Center on Health Policy at BROOKINGS

July 1, 2024

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Director, Center for Medicare

Center for Medicare & Medicaid Services

Dear Dr. Seshamani,

Thank you for the opportunity to comment on the Medicare Drug Price Negotiation Program Draft Guidance issued on May 3, 2024. In what follows, we comment on several proposed provisions of the guidance, including some of those where comments were specifically requested. Our comments are organized into four groupings: 1) competitive entry standards; 2) payment and price components; 3) negotiation factors; and 4) negotiation process.

1. *Competitive Entry Standards*

The draft guidance sets forth a process for the Centers for Medicare & Medicaid Services (CMS) to assess whether generic or biosimilar competition has been established, which is relevant both for determining a drug's eligibility for selection into the negotiation program and for determining when a drug will be removed from the selected drug list. The guidance describes a holistic assessment of whether a generic or biosimilar is engaging in "bona fide" marketing. We recognize the challenges of trying to determine how the market will evolve.

The elements of information set forth in Section 30.1 (particularly on pages 10-12) and in Section 70 are generally sensible. In addition to the sources of information listed on page 11, CMS should be mindful of erroneous reporting of information in the U.S. Food and Drug Administration (FDA) Orange Book. There have been numerous examples of invalid and expired patent being reported in the Orange Book that would cloud assessments of whether entry is even possible. The discussion of information to be examined includes agreements between a generic manufacturer and the Primary Manufacturer of a selected drug. We suggest that specific attention be given to settlement agreements of patent litigation and discussion of expected and realized competition in Primary Manufacturer 10K and 10Q filings with the Securities and Exchange Commission (SEC). Bona fide entry of biosimilars involves similar issues. It is important to recognize that the Purple Book has less complete information to inform an analysis of bona fide marketing than the Orange Book and is likely equally prone to errors. That may result in distorted assessments of whether market entry by the biosimilar is likely.

The biosimilar delay portion of the negotiation program in Section 11002 of the IRA allows for a potential delay in selection of a biological product for negotiation if the Secretary determines that

there is a "high likelihood" that a biosimilar for that biologic would be licensed and marketed within two years of the relevant date. The process by which CMS will determine whether there is a "high likelihood" of such licensure and marketing is detailed in Section 30.3.1 of the draft guidance. Section 30.3.1.2 of the draft guidance, referencing section 1192(f)(3)(B) of the Social Security Act, identifies SEC filings and comparable communications with shareholders of privately held companies as relevant in determining whether the "high likelihood" threshold is met. We would suggest that CMS also obtain data from the FDA and private vendors to track progress of clinical trials involving potential biosimilar entrants in assessing the likelihood of timely launch and marketing. While the statute requires CMS to obtain data on manufacturing schedules, private vendors and the FDA also receive data on the progress of clinical trials and details on potential risks that may be relevant to assessing the likelihood of launch. Examining the timing and details of patent settlement agreements should also be incorporated into the assessment. Finally, monitoring bona fide marketing should involve monitoring of agreements between pharmacy benefit managers (PBMs) and manufacturers. This may be important because such agreements may serve to limit the ability of a biosimilar product to effectively penetrate the market.

In assessing an Initial Delay Request from a biosimilar manufacturer, the draft guidance sets out the conditions that a written agreement that permits the biosimilar manufacturer to market the biosimilar before February 1, 2027, would need to meet to constitute support for an application (Section 30.3.1.2). We would suggest that as a complement to the review of a written agreement CMS also examine the biosimilar manufacturer production plans, that they are required to obtain, to ensure that no tacit agreement on volume of production has been made in connection to the written agreement.

If, after consideration of all the listed sources, there is residual uncertainty regarding whether the biosimilar is going to be launched and bona fide marketed in the required time frame, we suggest that CMS adopt a presumption to resolve this uncertainty against the applicant, declining to remove the relevant biologic from the list of negotiation-eligible drugs. Otherwise, there is the real possibility of a sham launch.

2. *Payment and Price Components*

We identify several issues regarding the primary manufacturers whose products are selected for the negotiation program and the elements that will be considered in constructing the initial offers.

