What do the new Medicare negotiations mean for pipeline orphan therapies?

Exploring the impact of the Inflation Reduction Act on orphan drugs

Background

- The **first round of CMS drug price negotiations led to an average cut of 63% to the list price** of the selected Part D drugs, effective from 2026; in January 2025, the next 15 drugs selected for negotiations were announced, with prices effective from 2027
- The final **CMS guidance**[1] (released in October 2024) outlines the eligibility criteria for negotiations and notably **allows for OMP inclusion in negotiations**, **under certain conditions**. Although the first round of negotiations were concerned with mostly highly prevalent conditions, it is **possible that OMPs could be selected for future rounds**, particularly multi-indication OMPs with higher cumulative sales
- Given the more challenging clinical development and commercialization environment for OMPs, there is a risk that their eligibility for **price negotiations could threaten continued rare disease drug development and indication expansion**, impacting innovation and access not only in US, but also globally [2]
- Therefore, Dolon has conducted a **holistic assessment of the CMS drug price negotiation process**, to characterise the **potential implications for OMPs with multiple indications that may be eligible for future negotiation**

Medicare negotiation pathway, methodology and OMP considerations

Negotiation eligible

- **Part B** and **Part D** drugs that are ≥7 years old for small molecules and ≥11 years for biologics, and **do not have generic or biosimilar competition**
- Selected from among the **top 50 highest-spend Medicare drugs**

Negotiation exempt

- Drugs with **generic alternatives or biosimilars available**
- Drugs with **all FDA-approved and orphan designated indications** within a **single rare disease** or condition

Many OMPs will be eligible for negotiation. An OMP will not be exempt unless all indications are within the same disease area (e.g., different lines of therapy or subgroups). Indications in development are also considered, even if they have not yet launched

Medicare negotiations are initiated with a two-step process[1]:

1 CMS calculates the Maximum Fair Price (MFP) ceiling

Choose the lower of

- **PART D:** Enrolment-weighted net price
- **PART B:** Average sales price
- **NON-FAMP DISCOUNT** **-25%** for drugs ≤ 15 years post-approval **-60%** for drugs 16+ years post approval

1 **A maximum ceiling price** is set based on the lower of the average Medicare net price or a statutory discount to the non-FAMP price, adjusted according to the length of time the drug has been on the market

OMP considerations

OMPs without a non-rare indication are less likely to be heavily rebated, therefore, the **ceiling will most likely be set by statutory non-FAMP discount**. Dolon analysis of first round of negotiations indicates no further negotiations may occur, thus the final MFP could be aligned to MFP ceiling (i.e. final MFP could be aligned to the non-FAMP statutory discount price)

If the **ceiling is set by the average Medicare net price**, then the final MFP could be below the MFP ceiling, to generate Medicare savings

2 CMS makes the initial MFP price offer

Tx alternatives available — **a) Are Tx alternatives available?** — *no Tx alternatives or Tx prices > MFP ceiling*

Yes

- **Net / sales price of alternatives**

No

Choose the lower of

- **FSS price**
- **Big 4 price**

b) Adjust offer according to

- **Outcomes**, especially in vulnerable populations
- **Clinical benefit** vs. therapeutic alternatives
- **Utilisation of product** vs. therapeutic alternatives
- **Unmet need**
- **Costs** (R&D, production)
- Level of **federal funding used in R&D**
- Revenues and market data on **volume**

Note: *Weightings of each factor are not specified in the IRA legislation*

MFP negotiations with manufacturers begin

2 **CMS calculates an initial price offer based on benchmarking** to therapeutic alternatives (if available) or Federal prices (FSS or Big 4), **with adjustments** then made according to several factors, including patient outcomes, unmet need, and level of utilisation vs. therapeutic alternatives

OMP considerations

OMPs may follow the Federal price path, as they often launch in non-competitive spaces. However, since Medicare negotiations focus on older drugs, the **likelihood of alternative treatments being available increases**, which may exert significant downward pressure in negotiations

Manufacturers may be able to influence which therapeutic alternatives CMS views **as clinically relevant** by submitting evidence at the beginning of this process in negotiations

The level **of unmet need and therapeutic benefit is determined based on Tx available at time of negotiation**. Although an OMP may launch as a first-in-class drug in an area of high unmet need, this may change by the time negotiations commence, leading to further erosion of the OMP price

The lack of transparency in net prices and federal agency pricing, combined with CMS's right to make discretionary, qualitative adjustments, make it impossible to accurately predict which price benchmark pathway will result in the greatest price reductions

Forward looking implications for OMPs

- The Orphan Drug Act, which was introduced to incentivise drug development for rare diseases, provides OMPs, amongst other things, market exclusivity for seven years from FDA approval, essentially providing price protection for this period
- **These incentives are crucial for continued innovation in rare diseases**, given their high risk of failure, challenges in development and uncertain return on investment[2, 5]; before the Act was passed, very few OMPs had been developed[3, 4]
- However, the **IRA effectively reduces the protection offered to OMPs** under the Orphan Drug Act for small molecules. Small molecule OMPs are now eligible for negotiations in a shorter time (six years)
- Additionally, the likelihood that OMPs are selected for negotiations will increase for future negotiations, as the negotiations for drugs with high Medicare sales move towards less prevalent therapeutic areas
- These factors, alongside becoming eligible for negotiations if the OMP gains an additional indication in a separate disease or condition, will likely **discourage OMP manufacturers from expanding into further rare diseases** with **high Medicare part B/D sales potential**
- Furthermore, with the difficulty in predicting the impact of potential price negotiations, manufacturers may start **to prioritise** the US **launch of larger, non-rare indications** with larger **non-Medicare components,** to minimise future risk to business
  - This could place further **pressure on the EU launch environment** by reducing the launch of novel orphan indications
- As a result, **R&D in OMPs could decline in the long-term limiting future patient access** to potentially life-changing therapies

Summary of Implications for OMPs

Inflation Reduction Act (**2022**) limits the price protection of OMPs to 6 years for small molecules and 10 years for biologics

Likelihood of OMPs being selected for negotiation **increases** over time

Limited expansion of OMPs into additional rare diseases due to qualifying for price negotiations

Decline in OMP R&D investment

Prioritization of launches for larger, non-rare indications

Limited future patient access to orphan drugs

What can be done?

Dolon's market access policy team can build policy engagement on IRA implications, address the decline in willingness to pay for rare disease innovation, and highlight the importance of continued investment in orphan medicine development. Dolon's pricing strategy team integrates IRA considerations into product pricing strategy for orphan medicines.

Abbreviations

B4: Big 4 [agencies]; CMS: Centers for Medicare and Medicaid Services; FAMP: Federal average manufacturer price; FDA: Food and Drug Administration; FFS: Federal Supply Schedule; IRA: Inflation Reduction Act; MFP: Maximum Fair Price; OMP: orphan medicinal product; R&D: research and development; Tx: treatment

References

1. CMS (2024); 2. Laurence et al. (2020); 3. FDA (2013); 4. King's Fund (2023); 5. Wong et al. (2018).