Qualifying Single Source Drug Policy and Incentives for Post-Approval Innovation

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Executive Summary

In June 2026, the Centers for Medicare & Medicaid Services (CMS) proposed a rule that would change how medicines are grouped for Medicare price negotiation. [1]
The proposed rule would group certain fixed-dose combination products with older medicines that share their active ingredients. The group would be considered one "qualifying single source drug" (QSSD), making all drugs in the group eligible for price negotiation at the same time as the oldest drug. If the group is selected for negotiation, a newer combination therapy could become subject to a negotiated price on an older medicine's timetable, rather than its own.

CMS intends to prevent companies from evading price negotiation by introducing minor product changes -- a legitimate concern. However, its proposal does not adequately distinguish such changes from combinations that require substantial new research and provide meaningful benefits to patients -- for example, replacing lengthy intravenous infusions with less burdensome injections. If genuinely beneficial medicines face earlier exposure to price negotiation, developing them could become less viable.

This tension illustrates a challenge facing CMS that extends far beyond the proposed rule. Medicare has an obligation to secure fair prices for medicines, and the program's QSSD groupings are intended to fulfill that obligation by streamlining price negotiations. However, the program also serves many patients who are waiting for new and better treatments. As such, CMS has a responsibility to ensure its QSSD policies preserve incentives for valuable post-approval innovation, including not only fixed-dose combinations but also post-approval indications and other forms of follow-on innovation.

CMS should reconsider its proposed fixed-dose combination policy and develop a targeted standard that accounts for additional research, patient benefit, and the risk of circumvention. It should work with the FDA and Congress to ensure separate price

negotiation treatment and strong incentives for meaningful post-approval innovation. These changes would prevent gamesmanship in price negotiation while promoting the continued development of improved treatments and new uses for existing medicines.

Background: The CMS Grouping Rule

Under the Inflation Reduction Act, small molecule drugs generally become eligible for Medicare price negotiation seven years after FDA approval under a new drug application (NDA), while biological products become eligible eleven years after licensure under a biologics license application (BLA). After factoring in expenditure rankings, competition, exclusions, and other statutory provisions, CMS then selects a certain number of eligible drugs each year and negotiates Maximum Fair Prices (MFP), which take effect in a later year. [2]

Importantly, CMS does not treat every FDA-approved product as a separate qualifying single-source drug (QSSD). It generally groups different dosage forms and strengths that share an active moiety and NDA holder, even when they have separate NDAs, and uses the earliest applicable approval date to calculate the entire group's eligibility for negotiation. This grouping process does not account for whether or not the grouped medicines are therapeutically interchangeable. [3]

In August 2026, in Teva Pharmaceuticals v. Kennedy, the D.C. Circuit Court of Appeals upheld CMS's grouping of Austedo and Austedo XR, an extended-release product approved under a separate NDA. The decision reinforces that a new application number alone does not entitle a manufacturer to a new negotiation clock. However, it does not resolve how QSSD groupings should account for more substantial therapeutic differences. [4]

The 2029 Proposal and Its Reach

In June 2026, CMS published a proposed rule that would expand QSSD aggregation beginning in 2029 for certain fixed-dose combination products. Under proposed § 429.125(b)(4)(i), when products share the same NDA or BLA holder, and an added component enables a different route of administration for the shared active components, CMS could group the combination with the older product. As an example, the agency cites hyaluronidase, which can enable subcutaneous delivery of medicines previously administered intravenously. [1]

The proposed rule marks a significant departure from current policy, under which fixed-dose combination products with different sets of active ingredients are generally considered separate QSSDs. CMS argues that its new approach would close a loophole by preventing manufacturers from introducing a drug with a slightly altered delivery mechanism simply to avoid price negotiation.

However, the proposed rule also risks sweeping in delivery innovations that provide meaningful benefits to patients. CMS states that it recognizes the value of clinical improvements in its price negotiation calculations. Still, the proposed rule could deprive new combination products of valuable time on the market prior to negotiation, which would inevitably change incentives for investment.

How the Proposal Could Weaken Innovation Incentives

The proposal would change investment incentives by allowing a new combination to inherit an older product's negotiation timeline. If a new product is incorporated into an older QSSD, it may become subject to negotiated prices much sooner than if it were evaluated separately -- reducing developers' opportunity to recoup the high costs of research, clinical trials, manufacturing changes, and regulatory review.

CMS's regulatory analysis shows how large the difference in timing could be. In its hypothetical example, a hyaluronidase-containing formulation could come under an existing group's MFP in 2029. But without the proposed aggregation, the later biologic might not be eligible for price negotiation until 2039. [1]

For companies evaluating whether to fund post-approval investment, research, and development, that difference could be decisive. Costly studies involving smaller populations or medicines used heavily by Medicare beneficiaries could become particularly difficult to finance. Ultimately, patients could lose out on potentially valuable combination therapies that could have materially improved convenience and, potentially, adherence to treatment. [5]

Case Study: PHESGO

The breast cancer treatment PHESGO illustrates the type of innovation that patients could lose out on under CMS's proposal. PHESGO combines pertuzumab and trastuzumab, two medications used in specified HER2-positive breast cancer settings, with hyaluronidase-zzxf. It allows patients to receive the two treatments through a subcutaneous injection rather than through intravenous infusion.

