PORTAL Program On Regulation, Therapeutics, And Law
Division of Pharmacoepidemiology and Pharmacoeconomics
Harvard Medical School | Brigham and Women's Hospital
www.portalresearch.org

March 1, 2026

Dr. Mehmet Oz, Administrator
Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Anoro Ellipta (umeclidinium-vilanterol)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Anoro Ellipta (umeclidinium-vilanterol) and its therapeutic alternatives:

Comparative Effectiveness and Safety of LAMA-LABA Inhalers in Chronic Obstructive Pulmonary Disease[1]
In an active-comparator cohort study, Portela et al. compared the effectiveness and safety of three commonly used fixed-dose LAMA-LABA inhalers in COPD, including umeclidinium-vilanterol. Across more than 55,000 propensity-score-matched patient pairs, initiation of umeclidinium-vilanterol was associated with a lower risk of first moderate or severe COPD exacerbation compared with both glycopyrrolate-formoterol (14% lower hazard) and tiotropium-olodaterol (3% lower hazard), with no meaningful differences in major adverse cardiovascular events, pneumonia hospitalization, or urinary tract infection across regimens.

Chronic Obstructive Pulmonary Disease Exacerbations and Pneumonia Hospitalizations Among New Users of Combination Maintenance Inhalers[2]
In a cohort study of more than 60,000 patients with COPD, Feldman and colleagues assessed if combination inhalers with long-acting muscarinic antagonists (LAMAs) and long-acting beta-agonists

[1] Portela GT, Wang SV, Suissa S, Feldman WB. Comparative Effectiveness and Safety of LAMA-LABA Inhalers in Chronic Obstructive Pulmonary Disease. JAMA Intern Med. 2026 Feb 23. doi:10.1001/jamainternmed.2025.8087 PubMed PMID: 41729543.
[2] Feldman WB, Avorn J, Kesselheim AS, Gagne JJ. Chronic Obstructive Pulmonary Disease Exacerbations and Pneumonia Hospitalizations Among New Users of Combination Maintenance Inhalers. JAMA Intern Med. 2023 Jul 1;183(7):685. doi:10.1001/jamainternmed.2023.1245 PubMed PMID: 37213116; PubMed Central PMCID: PMC10203971.

(LABAs), include umeclidinium-vilanterol, were associated with reduced incidence of COPD exacerbations and pneumonia hospitalization versus inhalers with LABAs and inhaled corticosteroids (ICSs). They found that patients receiving LAMA-LABA inhalers had an 8% lower rate of moderate or severe COPD exacerbations and a 20% lower rate of pneumonia hospitalization compared to those receiving ICS-LABA therapy.

Added Therapeutic Benefit of Top-Selling Brand-Name Drugs in Medicare[3]
Egilman and colleagues examined the added therapeutic benefit of the 50 highest-selling drugs in Medicare in 2020 as assessed by the national health technology assessment agencies in France, Germany, or Canada. They found that 27 drugs (55%) had a low added therapeutic benefit rating by at least one country's HTA, representing $19.5 billion (35%) of estimated net Medicare spending in 2020 on the top 50 single-source drugs. Umeclidinium-vilanterol received a "low" added therapeutic benefit rating in Canada, France, and Germany, with a "Moderate" absolute therapeutic benefit rating in France.

Patents and Regulatory Exclusivities on Inhalers for Asthma and COPD, 1986–2020[4]
Feldman et al. examined patents and FDA regulatory exclusivities on inhalers approved for asthma and COPD between 1986 and 2020, finding that brand-name inhalers received a median of 16 years of protection from generic competition. More than half of all listed patents were on inhaler devices rather than active ingredients, and manufacturers frequently extended exclusivity through "device hopping," in which the same drugs were reformulated into new delivery devices with new patent protection. The study identifies umeclidinium-vilanterol as part of the Ellipta line, which spans multiple inhaler classes and benefits from overlapping device patents which contribute to prolonged market exclusivity.

Tertiary Patents on Drugs Approved by the FDA[5]
Teng and colleagues analyzed patenting practices on FDA-approved drug–device combination products from 1986 to 2023, focusing on the role of tertiary patents (patents covering drug delivery devices). Among 331 drug–device combinations, the authors identified 3,241 listed patents, of which 54% were tertiary patents. Nearly 60% of tertiary, and more than half of products had tertiary patents that extended expected market protection beyond primary and secondary patents, including umeclidinium-vilanterol. Inhalers had among the highest numbers of tertiary patents and longest protection periods, reflecting the central role of device patents in delaying competition for these therapies.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Anoro Ellipta. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