- Prescription drug markets are dynamic. Thus, price levels depend on a variety of market conditions that can change in significant ways over time. Given that there is a notable time lag between the time at which drug prices are negotiated and the date that the maximum fair price (MFP) applies, much can change. This means that the marketplace for a negotiated drug may look quite different on the day the MFP goes into practice from when it was negotiated. CMS should anticipate changes to the structure and conduct in the market in developing its stance on individual drug negotiations.
- The guidance in section 60.5.1 describes procedures for addressing how new formulations and dosage forms of negotiated drugs with an MFP and new drug applications (NDAs) or biologics license applications (BLAs) will be incorporated into the pricing scheme. The guidance proposes to identify comparable NDAs and BLAs and

project volume to rescale prices. The guidance does not explain in detail how CMS proposes to identify what drugs are comparable. Similarly, for cases without a comparable NDA or BLA, an imputation will be implemented. The guidance offers only minimal information on any principles guiding the imputation. One approach might assign the existing weighted average price for a period of at least one year. That would be followed by a rescaling.

- The guidance defines a method for calculating retrospective refunds to pharmacies in Section 40.4.3, on pages 50-51. The refund uses wholesale acquisition cost (WAC) to estimate the pharmacy acquisition cost. The Congressional Budget Office has provided evidence that WAC typically exceeds what Medicare Part D plans pay pharmacies.[1] Since WAC is a list price and not a transaction price, manufacturers control the size of the refunds given to pharmacies. While in many cases the ability to steer prescriptions by pharmacies is quite limited (e.g., many retail pharmacies) that may be less so in the case for pharmacies connected to vertically integrated health care organizations (e.g., some retail pharmacies, mail order- and specialty pharmacies). Thus, pharmacies would have an incentive to favor negotiated drugs. The net impact for consumers and Medicare spending would depend on the alternatives available and their prices. An acquisition cost measure that is not controlled by manufacturers and more reflective of transaction prices may be preferable. Alternative metrics might include national average drug acquisition cost (NADAC), average sales price (ASP) (when available), and federal supply schedule prices. These metrics attempt to reflect transaction prices and are less able to be controlled by manufacturers.
- In considering facilitation of payments to pharmacies, the guidance offers two options for doing so in Section 40.4.4, page 53. Option 1 establishes a direct financial link between the manufacturer and the dispensing pharmacy. It also has the potential to provide proprietary data about the pharmacies to the manufacturers. In effect, the financial links creates new risks from the facilitation of coordination between pharmacies and manufacturers. For example, agreements between manufacturers and PBMs (owners of mail order and specialty pharmacies) can facilitate limited entry arrangements related to both generic and biosimilar marketing. This is especially the case with specialty pharmacies and mail order pharmacies. CMS notes that Option 1 facilitates more efficient payment of pharmacies. Option 2 retains a more arm's length relation of manufacturer and pharmacy. The downside risks associated with coordinated conduct and reduced competition may make Option 2 worth pursuing.
- Weighting prices: CMS interprets Section 1196(a)(2) of the statute as calling for negotiation of a single price per drug product (based on active ingredient or moiety). This requires developing a weighting scheme to arrive at a single weighted average price. Creating that weighted average requires information on volume of sales for individual formulations and dosages plus information about the relative prices across dosage forms and strengths. The guidance proposes using WAC to construct the relative price weights (page 98). As noted earlier, WAC is a list price controlled by manufacturers. It would be preferable to base the aggregation and eventual disaggregation on something close to transaction prices such as Medicare net prices.

[1] Congressional Budget Office, A Comparison of Brand-Name Drug Prices Among Selected Federal Programs, September 2021; Table 2 provides the comparisons between various Medicare prices and WAC.

Since the aggregation would be done by applying ratios CMS would not be revealing any individual product net prices.