PHESGO brings real patient benefits. The initial injection takes approximately eight minutes, and subsequent injections take about five minutes. Required observation adds thirty minutes after the initial dose and fifteen minutes after maintenance doses. By contrast, intravenous delivery of pertuzumab and trastuzumab typically takes more than an hour. [6]

For patients, the time savings may mean less time away from work and family responsibilities. They can make clinic visits less burdensome, potentially increasing the likelihood that patients adhere to regular appointments and treatment. More efficient delivery may also free clinical capacity for providers.

PHESGO also required substantial new clinical evidence. The medication was tested in a randomized study involving 500 patients, which assessed whether the subcutaneous combination could deliver the antibody treatments safely and effectively. This was a clinical development program, even though the antibodies were already known. [7]
If CMS's proposal exposes combination therapies like PHESGO to higher pricing risks, convenient treatment options may receive less investment in the future.

PHESGO is an illustration of the development issue, not a determination of its negotiation status. Whether and how the proposed rule would apply requires review of the relevant BLA holders, component products, licensure histories, exclusions, and selection rules. No specific selection date or MFP date is assigned here. The concern is that a qualifying delivery-enabling combination could inherit an older product's timetable, reducing the prospective return available to finance the new program.

Ultimately, CMS's proposal risks disincentivizing meaningful advances in care by treating them the same as minor product changes. While preventing manufacturers from circumventing price negotiation is an important goal, the agency should not pursue it at the expense of innovations that offer real benefits to patients.

Recommendations for More Targeted Policy

CMS should reconsider its proposed rule and instead pursue a narrower approach that protects Medicare's negotiating authority without discouraging meaningful development. Three steps would help.

1. Distinguish substantial advances from minor modifications
CMS should work with the FDA to determine the work that contributed to a follow-on drug, as well as the new clinical benefits it offers, and use that information to determine whether the new drug warrants separate QSSD treatment. The following questions could guide the agencies' assessment.

Key Question	**Evaluation Criteria**
Does the product address a distinct therapeutic or patient need?	The product should treat a different disease or patient population, or address a meaningful treatment limitation, such as burdensome administration.
Did development require substantial new research?	The product should have involved meaningful additional research, such as additional clinical trials, formulation research, pharmacokinetic studies, and safety assessments.
Does the product offer meaningful benefits to patients?	The product should offer evidence of improved clinical outcomes, reduced

	treatment burden, or an important new treatment option.
Does the new administration method represent a real improvement?	The product's delivery mechanism should meaningfully improve on existing options in factors such as dosing, drug exposure, safety, administration time, or observation requirements.
Was significant additional investment necessary?	The manufacturer should provide evidence of increased development costs, timelines, and financial commitments for the new product.
Could special treatment undermine negotiation?	Separate QSSD treatment for the new product should not reset an older product's negotiation timeline or shelter its established sales.

2. Preserve a separate clock for qualifying later products

A later product that required substantial independent development and demonstrates meaningful patient benefits should be eligible for a separate negotiation timetable where statute allows. The Department of Health and Human Services should first evaluate whether current law permits narrower grouping for such products. If it does not, CMS should identify the needed change and recommend that Congress authorize a targeted exception.

Congress should receive proposed eligibility criteria, a budget analysis, and safeguards that preserve the older product's negotiation status. That would turn an innovation concern into a proposal lawmakers can evaluate. Any resulting legislation should clearly define eligibility, the start and length of any new period, limits on repeated exceptions, and treatment of products already selected for negotiation.

The exception should apply only to the qualifying later product, not reset the original medicine's clock. This would prevent companies from abusing separate QSSD treatment to indefinitely shelter established sales.

3. Make decisions transparent and test their effects

CMS should publish its evaluation criteria and worked examples covering routine formulation changes, delivery-enabling combinations, separately developed products for different diseases, and supplemental indications. Each example should show how CMS arrived at its decision so that manufacturers can make informed choices about future development programs.

CMS should also explain how it accounts for new research, development costs, and patient benefits when negotiating prices. The agency should evaluate how its own policies affect decisions to fund clinical trials, patient access to treatment, and the use of older versus newer medicines. It should weigh the risk of discouraging innovation against the risk of manufacturers using minor product changes to avoid negotiation.

Finally, CMS should establish a formal process for consulting the FDA on complex grouping decisions and clearly identify each agency's responsibilities. Where permitted by law, it should allow manufacturers to correct factual errors or submit missing clinical evidence before determinations are finalized. This would improve the accuracy and transparency of QSSD classifications while giving manufacturers greater certainty about how their products will be evaluated.