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[3] Egilman AC, Rome BN, Kesselheim AS. Added Therapeutic Benefit of Top-Selling Brand-name Drugs in Medicare. JAMA. 2023 Apr 18;329(15):1283. doi:10.1001/jama.2023.4034 PubMed PMID: 37071095; PubMed Central PMCID: PMC10114018.
[4] Feldman WB, Bloomfield D, Beall RF, Kesselheim AS. Patents And Regulatory Exclusivities On Inhalers For Asthma And COPD, 1986–2020. Health Aff (Millwood). 2022 Jun 1;41(6):787–96. doi:10.1377/hlthaff.2021.01874 PubMed PMID: 35579925; PubMed Central PMCID: PMC10328096.
[5] Teng TW, Tu SS, Mooney H, Bendicksen L, Gabriele SME, Wouters OJ, et al. Tertiary Patents on Drugs Approved by the FDA. JAMA Health Forum. 2026 Jan 2;7(1):e255909. doi:10.1001/jamahealthforum.2025.5909 PubMed PMID: 41481325; PubMed Central PMCID: PMC12761334.

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Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Biktarvy (bictegravir-emtricitabine-tenofovir alafenamide)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Biktarvy (bictegravir-emtricitabine-tenofovir alafenamide) and its therapeutic alternatives:

Added Therapeutic Benefit of Top-Selling Brand-Name Drugs in Medicare[1]
Egilman and colleagues examined the added therapeutic benefit of the 50 highest-selling drugs in Medicare in 2020 as assessed by the national health technology assessment agencies in France, Germany, or Canada. They found that 27 drugs (55%) had a low added therapeutic benefit rating by at least one country's HTA, representing $19.5 billion (35%) of estimated net Medicare spending in 2020 on the top 50 single-source drugs. Bictegravir-emtricitabine-tenofovir alafenamide received a "low" added therapeutic benefit rating in Canada, France, and Germany, with an "Important" absolute therapeutic benefit rating in France.

Patent Portfolios Protecting 10 Top-Selling Prescription Drugs[2]
Horrow and coauthors examined the patent portfolios protecting the 10 highest-selling prescription drugs in the United States as in 2021, including Biktarvy. They found that 58% of patent applications for small-molecule drugs were filed after FDA approval, with post-approval patenting concentrated in the first 5 years after approval. Patent thickets for small-molecule drugs peaked at a median of 62 active

[1] Egilman AC, Rome BN, Kesselheim AS. Added Therapeutic Benefit of Top-Selling Brand-name Drugs in Medicare. JAMA. 2023 Apr 18;329(15):1283. doi:10.1001/jama.2023.4034 PubMed PMID: 37071095; PubMed Central PMCID: PMC10114018.
[2] Horrow C, Gabriele SME, Tu SS, Sarpatwari A, Kesselheim AS. Patent Portfolios Protecting 10 Top-Selling Prescription Drugs. JAMA Intern Med. 2024 Jul 1;184(7):810. doi:10.1001/jamainternmed.2024.0836 PubMed PMID: 38739386; PubMed Central PMCID: PMC11091822.

patents around 12 years after FDA approval, about half of which were filed post-approval. Visualizations of the patent thicket surrounding Biktarvy are presented in eFigure 1 and eFigure 2 in the study supplement.

The Strength and Importance of Government-Funded Patents for Approved Drugs[3]
Gabriele and colleagues analyzed the prevalence and strength of US government-funded patents associated with FDA-approved drugs. Between 1984 and 2023, the authors identified 254 government-funded patents tied to 137 approved drugs, including bictegravir-emtricitabine-tenofovir alafenamide, accounting for 32% of all patents protecting those products. Compared with industry-funded patents, government-funded patents were more likely to be primary patents covering the active ingredient (28% vs 13%) and more likely to receive patent term extensions, indicators of the patent's strength and commercial value. Most government-funded patents were filed before FDA approval, underscoring the public sector's role in core drug discovery.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Biktarvy. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

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[3] Gabriele SME, Martin MJ, Kesselheim AS, Tu SS. The strength and importance of government-funded patents for approved drugs. Nat Biotechnol. 2025 Jul;43(7):1050–2. doi:10.1038/s41587-025-02724-7 PubMed PMID: 40664847.

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Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Botox; Botox Cosmetic (onabotulinum toxin A)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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Below, we have included a summary of apeer-reviewed publication from our group that we think may be valuable to CMS' evidence-based assessment of Botox (onabotulinum toxin A) and its therapeutic alternatives:

Variation in Endpoints in FDA Medication Approvals: A Review of Acute and Preventive Migraine Medications[1]
Sharpless et al. examined the primary endpoints used in pivotal trials supporting FDA approval of migraine medications from 2001 to 2022, including onabotulinum toxin A, and found substantial heterogeneity across drugs approved for similar indications. Among 16 migraine medications supported by 45 pivotal trials, endpoints varied in both type (e.g., migraine days vs headache days) and timing of assessment, complicating comparative assessment of clinical benefit across preventive migraine options.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Botox. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

[1] Sharpless LK, Kesselheim AS, Orr SL, Darrow J. Variation in Endpoints in FDA Medication Approvals: A Review of Acute and Preventive Migraine Medications. Neurology. 2023 Sep 5;101(10):989–1000. doi:10.1212/WNL.0000000000207544 PubMed PMID: 37438124; PubMed Central PMCID: PMC10491441.

