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I. Introduction

Thank you Mr. Chairman. My name is Eric Ketcham, M.D., F.A.C.E.P., and I am an Emergency Department Medical Director, an EMS Medical Director, a Medical Director for an Opioid Addiction Treatment Clinic, and the Immediate Past-President of the New Mexico Chapter of the American College of Emergency Physicians (ACEP). On behalf of the 37,000 members of ACEP, I would like to thank you for this opportunity to testify today about the high and rising prices of two medications, buprenorphine and naloxone, critical to the treatment of opioid addiction and overdose, respectively. The unnecessarily high price attached to these medications increases the cost of healthcare, and reduces patient access to these medications. The pricing of these medications by several pharmaceutical companies obstructs access to treatment for opioid addiction and overdose in America, and thus prolongs the scourge of heroin and prescription opioid addiction, and puts American lives at risk.

The United States currently faces a steadily growing crisis of opioid abuse and addiction that has reached epidemic proportions. According to the CDC, for the year 2013:

> "The total economic burden is estimated to be $78.5 billion. Over one third of this amount is due to increased health care and substance abuse treatment costs ($28.9 billion). Approximately one quarter of the cost is borne by the public sector in health care, substance abuse treatment, and criminal justice costs."[1]

Furthermore, more Americans have died each year during the past decade from drug overdoses than motor vehicle accidents.[2] In 2014, more than 28,000 Americans died of opioid overdoses alone.[3] This opioid abuse epidemic claims the lives of more than 78 Americans every day.[3]

We could endlessly debate the factors that have contributed to the rise of this widespread and deadly epidemic in America, and how best to curb its growth. However, today we must focus on two unique, specific treatments for this epidemic.

First, use of buprenorphine, which should be a low-cost medication, ought to be expanded so that more Americans could be successfully treated for the affliction of opioid dependence. These treatments would help alleviate a great burden on society by ameliorating crime, incarceration and healthcare expenses, including complications from intravenous drug use (HIV, Hepatitis C, infections, etc.), but most important, access to buprenorphine means more potentially deadly overdose deaths could be avoided.

Second, access to naloxone, which also should be a low-cost medication, must be increased. This is truly a life-saving drug that when used properly can reverse opioid overdoses and save lives.

Congress must ensure that buprenorphine, and buprenorphine/naloxone combination medications are affordable as prescriptions. Congress must also act to ensure naloxone is widely available and affordable for EMS and law enforcement agencies, as well as for patients and their caregivers.

II. Buprenorphine

Buprenorphine was developed in 1966 for the purpose of treating opioid dependence, but was first licensed, however, as an effective analgesic for severe pain.[4] The injectable form was licensed in Europe in 1978 and the oral dissolvable (sublingual) form followed in 1982.[4] By 1985, buprenorphine was licensed in 29 countries and was approved by the U.S. Food and Drug

Administration (FDA) the same year.[4] Although this medication was originally researched and developed for the purpose of treating opioid addiction, it was not successfully brought to market for this indication until 1996 when France implemented an off-label program of medication assisted treatment (MAT) for heroin addiction.[4,5] The results in France were astounding:

- The incidence of deaths from heroin overdoses dropped dramatically (by 2004, deaths from heroin overdoses had dropped over 80%) and
- The rate of HIV transmission through injection drug use (IDU) dropped by 50%.[5]

This dramatic success inspired the original developer of the medication, Reckitts Benckiser Pharmaceuticals, to return to its pursuit of licensing buprenorphine for the treatment of opioid addiction.[4] In 2002, the manufacturer obtained FDA approval for both the mono-agent buprenorphine (*Subutex*) and the combination medication buprenorphine/naloxone (*Suboxone*).[4]

Buprenorphine is an opioid medication known as a "partial agonist" and as an "agonist-antagonist." Essentially, this means that, similar to opioids, buprenorphine produces effects such as euphoria or respiratory depression. However, with this medication these effects are weaker than those of normal opioids such as heroin and methadone.[6]

Because of these properties, and even though it has an analgesic potency 25 times greater than morphine, there is a ceiling limit to its adverse effects.[4,7,8,9] With the exception of small children, buprenorphine causes only limited respiratory and central nervous system depression. When properly prescribed, this medication is a very safe alternative to methadone and thus can be effectively utilized to treat opioid abuse and addiction by a variety of physicians in a variety of

settings, as opposed to methadone, which must be administered in a licensed opioid addiction treatment clinic.[4,10,11,12]

One would think that a life-saving and life-transforming medication such as buprenorphine, which has a well-established safety profile as well as generic equivalents, would be accessible by hundreds of thousands more opioid dependent patients. Unfortunately, that is not the case.

Although access to buprenorphine can be diminished due to a shortage of properly trained physicians, many patients are unable to access this medication simply based on cost. Even more distressing, the cost of the generic version has more than doubled during the last six months, even though there are now multiple generic producers of buprenorphine.

