Attachments—Additional Questions for the Record

Subcommittee on Health
Hearing on
"Improving Safety and Transparency in America's Food and Drugs"
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The Honorable Ann Kuster (D-NH)

Dr. Chua, in 1994 the FDA granted Subutex, commonly known as buprenorphine, orphan drug status even though opioid use disorder is not a rare disease. Your testimony described Sublocade's orphan approval as an abuse of orphan drug policy, but also a catastrophe in the treatment of opioid use disorder.

1. Can you detail how the cost of buprenorphine is a barrier to opioid use disorder treatment, and how the gaming of the orphan drug act has contributed to that prohibitive cost

   Thank you for the opportunity to address these excellent questions. There are two main ways in which high prices can impede access to buprenorphine-based treatment of opioid use disorder. The first is that high prices may prompt insurers to not cover buprenorphine drugs or to enact barriers such as prior authorization. Some insurers, for example, refuse to cover Sublocade due to its high price.

   The second is that high prices can increase the amount that patients have to pay out-of-pocket. For example, when insurance plans have deductibles for prescription drugs, patients often have to pay the full list price of drugs until they meet the deductible. Even after the deductible is met, patients often have to pay a percentage of a drug's price through co-insurance. Recently, we analyzed out-of-pocket spending for buprenorphine among a national sample of privately insured patients with opioid use disorder (https://www.healthaffairs.org/do/10.1377/hblog20200302.846103/full). In this analysis, we found that patients paid an average of $48 every time they filled a Suboxone prescription and $101 every time they had a monthly injection of Sublocade. This substantial out-of-pocket spending suggests that the high prices charged for buprenorphine products may deter initiation of buprenorphine treatment and/or adherence to treatment.

   The question regarding how orphan drug policy has contributed to the high prices of buprenorphine products is an important one. U.S. drug prices are strongly correlated with

market power. When there is a monopoly with no competitors, drug companies can charge whatever the market will bear. The 1994 orphan drug designation for Subutex and Suboxone, coupled with their 2002 orphan approvals under these designations, effectively gave their sponsor Reckitt-Benckiser a monopoly by providing seven years of orphan drug exclusivity. During this period, no competitors were able to make an alternative version of Subutex or Suboxone to treat opioid use disorder. Both of the 1994 designations for Subutex and Suboxone were granted via the "cost-recovery" prong because the drugs supposedly had limited sales potential, but both drugs ultimately had strong sales – particularly Suboxone.

Indivior's Sublocade was grandfathered Subutex's orphan drug designation upon approval in 2017. Consequently, Sublocade was entitled to orphan drug exclusivity. Had this exclusivity been granted, competitors would have been blocked from marketing alternative buprenorphine products to treat opioid use disorder until 2024, thus allowing Indivior to charge high prices for a prolonged period. Fortunately, because FDA revoked Subutex's designation, Sublocade is no longer eligible for orphan drug exclusivity, and competing buprenorphine products will now be able to enter the market in December 2020 (including Braeburn Pharmaceutical's extended-release buprenorphine injection product, Brixadi). Based on prior experience, the entry of competitors should decrease prices for extended-release buprenorphine products, facilitating access to buprenorphine-based treatment of opioid use disorder.

One of the greatest challenges associated with medication assisted treatment in the criminal justice setting has been the fear of diversion. Subutex and Suboxone were tablets placed under the tongue, while newer, extended release formulations by another company could not enter the market due to the monopoly established by the gaming of the Orphan Drug Act.

2. Dr. Chua, how might the entrance of new formulations of buprenorphine improve treatment in vulnerable populations?

   This is a very important question. There are two major advantages of extended-release buprenorphine products. The first is that they can increase adherence to treatment. Most buprenorphine products must be taken daily. In contrast, Sublocade is given monthly, and Braeburn's Brixadi is given either weekly or monthly. For some patients, it will be easier to receive an injection in an office every week or every month than to remember to take buprenorphine every day.

   The second advantage is that extended-release buprenorphine products stay in the provider's office, making them hard to divert. In contrast, immediate-release buprenorphine products such as Subutex and Suboxone are in the patient's possession. While the majority of patients do not divert buprenorphine, increased reliance on extended-release buprenorphine products and decreased reliance on immediate-release products could decrease the risk of diversion among the few patients who engage in this behavior.

3. And is the legislation that we considered at this hearing effective in closing the loophole that has prevented other companies from entering the market with new formulations?

   Yes. HR 4712 and its companion bill in the Senate would permanently close the loophole that allowed Sublocade to become an orphan drug. Under the legislation, sponsors of a new drug who apply for orphan approval under a previously granted cost-recovery prong designation would have to prove there is no reasonable expectation *at the time of approval* that the lifetime sales of the new drug would be sufficient to recover development and production costs. Under current policy, Indivior theoretically could develop a new formulation of buprenorphine-naloxone (Suboxone) and automatically obtain orphan approval under Suboxone's 1994 cost-recovery prong designation, just as it did for Sublocade under Subutex's cost-recovery prong designation. If the bills were enacted, Indivior would have to argue that the new formulation of Suboxone was unlikely to be profitable, but this would be challenging because Suboxone is a blockbuster drug with billions of sales to date.

   Additionally, HR 4712 and its companion bill in the Senate would permanently block the possibility of Sublocade receiving orphan drug exclusivity even in the event of successful litigation by Indivior. Within 60 days of the legislation's enactment, sponsors of orphan drugs approved under a prior cost-recovery prong designation would be required to submit cost-recovery analyses proving that there was no reasonable expectation at the time of approval that lifetime sales of the drug would be sufficient to recover development and production costs. Under current policy, if Indivior successfully sues FDA for revoking Subutex's orphan drug designation, Sublocade would again be entitled to orphan drug exclusivity. If the bills were enacted, Indivior would not receive exclusivity for Sublocade unless the company could argue that the drug was unlikely to be profitable based on data available at the time of approval in November 2017. Such an argument would be difficult to make, as Indivior projected in February 2018 that Sublocade's peak annual sales would exceed $1 billion.