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Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Cimzia (certolizumab pegol)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Cimzia (certolizumab pegol) and its therapeutic alternatives:

Use of Efficiency Frontiers to Align Prices and Clinical Benefits of Biologic Therapies for Plaque Psoriasis[1]

Egilman and coauthors assessed whether an efficiency frontier (EF) approach could better align the prices of biologic therapies for moderate to severe plaque psoriasis with their clinical benefits. The study compared 11 biologics and 2 biosimilars across the US, Australia, Canada, France, and Germany using PASI 90 response rates as the measure of efficacy and annual treatment costs as of January 2023. Aligning US prices with the EF would require a median price reduction of 71%. Certolizumab was found to have a PASI 90 response rate of 45.6% and require an US annual net price reduction of 96% from $31,910 to $1,322 to align with the EF. International price estimates are provided in the eTable of the supplement.

[1] Egilman AC, Kesselheim AS, Avorn J, Raymakers AJN, Rome BN. Use of Efficiency Frontiers to Align Prices and Clinical Benefits of Biologic Therapies for Plaque Psoriasis. JAMA Dermatol. 2024 Apr 1;160(4):409. doi:10.1001/jamadermatol.2023.6236 PubMed PMID: 38381418; PubMed Central PMCID: PMC10882509.

Use and Cost of First-Line Biologic Medications to Treat Plaque Psoriasis in the US[2]
Rome et al. examined trends in the use and cost of first-line biologic medications for plaque psoriasis in the US from 2007 to 2021 using a large national commercial claims database. Over the study period, treatment patterns shifted markedly from older TNF inhibitors toward newer IL-17 and IL-23 inhibitors, with IL-23 inhibitors accounting for 42% of new initiations in 2021. During the same period, the average annual net cost of biologic treatment more than doubled, rising from $21,236 in 2007 to $47,125 in 2021. If patients had initiated the lowest-cost biologic within each mechanistic class, average treatment costs in 2021 would have been an estimated 44% lower.

Identifying Therapeutic Alternatives in Medicare Drug Price Negotiation: The Case of Etanercept[3]
Mooney and colleagues developed a systematic, clinical guideline-based approach to identify therapeutic alternatives for drugs selected for Medicare drug price negotiation, using etanercept as an example. The authors identified 22 potential therapeutic alternatives across etanercept's indications, including 4 other TNF inhibitors, 10 biologics with different mechanisms of action, and 8 small-molecule drugs, with the number of alternatives varying by indication. As a TNF inhibitor, certolizumab pegol (Cimzia) was considered a within-class therapeutic alternative for etanercept for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and adult plaque psoriasis.

Utilization and Treatment Costs of Tumor Necrosis Factor Inhibitors After the Introduction of Biosimilar Infliximab in the United States[4]
Kim and coauthors examined utilization patterns and insurer treatment costs for tumor necrosis factor inhibitors (TNFi) in the US from 2016 to 2019 following the introduction of biosimilar infliximab. Using claims data from a large national commercial insurer, the authors found that originator TNF inhibitors continued to dominate the market, while biosimilar infliximab uptake remained below 1% throughout the study period. Across all originator TNFi, mean quarterly insurer costs per treated patient increased over time, and early biosimilar infliximab prices were similar to those of originator infliximab, limiting incentives for switching. Certolizumab accounted for a smaller share of TNFi use than adalimumab and etanercept, but experienced cost increases comparable to other originator biologics.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Cimzia. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

PORTAL Program On Regulation, Therapeutics, And Law

[2] Rome BN, Han J, Mooney H, Kesselheim AS. Use and Cost of First-Line Biologic Medications to Treat Plaque Psoriasis in the US. JAMA Dermatol. 2025 Jun 1;161(6):622. doi:10.1001/jamadermatol.2025.0669 PubMed PMID: 40238112; PubMed Central PMCID: PMC12004245.
[3] Mooney H, Martin MJ, Bendicksen L, Kesselheim AS, Rome BN, Lalani HS. Identifying therapeutic alternatives in Medicare drug price negotiation: The case of etanercept. JMCP. 2024 Mar 1;30(3):226–33. doi:10.18553/jmcp.2023.23209 PubMed PMID: 38088900; PubMed Central PMCID: PMC10906443.
[4] Kim SC, Sarpatwari A, Landon JE, Desai RJ. Utilization and Treatment Costs of Tumor Necrosis Factor Inhibitors After the Introduction of Biosimilar Infliximab in the United States. Arthritis Rheumatol. 2020 Jun;72(6):1036–8. doi:10.1002/art.41201 PubMed PMID: 31943866.

