RE: Orphan Drug Exclusion from the "Line Extension" Rebate

Dear Mr. Coster:

We are writing to encourage the Centers for Medicare and Medicaid Services (CMS) to revise its proposed rule on Medicaid “line extension” rebates, and exclude orphan drugs from the scope of this policy. This discretionary decision would greatly encourage the development of new treatments for rare diseases, while maintaining the intent and appropriate scope of the line extension rebate. As CMS promulgates its final rule, the agency clearly has the discretionary authority to reinstate the orphan drug exclusion as a reasonable agency interpretation of the clear congressional intent underlying the provision.

As you know, section 2501(d) of the Affordable Care Act authorizes an additional Medicaid rebate to be imposed on line extension products. Congress intended this provision to prevent manufacturers from resetting their Average Manufacturer’s Price (AMP) to avoid the statutory inflation-based rebate described in section 1927(c)(2) of the Social Security Act by making a "slight alteration" to an existing product, such as creating an extended-release formulation. The provision defines the term “line extension” as “a new formulation of the drug, such as an extended release formulation.”

The legislative history of the provision establishes that Congress was targeting a very narrow subset of drugs and enacted it to ensure that a new formulation that is simply a “slight alteration” or “minor change” made by a single manufacturer to an existing covered outpatient drug is still subjected to a form of the inflation penalty rebate under the Medicaid Drug Rebate Program.

2 See, e.g., K Mart Corp. v. Cartier, Inc., 486 U.S. 281, 291 (1988) (courts should look “to the particular statutory language at issue, as well as the language and design of the statute as a whole” in order to ascertain statute’s “plain meaning”).
4 Congressional Budget Office, Budget Options Volume 1: Health Care 143 (2008).
It is well understood that Congress acted to prevent such manufacturers from circumventing the intent and operation of the Medicaid Drug Rebate Program.

It is just as well established that treatments against rare diseases were never an intended target of the line extension policy. Congress explicitly exempted orphan drugs from this provision under the Affordable Care Act; however, this exemption was repealed as part of a broader restatement of the provision in question under the Health Care and Education Reconciliation Act.\(^6\) The repeal of the orphan drug exemption was unintended and wholly collateral to Congress’ reversal in the reconciliation bill to earlier House language, which was adopted in order to limit the scope of the policy to oral solid dosage form drugs.\(^7\)

We strongly encourage you to restore the exemption in the final rule in order to ensure that Medicaid beneficiaries suffering from rare diseases retain access to life-saving therapeutic choices. The current CMS interpretation creates an economic barrier that is contrary to stimulating orphan drug development, which is in critical need of additional therapies for many devastating orphan diseases. Abiding by Congress’ original intent to exclude orphan drugs, and target extended-release and similar drug products, would greatly improve the prospects for new cures and treatments for rare diseases, which together they affect nearly 30 million - or almost 1 in 10 - Americans. In the face of significant economic barriers to innovation, only a few hundred of the nearly 7,000 rare diseases currently have FDA-approved therapies.

Because rare diseases affect such small patient populations, a significant share of the innovation in orphan drugs is upon the basis of previously approved drugs.\(^8\) For example, both the Food and Drug Administration (FDA) and National Institutes of Health (NIH) are pursuing a drug repurposing initiative intended to facilitate development or improvement of treatments for rare diseases that lack an FDA-approved treatments as well as improvements to existing rare disease therapies.\(^9\) Yet the 2012 proposed rule would even apply the line extension rebate to orphan drugs where the manufacturer of the FDA-approved, 'line extension' orphan drug is different from, and has no commercial relationship with, the manufacturer of the original drug. This is clearly an unintended consequence, and unjustifiable,

Moreover, in sharp contrast to the “slight alterations” or “minor changes” targeted by Congress in the line extension rebate, FDA approves orphan drugs that are the same drug for the same disease as a previously approved drug only upon a finding of clinical superiority to the earlier drug. For example, FDA has determined under its orphan drug policies that extended release cy steamine bitartrate capsules and extended release hydrocortisone tablets to be the “same” drug as the previously approved immediate release versions, and consequently subject to the standard of

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\(^7\) See HCERA § 1206.

\(^8\) A. Kesselheim et al. "The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs." Health Aff (Millwood). 2015 Feb;34(2):286-93. ("Nine of the twenty-six (35 percent) [drugs approved by the Food and Drug Administration between 1984 and 2009 that were judged by expert physicians to be transformative] were repurposed from products developed for other indications, and ten (38 percent) were developed for rare diseases before much broader applicability was found.")

clinical superiority. Yet the 2012 proposed rule would even apply the line extension rebate to these orphan drugs.

We are deeply concerned with the Agency’s proposed rule, which expressly includes orphan designated and approved drugs in the scope of the line extension rebate. By proposing a policy that is inconsistent with congressional intent and the clinical significance of many orphan drugs, the regulation would inadvertently but detrimentally affect the development of significant new medicines for millions of American patients with life threatening and debilitating rare diseases, including thousands of Medicaid beneficiaries nationwide. For this reason, consistent with congressional intent, we ask that CMS use its discretionary authority to expressly exempt orphan drugs from the line extension rebate.

We appreciate your attention to this matter of importance to Americans with unmet medical needs, and look forward to your response.

Sincerely,

Jeff Larimore, President, Cystinosis Research Network

Kym Kilbourne, Vice President of Patient Advocacy, Global Genes

Paul Melmeyer, Associate Director of Public Policy, National Organization for Rare Disorders (NORD)

Jay Greissing, Director, U.S. Government Relations and Public Policy, Shire