medications.

Risk Evaluation and Mitigation Strategies

Although opioids are the principle analgesics for moderate to severe cancer pain, NCCN recognizes that they also pose significant risk to society and, as such, must be prescribed in a responsible manner. In 2013, there were 43,982 drug-poisoning deaths in the United States, including 16,235 that involved opioid analgesics.⁴ Most people who have overdosed on prescription opioids not prescribed to them have been given (not bought or stolen) the opioids from friends or family⁵, indicating a need for greater patient

³Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The Effect of Prescribed Daily Dose Frequency on Patient Medication Compliance. *Arch Intern Med.* 1990;150(9):1881-1884. doi:10.1001/archinte.1990.00390200073014

⁴Hedegaard, H; Chen, LH; Warner, M- Drug poisoning deaths involving heroin: United States, 2000-2013-NCHS Data brief. 2017 Nov <https://www.cdc.gov/nchs/products/databriefs/db190.htm>

⁵National Comprehensive Cancer Network. Adult Cancer Pain Guidelines (Version 2.2017). 2017 Nov https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf

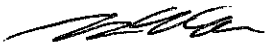
education regarding safe drug disposal, including the significant consequences of drug sharing.

Patients living with cancer, although in need of appropriate pain management, are also at risk for developing dependence on opioids and must be regularly monitored for signs of misuse/abuse. To reduce this risk, the NCCN Guidelines for Adult Cancer Pain recommends the use of state prescription drug monitoring databases, prescribing the lowest possible dose to minimize pain and maximize function, an initial assessment for risk of aberrant use of pain medications, and ongoing monitoring for aberrant drug-taking behaviors. Additionally, the Guidelines discuss the FDA's Risk Evaluation and Mitigation Strategies (REMS) for select opioid products. As discussed in REMS, prescribers should educate patients on the safe use, storage, and disposal of opioid, including community take back programs, as well as the addictive potential associated with opioids to prevent misuse and abuse.

NCCN supports efforts to reduce the risk of opioid addiction while also protecting access to appropriate pain management tools for cancer patients. If the FDA considers implementing the restrictions proposed in the Citizen Petition, we believe there should be an exemption made for patients with cancer and patients receiving palliative or hospice care.

We appreciate the opportunity to respond to this Citizen Petition to the FDA. If the FDA does approve this policy, NCCN respectfully requests that an exemption for patients with cancer and patients in hospice and palliative care be included. To do otherwise is to subject a number of patients with cancer to unnecessary suffering and decreased quality of life. If you have any questions, we would welcome the chance to discuss our comments further and work together to enhance the quality of life of patients with cancer pain while also preventing the misuse and abuse of prescription opioids.

Sincerely,



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