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7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Cosentyx (secukinumab)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Cosentyx (secukinumab) and its therapeutic alternatives:

Use of Efficiency Frontiers to Align Prices and Clinical Benefits of Biologic Therapies for Plaque Psoriasis[1]

Egilman and coauthors assessed whether an efficiency frontier (EF) approach could better align the prices of biologic therapies for moderate to severe plaque psoriasis with their clinical benefits. The study compared 11 biologics and 2 biosimilars across the US, Australia, Canada, France, and Germany using PASI 90 response rates as the measure of efficacy and annual treatment costs as of January 2023. Aligning US prices with the EF would require a median price reduction of 71%. Secukinumab was found to have a PASI 90 response rate of 61.4% and require an US annual net price reduction of 70% from $36,926 to $11,019 to align with the EF. International price estimates are provided in the eTable of the study supplement.

[1] Egilman AC, Kesselheim AS, Avorn J, Raymakers AJN, Rome BN. Use of Efficiency Frontiers to Align Prices and Clinical Benefits of Biologic Therapies for Plaque Psoriasis. JAMA Dermatol. 2024 Apr 1;160(4):409. doi:10.1001/jamadermatol.2023.6236 PMID: 38381418; PMCID: PMC10882509.

Use and Cost of First-Line Biologic Medications to Treat Plaque Psoriasis in the US[2]
Rome et al. examined trends in the use and cost of first-line biologic medications for plaque psoriasis in the US from 2007 to 2021 using a large national commercial claims database. Over the study period, treatment patterns shifted markedly from older TNF inhibitors toward newer IL-17 and IL-23 inhibitors, with IL-23 inhibitors accounting for 42% of new initiations in 2021. During the same period, the average annual net cost of biologic treatment more than doubled, rising from $21,236 in 2007 to $47,125 in 2021. The authors estimated that if patients had initiated the lowest-cost biologic within each mechanistic class, average treatment costs in 2021 would have been 44% lower.

Identifying Therapeutic Alternatives in Medicare Drug Price Negotiation: The Case of Etanercept[3]
Mooney and colleagues developed a systematic, clinical guideline-based approach to identify therapeutic alternatives for drugs selected for Medicare drug price negotiation, using etanercept (Enbrel) as an example. The authors identified 22 potential therapeutic alternatives across etanercept's indications, including 4 other TNF inhibitors, 10 biologics with different mechanisms of action, and 8 small-molecule drugs, with the number of alternatives varying by indication. Secukinumab was recommend in clinical guidelines in the same treatment as etanercept for multiple indications, highlighting how drugs in other therapeutic classes may be reasonable comparators.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Cosentyx. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

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[2] Rome BN, Han J, Mooney H, Kesselheim AS. Use and Cost of First-Line Biologic Medications to Treat Plaque Psoriasis in the US. JAMA Dermatol. 2025 Jun 1;161(6):622. doi:10.1001/jamadermatol.2025.0669 PMID: 40238112; PMCID: PMC12004245.
[3] Mooney H, Martin MJ, Bendicksen L, Kesselheim AS, Rome BN, Lalani HS. Identifying therapeutic alternatives in Medicare drug price negotiation: The case of etanercept. JMCP. 2024 Mar 1;30(3):226–33. doi:10.18553/jmcp.2023.23209 PMID: 38088900; PMCID: PMC10906443.

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Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Entyvio (vedolizumab)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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Below, we have included a summary of a peer-reviewed publication from our group that we think may be valuable to CMS' evidence-based assessment of Entyvio (vedolizumab) and its therapeutic alternatives:

Public-Sector Contributions to Novel Biologic Drugs[1]
Nayak and colleagues examined the extent of public-sector contributions to the late-stage development of novel biologic drugs approved by the FDA between 2008 and 2017. Among 69 new biologic drugs, the authors found that 29 drugs (42%) had evidence of late-stage financial or intellectual support from public-sector institutions, such as government agencies, universities, or nonprofit research centers. This includes vedolizumab, for which research conducted at Massachusetts General Hospital was instrumental (see Supplement eTable 2).

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Entyvio. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

[1] Nayak RK, Lee CC, Avorn J, Kesselheim AS. Public-Sector Contributions to Novel Biologic Drugs. JAMA Intern Med. 2021 Nov 1;181(11):1522–5. doi:10.1001/jamainternmed.2021.3720 PubMed PMID: 34279545; PubMed Central PMCID: PMC8290329.

