ADAPT PHARMA

The Honorable Orrin G. Hatch
Chairman
Senate Committee on Finance
219 Dirksen Senate Office Building
Building
Washington, DC 20510

The Honorable Ron Wyden
Ranking Member
Senate Committee on Finance
219 Dirksen Senate Office

Washington, DC 20510

Dear Chairman Hatch and Ranking Member Wyden:

Thank you for your February 2nd request for input on the Committee's efforts to address the nation's opioid crisis through actions in the Medicare and Medicaid programs. Adapt Pharma appreciates the opportunity to share our thoughts and ideas with the Committee.

We believe our response to the Committee's solicitation is best captured in Adapt Pharma's February 6, 2018 submission (attached) to the Centers Medicare and Medicaid Services (CMS) in response to their proposed new safety edits for certain high-risk opioid prescriptions. The proposed safety edits would be triggered at the pharmacy and would flag higher risk opioid prescriptions. Where these hard and soft safety edits are flagged and subsequently overridden by either the Medicare Part D Sponsor or the pharmacist, we strongly recommend that CMS require that a FDA approved community-use naloxone product be dispensed to the beneficiary alongside the higher risk opioid prescription as an opioid overdose risk mitigation step. This would rapidly expand naloxone access targeted at highest risk opioids which is a key metric outlined in priority area #2 of the CMS Opioid Misuse Strategy published in 2017.

We make this recommendation for the following reasons:

1. Higher risk opioid prescriptions are associated with a higher risk of opioid overdose. Most opioid overdoses occur at home and many are witnessed. Co-prescribing of naloxone is supported by myriad medical associations and societies, as well as federal agencies such as SAMHSA, FDA and NIDA. And is also recommended by the Centers for Disease Control and Prevention (CDC) in their Opioid Prescribing Guidelines. Indeed, the Comprehensive Addiction and Recovery Act (CARA) includes provisions recommending prescribers follow the CDC Guideline. Unfortunately, due to stigma and low awareness, adoption of this recommendation has been low and at the end of 2017 there were just 8 naloxone prescriptions for every 1,000 higher risk opioid prescription.

2. The Veteran's Administration and two states (Virginia and Vermont) took a more proactive approach and in 2017 required (rather than requested) co-prescribing of

naloxone with higher risk opioid prescriptions and achieved dramatically different outcomes. For example, in Vermont, there are approximately 100 naloxone prescriptions per 1,000 high dose (>90 MME) opioid prescriptions compared to a national average of 15:1,000. Details regarding their success are outlined in our attached letter to CMS.

While States have implemented a wide array of policy responses, Congress and federal agencies are best suited to implement policies nationally, so that all Americans have timely and equal access to potentially lifesaving overdose reversal drugs in the event of an opioid overdose emergency.

As the Committee has oversight of CMS, we strongly recommend the Committee consider directing CMS to require that an FDA approved community-based overdose reversal drug be dispensed alongside higher risk opioid prescriptions, following a soft or hard edit override. In so doing, CMS would be following the guideline that CDC, NIDA and the AMA, amongst many other bodies, have promoted as best practice. The argument is simple, when you provide a beneficiary an opioid prescription associated with an elevated risk of opioid overdose, and a risk mitigation tool (community-use naloxone) exists, shouldn't CMS require it be dispensed as well?

Attached is the recommendation from Adapt Pharma to CMS which details how CMS can make a positive impact by expanding naloxone access for patients who need it most.

We look forward to discussing this with you and providing the evidence-based data which will contribute to the goal of expanding access to naloxone where higher risk opioids are present in Medicare and Medicaid settings.

Sincerely

Mike Kelly

President US Operations

Adapt Pharma Submitted via email to: opioids@finance.senate.gov

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Demetrios Kouzoukas
Principal Deputy Administrator and Director
Center for Medicare

6 February 2018

Docket No. CMS-2017-0163 for "Advance Notice of Methodological Changes for Calendar Year (CY) 2019 for Medicare Advantage (MA) Capitation Rates, Part C and Part D Payment Policies and 2019 draft Call Letter"

Dear Sir,

We write regarding the proposal to implement additional drug utilization review controls for certain opioid prescriptions. Specifically, for 2019 CMS proposes a hard safety edit for high dose opioid prescriptions (>90 MME) and soft safety edits for (i) duplicative long acting opioid therapy and (ii) concurrent benzodiazepine and opioid use.