Broader Ramifications for Post-Approval Innovation

Drug innovation typically does not occur in a single "Eureka!" moment. Researchers continually build on existing knowledge, discovering new ways to use established medicines to treat different diseases, reach new patient populations, or improve outcomes. Researchers learn more about a mechanism, an organ system, a dose, or a patient population and discover a use that the original development program never established.

This is true not only of combination therapies, but also of many other innovative medicines developed by modifying existing products or finding new uses for familiar active ingredients.

CMS's proposal for fixed-dose combination products therefore underscores a broader issue with the agency's QSSD grouping policies. Existing grouping policies may discourage other forms of post-approval innovation, including the development of new medicines that share active ingredients with earlier products and research into additional uses for existing treatments.

Risks to separately approved products

Current QSSD rules risk treating clinically distinct products as a single drug simply because they share an active ingredient and application holder.

Case Study: Pegcetacoplan

Pegcetacoplan, a medication used to treat rare blood, kidney, and eye disorders, illustrates this concern. In 2021, the FDA approved EMPAVELI, a pegcetacoplan product, for paroxysmal nocturnal hemoglobinuria (PNH). In 2023, the agency approved SYFOVRE, another pegcetacoplan product, for geographic atrophy secondary to age-related macular degeneration.

Although these products share an active moiety, they use different administration routes and treat different patient populations. EMPAVELI is administered through subcutaneous infusion and can treat PNH in addition to C3 glomerulopathy and glomerulonephritis, two diseases that can lead to kidney failure. The development question was whether pegcetacoplan could treat systemic disease.

SYFOVRE, meanwhile, is injected into the eye. The development question was whether local ocular treatment could improve a patient's geographic atrophy. [8,9] The products also required different clinical evidence. Although SYFOVRE's development drew on some earlier nonclinical information, existing evidence supporting a systemic use did not establish the benefit of an ocular treatment. Its approval required two pivotal phase 3 studies assessing geographic-atrophy lesion growth.

That is how development can work: earlier knowledge supports a later program, which must still establish its own disease-specific evidence.

EMPAVELI and SYFOVRE are therefore clinically distinct products. Yet under CMS's grouping framework, products this different could potentially be treated as a single QSSD if they meet the applicable ownership and eligibility requirements. Grouping them could reduce the expected return on the later development program, discouraging investment in treatments that could benefit patients.

Like the proposed fixed-dose combination rule, CMS's existing QSSD framework risks subjecting newer products to older negotiation timelines, even when they require substantially different clinical research. CMS should examine that additional work rather than treating shared knowledge as evidence that little new research was needed.
The approach proposed earlier -- allowing qualifying products that require substantial independent development to receive separate negotiation timelines -- could help address this problem. Such a policy would recognize the investment required to develop distinct treatments without delaying negotiation for their predecessors.

Risks to supplemental indications
A related but more complicated problem arises when post-approval clinical trials establish a new use for an existing medicine.

The fact that a medicine works in one disease can make another program scientifically attractive. It cannot make that program financially viable on its own. An additional cancer indication, for example, may require years of research and sizable investment.
If the FDA approves it through a supplement to the existing NDA or BLA, however, the medicine generally retains the original negotiation timetable. The additional indication therefore receives no separate period before negotiation eligibility, which may leave manufacturers little time to earn a return on their investments in research and development.

Some programs could remain attractive under earlier negotiated pricing. A large market, manageable trial costs, or substantial demand outside Medicare may sustain investment. A small population, expensive study, lengthy recruitment, and heavy Medicare exposure can push a different program below the financing threshold. That is the trial CMS should worry about: scientifically worth pursuing, but no longer worth funding under the expected economics.

Addressing this problem would therefore require a different approach. CMS should more explicitly recognize the additional research and clinical benefits associated with new indications when negotiating prices. Congress should also consider targeted incentives that reward substantial research into supplemental indications without extending the negotiation timeline for a medicine's existing uses.

More broadly, these examples illustrate why QSSD policy must distinguish between minor product modifications and meaningful advances that build on existing medicines. Medicare's negotiation framework should recognize the additional research required to deliver those advances, rather than discouraging investment simply because a treatment builds on an earlier discovery.

Conclusion

Medicare can count the savings from a lower drug price, but it cannot directly measure the cost to patients of a trial that never took place. That should make CMS cautious about adopting broad price negotiation policies that could discourage valuable innovation. CMS's proposed fixed-dose combination rule could make it harder to justify developing new, convenient treatments based on previous breakthroughs. The agency should reconsider this proposal and instead adopt a more targeted approach that accounts for each new drug's research investments and patient benefits.

Similarly, CMS should reevaluate its broader QSSD policy. New medicines built on familiar ingredients can offer substantial benefits to patients and even enable treatment for additional diseases. Medicare pricing policies should ensure that innovations like these, which are functionally new medicines, remain viable for drugmakers to invest in. Patients depend on Medicare to make existing treatments affordable. But they also depend on manufacturers and researchers investing in the next clinical trial that could give them a better option tomorrow. Policymakers should ensure that Medicare's pricing rules support both goals.

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