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Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Erleada (apalutamide)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Cancer Innovation and Regulation Initiative and the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

As detailed in prior comments on CMS' Draft Guidance on the Medicare Drug Price Negotiation Program,[1] we recommend that the agency use the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in assessing section 1194(e)(2) factors relating to the therapeutic value and comparative effectiveness of negotiation-eligible cancer products.

Background on the ESMO Magnitude of Clinical Benefit Scale

ESMO (European Society for Medical Oncology, representing >40,000 cancer specialists from 177 countries) developed the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in 2015 to facilitate improved decision-making regarding the value of cancer therapies.[2] The ESMO-MCBS was developed in a rigorous and transparent process with peer review and feedback from patient representatives, clinicians, statisticians, and researchers. ESMO-MCBS scores for new drugs are incorporated into cancer guidelines, helping to provide patients and clinicians globally with the best care options for their conditions.

The ESMO-MCBS tool can be used to score cancer drugs using publicly available outcome data: overall survival, progression- and disease-free survival, quality of life, response rates, and toxicity. Separate

[1] Centers for Medicare and Medicaid Services. Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2028 and Manufacturer Effectuation of the Maximum Fair Price in 2026, 2027, and 2028. May 2025.
[2] The ESMO-MCBS Scorecards for approved cancer drugs and indications are available online at esmo.org; widely cited in the peer-reviewed scientific literature; and used as part of Health Technology Assessment (HTA) processes in >15 countries.

scoring forms are provided for the curative (scores range from A to C, with A representing the highest score) and non-curative (scores range from 5 to 1, with 5 indicating the highest score) settings. The ESMO-MCBS does not incorporate any cost-effectiveness or quality-adjusted life year information.

Section 1194(e)(2) of the Inflation Reduction Act directs CMS to consider evidence about alternative treatments to the selected drug, including the extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the comparative effectiveness of the selected drug and its therapeutic alternative(s). **In general, cancer medicines with ESMO-MCBS scores of A or B (for therapies with curative intent) and 4 or 5 (for those with non-curative intent) should be highlighted for high therapeutic value.**

ESMO-MCBS Scores for Selected Drugs for Price Applicability Year 2028

Please see below ESMO-MCBS scoring for apalutamide (Erleada) for all approved indications as of February 2026. This benefit scoring information could be relevant for CMS in adjusting the starting point for these selected cancer medicines (as well as comparison of scoring for therapeutic alternatives). ESMO-MCBS is a potentially useful tool for informing section 1194(e)(2) adjustment moving forward.

Drug	Indication	ESMO-MCBS Score
Apalutamide (Erleada)	Metastatic castration-sensitive prostate cancer	**4 (High Benefit)**
	Non-metastatic castration-resistant prostate cancer	**4 (High Benefit)**

Please also see below ESMO-MCBS scoring for potential therapeutic alternatives for apalutamide based on the relevant National Comprehensive Cancer Network (NCCN) practice guidelines.

Drug	Indication	ESMO-MCBS Score	Therapeutic Alternative	ESMO-MCBS Score for Alternative
Apalutamide (Erleada)	Metastatic castration-sensitive prostate cancer	**4 (High Benefit)**	Enzalutamide (Xtandi)	**4 (High Benefit)**
			Darolutamide (Nubeqa)	**4 (High Benefit)**
			Abiraterone (Zytiga; generics)	**4 (High Benefit)**
	Non-metastatic castration-resistant prostate cancer	**4 (High Benefit)**	Enzalutamide (Xtandi)	3
			Darolutamide (Nubeqa)	3

CONCLUSION

We thank CMS for the opportunity to provide comment on the selected drugs for Initial Price Applicability Year 2028. PORTAL is available to discuss these issues at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

These comments were prepared with input from: Thomas Hwang, M.D.; Ariadna Tibau, M.D.; and Aaron S. Kesselheim, M.D., J.D., M.P.H.

PORTAL Program On Regulation, Therapeutics, And Law

March 1, 2026

Dr. Mehmet Oz, Administrator
Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Kisqali (ribociclib)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Cancer Innovation and Regulation Initiative and the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

As detailed in prior comments on CMS' Draft Guidance on the Medicare Drug Price Negotiation Program,[1] we recommend that the agency use the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in assessing section 1194(e)(2) factors relating to the therapeutic value and comparative effectiveness of negotiation-eligible cancer products.

Background on the ESMO Magnitude of Clinical Benefit Scale

ESMO (European Society for Medical Oncology, representing >40,000 cancer specialists from 177 countries) developed the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in 2015 to facilitate improved decision-making regarding the value of cancer therapies.[2] The ESMO-MCBS was developed in a rigorous and transparent process with peer review and feedback from patient representatives, clinicians, statisticians, and researchers. ESMO-MCBS scores for new drugs are incorporated into cancer guidelines, helping to provide patients and clinicians globally with the best care options for their conditions.