Recommendation

In situations where a hard or soft safety edit is triggered and overridden by the Sponsor or pharmacist based on medical need, we **strongly recommend CMS to require that a community use naloxone be dispensed alongside the triggering opioid prescription**. This risk-mitigation strategy is recommended by the CDC Opioid Prescribing Guideline as well as multiple other medical associations, societies and federal health agencies.

This initiative would also meet CMS' own Priority Action as set-out in Opioid Misuse Strategy 2016 which states:

> *"Today, when patients are prescribed opioids for long term therapy, the majority are prescribed stool softener medications to help manage a common anticipated side effect: constipation. Respiratory depression, another known side effect with the potential for far more devastating consequences, should be addressed with similarly routine practices.* ***As a first step toward this goal, CMS will need to identify standards to guide automatic co-prescribing of naloxone for patients whose opioid prescription reaches certain thresholds of dose, frequency, and/or duration****."*

In 2015 nearly half of all opioid overdose deaths involved a prescription opioid[1] while approximately 75% of persons who initiated heroin first misused prescription opioids.[2] Consequently, addressing overdose risk associated with prescription opioids is a critical component of the response to the wider opioid overdose crisis.

Adapt Pharma holds the NDA and distributes Narcan® (naloxone) Nasal Spray, the leading community-use, or take-home, naloxone product.

Naloxone co-prescribing is broadly supported but narrowly adopted

Broad support

Clinician co-prescribing of take-home naloxone alongside higher risk opioid prescriptions and to persons at higher risk of opioid overdose is broadly supported. Proponents include multiple health associations and societies including the American Medical Association[3] and the American Society of Addiction Medicine;[4] community based organisations such as Prescribe to Prevent;[5] and federal health organisations such as Substance Abuse and Mental Health Services Administration (SAMHSA) and the Veteran's Administration (VA). Co-prescribing naloxone is recommended by the CDC Guideline for Prescribing Opioids for Chronic Pain (Recommendation 8); the National Academies of Sciences, Engineering and Medicine (NAS) Pain Management and the Opioid Epidemic Report (Recommendation 5-9)[6]; the FDAs Prescriber Education Blueprint, which states "*HCPs should prescribe and discuss the use of naloxone products as a means of avoiding death due to overdose.*" [7]; and the FDA Consumer Update "What to Ask Your Doctor Before Taking Opioids?".[8]

The Vermont Health Department and Virginia Board of Medicine have successfully implemented a requirement for clinicians to prescribe naloxone alongside high dose opioid prescriptions, where there is concurrent benzodiazepines use and to persons at higher risk of opioid overdose.[9,10] As described below, this has led to a very significant expansion in naloxone prescriptions.

Narrow Adoption

Notwithstanding the broad support and encouragement, naloxone co-prescribing has been narrowly adopted. In 2016, 19.8 million opioid prescriptions exceeded 90 MMEs/day, equating to over 9.2% of all opioids prescriptions.[11] In contrast, according to IMS Health prescription data, naloxone prescriptions approximate just 337,000 (Jan-Dec 2017), or a ratio of approximately 15 naloxone prescriptions to every 1,000 high-dose (>90 MME) opioid prescriptions. In stark contrast, the ratios in the two states (Virginia and Vermont), which require clinicians to co-prescribe naloxone alongside higher risk opioid prescriptions, are multiple folds higher than this ratio[12]. This suggests that if naloxone prescribing was a required prescribing intervention, many more 'at-risk' individuals receiving higher risk opioid prescriptions would be dispensed naloxone. Published literature suggests this low level of adoption reflects stigma and low awareness.

Successful models and potential ancillary benefits

Vermont and Virginia implemented new rules in 2017 requiring naloxone prescribing with higher-risk opioid prescriptions and to at-risk persons. These policies have demonstrated that

such a requirement is both feasible and successful in expanding naloxone access. For example, in Vermont, there are approximately 100 naloxone prescriptions per 1,000 high dose (>90 MME) opioid prescriptions compared to a national average of 15:1,000. The higher risk opioid dose thresholds in Vermont and Virginia are 90 MME/day and 120 MME/day, respectively.

Co-prescribing naloxone has also been associated with ancillary benefits. A pilot naloxone co-prescribing intervention study funded by National Institute on Drug Abuse and published by Dr Phil Coffin demonstrated that opioid patients who received a naloxone prescription had 47% fewer opioid related emergency department visits per month in the 6 months after receipt of the prescription and 63% fewer visits after 1 year, compared with patients that did not receive naloxone.[13] The VA implemented a system wide opioid initiative, including naloxone prescribing broadly consistent with the CDC guideline, and achieved a 26% drop in VA patients prescribed opioids, 60% reduction in opioid/ benzodiazepines and a 40% reduction in veterans on long term opioid treatment.