Surveying local pharmacies in northwest New Mexico (all from national pharmacy chains), the wholesale price paid by the pharmacy for generic 8mg buprenorphine sublingual tablets recently increased from $2.37/tablet to $5.57/tablet. Most opioid dependent patients are treated with two tablets daily, and thus a 30-day supply costs $334.20. Although the pharmacies are providing this medication to the patients at near cost, with a margin of less than 2% (to cover the cost of packaging), if the uninsured or underinsured must also pay to see the prescribing physician, then for many this becomes unaffordable and many prescriptions go unfilled.

For Medicaid beneficiaries, that program is paying the full retail price and state Medicaid budgets are bearing a substantial burden trying to cover each patient's regular monthly supply of buprenorphine at an annual cost of more than $4,000 each. Many opioid addicted patients truly are safer if prescribed the combination medication of buprenorphine/naloxone (e.g. Suboxone,

Zubsolv, Bunavail) because it reduces the likelihood of injecting the medication rather than taking it sublingually. This is concerning, because, as of this week, in northwest New Mexico pharmacies, the average wholesale price (AWP), which is similar to the average retail price, for 8mg/2mg buprenorphine/naloxone (Suboxone) oral film strips is now up to $8.67 each, or $532.08 for 60 tablets (a 30-day supply). There are, however, "manufacturer coupons" sometimes available on-line, or from the pharmacy, to reduce this price by $50. Interestingly, however, the prices of the three brand names (Suboxone, Zubsolv, and Bunavail) at equipotent doses are all about the same, and after coupons, end up at roughly $470 (30-day supply).

Shockingly, the generic versions of Suboxone (buprenorphine/naloxone) tablets cost even more than the brand name prescriptions, despite the fact that it's a generic formulation and there are multiple manufacturers; this week they cost approximately $10.42 a tablet ($625.28 for a 30-day supply).

The high cost of buprenorphine, combined with the shortage of licensed prescribing physicians and the high rate of uninsured or underinsured individuals who are in need of this medication, has led many to turn to the "secondary market" for illegally diverted opioid addiction medications.[13,14] For the vast majority of opioid-dependent patients, whether addicted to heroin or prescription opioids (whose chronic pain and/or dependence is not managed by a physician or other healthcare provider), much of their life is spent securing the next supply, which might only be for the day, of heroin, oxycodone, etc. Rarely do these patients experience a "high," or state of euphoria.[13] The need to continue using heroin or other opioids is to avoid the extremely miserable condition of acute opioid withdrawal (abdominal pains, vomiting, diarrhea, severe

muscle cramps, tremor, twitching, headaches, dysphoria, and sometimes seizures).[12] Acute opioid withdrawal puts patients with certain underlying medical conditions (e.g. insulin dependent diabetes, epilepsy, heart failure) at particular risk of critical illness or death.

However, buprenorphine does not provide any significant euphoria even for those individuals who have never taken it before. As most addiction medicine physicians will attest and recent research supports, most patients who obtain buprenorphine on the secondary market do so simply for the purpose of self-managing their addiction.[12,13] Currently, in northwest New Mexico, the street price of buprenorphine is similar to the retail prices described earlier, usually marked up 50% or less above these current prescription prices.

III. Naloxone

Naloxone was patented over 55 years ago and approved for the treatment of opioid overdose by the FDA in 1971. Naloxone is on the World Health Organization's list of essential medicines, and thus is regarded as a medication necessary to the most basic health system. This medication can be administered intravenously, intramuscularly or intranasally and is effective within minutes. The response can be profound, literally producing a "Lazarus-like" effect. Victims of opioid overdose often completely stop breathing and without respiratory support death is imminent. However, after the prompt injection of naloxone, the victim begins to breathe again and may quickly become fully conscious, rescued from the edge of death.

Naloxone has been utilized in hospitals and by fire and EMS personnel for decades. In some communities where there has been a particularly high rate of opioid overdoses, law enforcement personnel carry naloxone in order to administer the medication while waiting for EMS to arrive, thus saving minutes and saving lives.

Recognizing the steady growth of opioid abuse and addiction in many communities around the country, there has been a movement, supported by the medical community, to further expand patient access to naloxone directly.[15] Some hospitals and clinics have begun to dispense naloxone kits to patients at risk of overdose and more physicians are writing prescriptions for at-risk patients to have naloxone kits available at home. In some regions, it is now legal for patients to purchase naloxone directly from a pharmacy, even without a prescription.[16]

While there has been a movement to increase prompt access to naloxone for opioid overdose victims over the last several years, the price of naloxone in nearly all forms of packaging has been steadily climbing in this country. Although the price of a pre-loaded 1 ml syringe of 0.4mg/ml of naloxone in India has risen to 78 Rupees (roughly $1.17 U.S.), the price of the same dose and concentration of naloxone in a single dose syringe device (carpuject) in northwest New Mexico has risen from approximately $12 in 2012 to ~$30 in 2016.[17] Without a hospital or municipal volume discount for a fire or EMS service, the Amphastar Inc. produced preloaded 2mg in 2ml syringe product (requires a fairly basic three-part assembly) used by many fire and EMS services is now priced at approximately $49/dose and has risen incrementally from approximately $17/dose in 2014 (and was reportedly about $1/dose in 2001).[18]