The ESMO-MCBS tool can be used to score cancer drugs using publicly available outcome data: overall survival, progression- and disease-free survival, quality of life, response rates, and toxicity. Separate

[1] Centers for Medicare and Medicaid Services. Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2028 and Manufacturer Effectuation of the Maximum Fair Price in 2026, 2027, and 2028. May 2025.
[2] The ESMO-MCBS Scorecards for approved cancer drugs and indications are available online at esmo.org; widely cited in the peer-reviewed scientific literature; and used as part of Health Technology Assessment (HTA) processes in >15 countries.

scoring forms are provided for the curative (scores range from A to C, with A representing the highest score) and non-curative (scores range from 5 to 1, with 5 indicating the highest score) settings. The ESMO-MCBS does not incorporate any cost-effectiveness or quality-adjusted life year information.

Section 1194(e)(2) of the Inflation Reduction Act directs CMS to consider evidence about alternative treatments to the selected drug, including the extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the comparative effectiveness of the selected drug and its therapeutic alternative(s). **In general, cancer medicines with ESMO-MCBS scores of A or B (for therapies with curative intent) and 4 or 5 (for those with non-curative intent) should be highlighted for high therapeutic value.**

ESMO-MCBS Scores for Selected Drugs for Price Applicability Year 2028

Please see below ESMO-MCBS scoring for ribociclib (Kisqali) for all approved indications as of February 2026. This benefit scoring information could be relevant for CMS in adjusting the starting point for these selected cancer medicines (as well as comparison of scoring for therapeutic alternatives). ESMO-MCBS is a potentially useful tool for informing section 1194(e)(2) adjustment moving forward.

Drug	Indication	ESMO-MCBS Score
Ribociclib (Kisqali)	Adjuvant treatment of HR+, HER2-, stage II/III early breast cancer at high risk of recurrence, in combination with an aromatase inhibitor	**A (High Benefit)**
	HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine therapy	**4 (High Benefit)**
	HR+, HER2- advanced or metastatic breast cancer with fulvestrant as initial endocrine therapy or following disease progression after endocrine therapy	**4 (High Benefit)**

Please also see below ESMO-MCBS scoring for potential therapeutic alternatives for ribociclib based on the relevant National Comprehensive Cancer Network (NCCN) practice guidelines.

Drug	Indication	ESMO-MCBS Score	Therapeutic Alternative	ESMO-MCBS Score for Alternative
Ribociclib (Kisqali)	Adjuvant treatment of HR+, HER2-, stage II/III early breast cancer at high risk of recurrence, with an aromatase inhibitor	**A (High Benefit)**	Abemaciclib** (Verzenio)	**A (High Benefit)**
	HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine therapy	**4* (High Benefit)**	Abemaciclib (Verzenio)	1
			Palbociclib (Ibrance)	2
	HR+, HER2- advanced or metastatic breast cancer with fulvestrant as initial endocrine therapy or following disease progression after endocrine therapy	**4 (High Benefit)**	Abemaciclib (Verzenio)	3
			Palbociclib (Ibrance)	**4 (High Benefit)**

Notes: ** ESMO-MCBS scores of 4 for both pre/peri-menopausal and postmenopausal patients for this indication (studied in the MONALEESA-7 and MONALEESA-2 clinical trials). ** Approved for adjuvant treatment of node-positive early breast cancer.*

CONCLUSION

We thank CMS for the opportunity to provide comment on the selected drugs for Initial Price Applicability Year 2028. PORTAL is available to discuss these issues at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

These comments were prepared with input from: Thomas Hwang, M.D.; Ariadna Tibau, M.D.; and Aaron S. Kesselheim, M.D., J.D., M.P.H.

PORTAL Program On Regulation, Therapeutics, And Law

March 1, 2026

Dr. Mehmet Oz, Administrator
Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Lenvima (lenvatinib)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Cancer Innovation and Regulation Initiative and the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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As detailed in prior comments on CMS' Draft Guidance on the Medicare Drug Price Negotiation Program,[1] we recommend that the agency use the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in assessing section 1194(e)(2) factors relating to the therapeutic value and comparative effectiveness of negotiation-eligible cancer products.

Background on the ESMO Magnitude of Clinical Benefit Scale

ESMO (European Society for Medical Oncology, representing >40,000 cancer specialists from 177 countries) developed the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in 2015 to facilitate improved decision-making regarding the value of cancer therapies.[2] The ESMO-MCBS was developed in a rigorous and transparent process with peer review and feedback from patient representatives, clinicians, statisticians, and researchers. ESMO-MCBS scores for new drugs are incorporated into cancer guidelines, helping to provide patients and clinicians globally with the best care options for their conditions.