Such a safety edit would not be unduly burdensome as it could be implemented using existing prescribing, distribution and reimbursement channels. Moreover, by targeting the requirement at those opioids that carry the greatest risk of overdose, the requirement would be commensurate with the serious identified risk. Additionally, such an initiative would be affordable: Narcan Nasal Spray is affordably priced at Wholesaler Acquisition Cost of $125 for a carton of two doses (before rebates), has extensive insurance coverage (94% of covered lives have access to Narcan Nasal Spray[14]) at affordable co-pays (77% of dispensed prescriptions had a co-pay of $10 or less[15]).

In closing, in situations where a hard or soft safety edit is triggered and overridden by the Sponsor or pharmacist based on medical need, we **strongly recommend CMS to require that a community use naloxone be dispensed alongside the triggering opioid prescription**.

Pilot studies and state level experience in Vermont and Virginia highlight the feasibility and success of such an intervention. The continuing loss of life underscores the urgency to act.

Sincerely

Seamus Mulligan

Chairman and CEO

Adapt Pharma

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1 Source CDC. Accessed October 2017 at https://www.cdc.gov/drugoverdose/index.html

[2] Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. N Engl J Med 2016;374:154–63.

[3] Help save lives: Co-prescribe naloxone to patients at risk of overdose. Accessed October 2017 at: chrome-extension://oemmndcbldboiebfnladdacbdfmadadm/https://www.end-opioid-epidemic.org/wp-content/uploads/2017/08/AMA-Opioid-Task-Force-naloxone-one-pager-updated-August-2017-FINAL.pdf

[4] Public Policy Statement on the Use of Naloxone for the Prevention of Opioid Overdose Deaths. Accessed October 2017 at: chrome-extension: //oemmndcbldboiebfnladdacbdfmadadm/https://www.asam.org/docs/default-source/public-policy-statements/use-of-naloxone-for-the-prevention-of-opioid-overdose-deaths-final.pdf?sfvrsn=4

[5] Website Accessed October 2017 at: http://prescribetoprevent.org/

[6] Report on Pain Management and the Opioid Epidemic (Recommendation 5-9). Accessed October 2017 at: chrome-extension: //oemmndcbldboiebfnladdacbdfmadadm/https://download.nap.edu/cart/download.cgi?record_id=24781

[7] FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain. Accessed October 2017 at: Chrome-extension: //oemmndcbldboiebfnladdacbdfmadadm/https://www.fda.gov/downloads/Drugs/NewsEvents/UCM557071.pdf

[8] FDA Consumer Update "What to Ask Your Doctor Before Taking Opioids?" Accessed October 2017 at: https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm529517.htm

[9] Virginia Board of Medicine Regulations Accessed October 2017 at: http://townhall.virginia.gov/l/ViewXML.cfm?textid=11462

[10] Vermont Department of Health Rule Governing the Prescribing of Opioids for Pain Accessed October 2017 at: chrome-extension: //oemmndcbldboiebfnladdacbdfmadadm/http://www.healthvermont.gov/sites/default/files/documents/pdf/REG_opioids-prescribing-for-pain.pdf

[11] CDCs 2017 Annual Surveillance Report of Drug Related Risks and Outcomes. Accessed October 2017 at:chromeextension://oemmndcbldboiebfnladdacbdfmadadm/https://www.cdc.gov/drugoverdose/pdf/pubs/2017-cdc-drug-surveillance-report.pdf

[12] Calculated as annualized naloxone state level prescription data post co-prescribing introduction per IMS Health NPA Extended Insights Audit as a ratio of state level high dose opioid prescriptions in 2016 per CDCs 2017 Annual Surveillance Report of Drug Related Risks and Outcomes. Accessed October 2017. For Virginia the ratio of 120MME:>90MME opioid prescriptions was estimated based on CMS data included in Analysis of Proposed Opioid Overutilization Criteria Modifications in Medicare Part D available at https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Revised-OMS-Criteria-Modification-Analysis.pdf

[13] Coffin et al. Annals of Internal Medicine August 2016 Nonrandomized Intervention Study of Naloxone Coprescription for Primary Care Patients Receiving Long-Term Opioid Therapy for Pain Accessed October 2017 at https://www.ncbi.nlm.nih.gov/pubmed/27366987

[14] MMIT Formulary Analytics

[15] IMS Health NPA Extended Insights Audit Jan – Nov 2017