Given the increasing incidence of opioid overdoses, some of which are massive overdoses (e.g. from heroin contaminated with fentanyl or other drugs that are much more powerful than standard opioids) that require much more than 0.4mg, or even more than 2mg, of naloxone to successfully resuscitate an opioid overdose victim, fire and EMS services are now having to pay much closer attention to naloxone in their pharmaceutical budget. The consequence of these rising prices may force naloxone out of the budget for the rural fire or EMS service that doesn't have the buying power of a hospital or larger municipal agency.

Furthermore, while lawmakers and the medical community have been making progress in expanding access to naloxone through education and focused naloxone program implementation, much of this targeted access remains significantly theoretical as naloxone products designed for the layperson are the most expensive of all naloxone formulations. For example, the cash price for the 4mg nasal spray product produced by Adapt Pharma has increased to $150 for the package of two nasal sprays in northwest New Mexico.[17],[19] The device certainly doesn't present any form of revolutionary technology and it includes a generic, and until recently, very inexpensive medication.

While the price of the Adapt Pharma product is cost prohibitive for individuals and outreach programs alike, it is the *Evzio* naloxone auto-injector product (built on the same basic technology of the *Epi-Pen* epinephrine auto injector), produced by Kaleo, Inc. that is truly astounding.[17,20] This product only includes 0.4mg per dose, which again may be insufficient as a rescue dose for many opioid overdoses, yet a two-pack of these devices is currently priced at $4,500.[17,19] It has

been reported that the cost of this device for EMS and law enforcement agencies is around $250 per two-pack, but this rate is significantly subsidized by federal grants.

There are also reportedly "patient-assistance programs" to help make the product affordable with commercial health insurance.[17,19] However, when I attempted to fill a prescription for this product; I was denied coverage even though I have a premium level employer-provided health insurance plan, with robust pharmaceutical coverage.

It must be noted that while ACEP applauds the great efforts to move naloxone closer to more patients at risk of overdose, with the concept of making naloxone an over-the-counter medication, we must acknowledge that there are several additional concerns and potential consequences related to this course of action, which must be carefully considered. First, unlike using an epinephrine auto-injector, almost no one ever saves his/her own life with naloxone. If not administered by EMS or law enforcement personnel, then naloxone must be administered by a bystander who could be a complete stranger, but who is more likely to be a friend, family member, or an off-duty EMT, nurse or physician. To rescue someone from a potential deadly opioid overdose, one must take action quickly and decisively, often with incomplete information.

For this reason, it is imperative that any directives or legislative efforts to expand naloxone to the public are accompanied by robust public education programs to improve the chances of correct patient selection and proper naloxone administration. Likewise, to encourage and ensure bystanders are not penalized for making a good faith effort to save someone's life, there must be an expansion of Good Samaritan laws because there are many other conditions that could cause

someone, including individuals who are opioid dependent, to be unconscious that are unrelated to an opioid overdose. If an opioid-dependent patient is not suffering from an acute overdose, but rather another condition, a dose of naloxone could force that patient into a state of acute opioid withdrawal and actually make the patient sicker despite the good intentions of the bystander administering the naloxone. The potential associated liability for placing individuals at risk for such an adverse event could certainly cause many physicians to be hesitant to prescribe naloxone kits for their patients.

Lastly, it cannot be emphasized often enough that the administration of a patient's naloxone auto injector or nasal spray empties the device and the device cannot be reused. The potential danger is that the opioids the patient overdosed on may have a much longer half-life than the naloxone administered to the patient. Thus, as the naloxone wears off, the patient may be at the same risk of relapsing into a deadly overdose. As advocates of patient safety, ACEP strongly recommends that whenever naloxone is administered by a bystander to treat an opioid overdose, EMS must be called. Ideally, any patient suffering from an opioid overdose should be evaluated in an emergency department.

IV. Conclusion

We are in the midst of an epidemic of opioid abuse and addiction that will take the lives of more than 28,000 Americans this year and keep many more Americans disabled. To help avert this tragedy, Congress first must act to ensure that buprenorphine, and buprenorphine/naloxone combination medications are affordable as prescriptions. Congress must also act to ensure access to naloxone is affordable and widely available to EMS and law enforcement agencies, as well as to patients and their caregivers who receive appropriate education and training. Finally, as we

push forward to make naloxone more readily available to patients, Congress must address the need for more robust patient and public education along with liability limitations for Good Samaritans and the prescribing physicians seeking to contain this disease. Thank you again for this opportunity to testify before your committee on these important issues.

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