The ESMO-MCBS tool can be used to score cancer drugs using publicly available outcome data: overall survival, progression- and disease-free survival, quality of life, response rates, and toxicity. Separate

[1] Centers for Medicare and Medicaid Services. Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2028 and Manufacturer Effectuation of the Maximum Fair Price in 2026, 2027, and 2028. May 2025.
[2] The ESMO-MCBS Scorecards for approved cancer drugs and indications are available online at esmo.org; widely cited in the peer-reviewed scientific literature; and used as part of Health Technology Assessment (HTA) processes in >15 countries.

scoring forms are provided for the curative (scores range from A to C, with A representing the highest score) and non-curative (scores range from 5 to 1, with 5 indicating the highest score) settings. The ESMO-MCBS does not incorporate any cost-effectiveness or quality-adjusted life year information.

Section 1194(e)(2) of the Inflation Reduction Act directs CMS to consider evidence about alternative treatments to the selected drug, including the extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the comparative effectiveness of the selected drug and its therapeutic alternative(s). **In general, cancer medicines with ESMO-MCBS scores of A or B (for therapies with curative intent) and 4 or 5 (for those with non-curative intent) should be highlighted for high therapeutic value.**

ESMO-MCBS Scores for Selected Drugs for Price Applicability Year 2028

Please see below ESMO-MCBS scoring for lenvatinib (Lenvima) for all approved indications as of February 2026. This benefit scoring information could be relevant for CMS in adjusting the starting point for these selected cancer medicines (as well as comparison of scoring for therapeutic alternatives). ESMO-MCBS is a potentially useful tool for informing section 1194(e)(2) adjustment moving forward.

Drug	Indication	ESMO-MCBS Score*
Lenvatinib (Lenvima)	Locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer	2
	Advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy	**4 (High Benefit)**
	Advanced RCC in combination with pembrolizumab	**4 (High Benefit)**
	Advanced endometrial carcinoma that is mismatch repair proficient or not microsatellite instability-high, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation	**4 (High Benefit)**
	Unresectable hepatocellular carcinoma	No Evaluable Benefit (NEB)

Please also see below ESMO-MCBS scoring for potential therapeutic alternatives for lenvatinib based on the relevant National Comprehensive Cancer Network (NCCN) practice guidelines.

Drug	Indication	ESMO-MCBS Score*	Therapeutic Alternative	ESMO-MCBS Score for Alternative
Lenvatinib (Lenvima)	Locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer	2	Sorafenib (Nexavar; generics)	2
	Advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy*	**4 (High Benefit)**	Nivolumab (Opdivo)	**5 (High Benefit)**
			Cabozantinib (Cabometyx)	3
			Ipilumab + nivolumab (Yervoy/Opdivo)	2
			Lenvatinib + pembrolizumab (Lenvima/Keytruda)	2
	Advanced RCC in combination with pembrolizumab	**4 (High Benefit)**	Axitinib + pembrolizumab (Inlyta/generic / Keytruda)	**4 (High Benefit)**
			Cabozantinib + nivolumab (Cabometyx/Opdivo)	**4 (High Benefit)**
	Advanced endometrial carcinoma that is mismatch repair proficient or not microsatellite instability-high, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation	**4 (High Benefit)**	Axitinib + avelumab (Inlyta/generic / Bavencio)	2
	Unresectable hepatocellular carcinoma**	No Evaluable Benefit (NEB)	Atezolizumab + bevacizumab (Tecentriq/Avastin)	**5 (High Benefit)**
			Tremelimumab + durvalumab (Imjudo/Imfinzi)	**5 (High Benefit)**

Notes: ** Therapeutic alternatives for subsequent therapy for patients with prior immunotherapy include belzutifan (ESMO-MCBS score 1) and tivozanib (ESMO-MCBS score 3). Per the NCCN guidelines, additional therapeutic alternatives for subsequent therapy for patients without prior immunotherapy include axitinib + pembrolizumab (not included in FDA approved labeling) and cabozantinib + nivolumab (not included in FDA approved labeling). ** Atezolizumab + bevacizumab and tremelimumab + durvalumab are the preferred regimens for first-line systemic therapy. Lenvatinib is listed for this indication in a less-favorable guideline position (other recommended regimens) alongside multiple other options.*

CONCLUSION

We thank CMS for the opportunity to provide comment on the selected drugs for Initial Price Applicability Year 2028. PORTAL is available to discuss these issues at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

These comments were prepared with input from: Thomas Hwang, M.D.; Ariadna Tibau, M.D.; and Aaron S. Kesselheim, M.D., J.D., M.P.H.