- New dosages, strengths, and formulations. As new products within a defined drug with an MFP enter the market, the guidance does not fully articulate the process for recalculating the weighted average prices under the negotiated MFP. While we propose that re-weighting use net prices, a related question is how long the new product should be on the market to ensure the market has adjusted to it and adequate data exist prior to the re-weighting calculations being made.
- The guidance does not offer sufficiently complete direction related to combination products. We are concerned with the potential for strategic development of combination products. For example, an easy way to create a product hop that might affect the construction of MFPs that would be to continue to produce the original negotiated drug and add a component that will make it a combination drug, but the combination would not be significantly different from the original. The guidance should add some additional direction about how combination products will be treated.
- Section 1860D-4(b)(3)(I) of the statute requires that Part D plans include on their formularies all selected drugs for which a negotiated MFP is in effect. In section 110 of the draft guidance, CMS is not establishing any substantive requirements about placement within formularies (page 121-123). CMS recognizes the potential to disadvantage drugs via formulary placement and application of utilization management techniques. The draft guidance notes that CMS will monitor formulary arrangements and may take enforcement actions if drugs with an MFP are disadvantaged. It should be recognized that doing so is costly and complex and may be less effective than establishing some directive for formulary placement and the application of utilization management mechanisms. This issue is in part evidenced by a recent finding that CMS does not use information on rebates and information on gross to net price gaps to monitor formulary practices in Part D.[2] CMS could stipulate that the negotiated drug be placed on the formulary in a favorable tier unless it can demonstrate to CMS that there is a therapeutic alternative with a lower price than the negotiated drug.

3. *Negotiation Factors*

In developing initial offers, Section 60.3.4 of the draft guidance discusses how CMS will use the 5 elements of manufacturer-specific data to adjust the preliminary price. The draft guidance identifies a variety of considerations for the five elements, and it highlights that the five elements will be viewed in their totality. However, it is unlikely that as a matter of economics, public education, or program management each of the five elements should be given equal weight. Some guidance on elements of most import would provide greater understanding and potentially greater credibility to the development of price offers.

Some specific comments on individual elements.

- Research and Development (R&D) Costs: There are a variety of complex accounting issues in making estimates of R&D spending attributable to a specific product. There are

[2] See U.S. GAO, CMS Should Monitor Effects of Rebates on Plan Formularies and Beneficiary Spending, September 2023, GAO-23-105270

difficult allocation assumptions related to so-called joint costs that must be made in such an exercise. The guidance set out on pages 127-129, does not provide direction on how this might be done. That means the results reported to CMS will depend on such assumptions and those assumptions can be based on strategic considerations related to the negotiations. It is likely that the intent of the provision was for CMS to be aware of the investments that a manufacturer has made in developing a drug to calibrate what might represent a fair return on investment. That intent is not well served by being permissive about assumptions made by a party to the negotiations.

- The guidance notes that CMS will use R&D costs along with revenues, including global revenues, to assess whether R&D costs have been recouped (page 87). The guidance states that if they have not been recouped, CMS might consider adjusting its preliminary price upward. Using a recoupment of costs standard is a complicated matter. That is because price adjustments would have to make judgements about the duration of time the drug in question would continue to be a sole source product and the expected volume of sales during that time. Furthermore, one might want to consider the reasons why costs were not recouped. Some guidance on how such information would be obtained and used would be important to outline.
- Federal financial Support for Drug Development. Existing evidence shows that nearly all prescription drugs have some federal financial support in their history.[3] Thus, if the point is to determine the extent to which taxpayers have a claim on the surplus produced by these drugs, then the level of federal support and where in the process it took place is relevant and those data should be collected.
- There are a variety of circumstances that would arise with respect to the market context where the range of possibilities with respect to therapeutic alternatives differ substantially. In considering alternatives that serve as a starting point for negotiations drugs that are lower priced that are therapeutic alternatives will give CMS the greatest leverage in the negotiations.

4. *Negotiation Process*

The draft guidance document solicits comments on the number of meetings and other communication there should be between CMS and manufacturers (Section 60.4). One of the most fundamental features of negotiation is communication and research has shown that face to face contacts and less constrained exchanges of views yield more satisfactory outcomes. This is especially true in circumstance where the issues and alternative views of the problems are complex and the markets in question are dynamic. Prescription drug markets have those attributes. Moreover, there are lots of intangible issues and important assumptions made by both sides in making formal price proposals. Understanding of those issues benefits from situations where there is free give and take. Given concerns aired by various stake holders about the degree to which the IRA negotiation are true negotiations, we support CMS continuing to hold up to

[3] Zhou EW, Jackson MJ, Ledley FD. Spending on phased clinical development of approved drugs by the US National Institutes of Health compared with industry. JAMA *Health Forum*. 2023;4(7):e231921. doi:10.1001/jamahealthforum.2023.1921

three negotiation meetings with each Primary Manufacturer. We support this in full recognition of the compressed schedule.

Thank you once again for the opportunity to comment on this critically important draft guidance document. We hope that you find these comments helpful to your work on this policy.

Sincerely,

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