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March 1, 2026

Dr. Mehmet Oz, Administrator
Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Orencia (abatacept)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of a peer-reviewed publication from our group that we think may be valuable to CMS' evidence-based assessment of Orencia (abatacept) and its therapeutic alternatives:

Added Therapeutic Benefit of Top-Selling Brand-Name Drugs in Medicare[1]
Egilman and colleagues examined the added therapeutic benefit of the 50 highest-selling drugs in Medicare in 2020 as assessed by the national health technology assessment agencies in France, Germany, or Canada. They found that 27 drugs (55%) had a low added therapeutic benefit rating by at least one country's HTA, representing $19.5 billion (35%) of estimated net Medicare spending in 2020 on the top 50 single-source drugs. Abatacept received a "high" added therapeutic benefit rating in Canada and France with an "Important" absolute therapeutic benefit rating in France.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Orencia (abatacept). PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

[1] Egilman AC, Rome BN, Kesselheim AS. Added Therapeutic Benefit of Top-Selling Brand-name Drugs in Medicare. JAMA. 2023 Apr 18;329(15):1283. doi:10.1001/jama.2023.4034 PubMed PMID: 37071095; PubMed Central PMCID: PMC10114018.

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Chris Klomp, Deputy Administrator
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7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Rexulti (brexpiprazole)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of a peer-reviewed publication from our group that we think may be valuable to CMS' evidence-based assessment of Rexulti (brexpiprazole) and its therapeutic alternatives:

Characteristics of Trials Preceding FDA Approval of Novel Psychiatric Drugs[1]
In a 2025 study, Ahn-Horst and colleagues examined the clinical trial evidence supporting all novel psychiatric drugs approved by the US Food and Drug Administration between 2013 and 2024. Among the 16 approved drugs, the FDA reviewed 73 efficacy trials, of which 62% were judged positive, and 46 were designated as pivotal, with a median of 3 pivotal trials per drug. Although most approvals were supported by multiple positive trials, 3 drugs were approved despite having more negative or failed efficacy trials than positive ones, including brexpiprazole as an adjunctive therapy for major depressive disorder, highlighting the variability in the strength of evidence underlying psychiatric drug approvals

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Rexulti. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

[1] Ahn-Horst RY, Turner EH, Kesselheim AS. Characteristics of Trials Preceding FDA Approval of Novel Psychiatric Drugs. JAMA Netw Open. 2025 Jan 27;8(1):e2456588. doi:10.1001/jamanetworkopen.2024.56588 PubMed PMID: 39869338; PubMed Central PMCID: PMC11774090.

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March 1, 2026

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7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Tradjenta (linagliptin)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Tradjenta (linagliptin) and its therapeutic alternatives:

Added Therapeutic Benefit of Top-Selling Brand-Name Drugs in Medicare[1]
Egilman and colleagues examined the added therapeutic benefit of the 50 highest-selling drugs in Medicare in 2020 as assessed by the national health technology assessment agencies in France, Germany, or Canada. They found that 27 drugs (55%) had a low added therapeutic benefit rating by at least one country's HTA, representing $19.5 billion (35%) of estimated net Medicare spending in 2020 on the top 50 single-source drugs. Linagliptin received a "low" added therapeutic benefit rating in Canada, France, and Germany, with an "Important" absolute therapeutic benefit rating in France.

Diabetes Drugs: List Price Increases Were Not Always Reflected In Net Price; Impact Of Brand Competition Unclear[2]
Sarpatwari et al. examined changes in list and net prices of three major classes of brand-name diabetes drugs (GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT-2 inhibitors) from initial market entry through 2017. Across all three classes, list prices increased by roughly 8-15% annually, but changes in net prices varied substantially. Net prices rose for GLP-1 agonists but declined for DPP-4 inhibitors (-

[1] Egilman AC, Rome BN, Kesselheim AS. Added Therapeutic Benefit of Top-Selling Brand-name Drugs in Medicare. JAMA. 2023 Apr 18;329(15):1283. doi:10.1001/jama.2023.4034 PubMed PMID: 37071095; PubMed Central PMCID: PMC10114018.
[2] Sarpatwari A, Tessema FA, Zakarian M, Najafzadeh MN, Kesselheim AS. Diabetes Drugs: List Price Increases Were Not Always Reflected In Net Price; Impact Of Brand Competition Unclear. Health Aff (Millwood). 2021 May;40(5):772–8. doi:10.1377/hlthaff.2020.01436 PubMed PMID: 33939506.

2% annually) and SGLT-2 inhibitors (-9% annually), suggesting that brand-brand competition affected net prices in some classes but not others. For DPP-4 inhibitors specifically, the introduction of multiple branded competitors, including linagliptin, was associated with stable or declining net prices despite continued list-price increases.

We thank CMS for the opportunity to submit our research for consideration during the re-negotiation of the maximum fair price for Tradjenta. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

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Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Trulicity (dulaglutide)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

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Below, we have included a summary of peer-reviewed publications from our group that we think may be valuable to CMS' evidence-based assessment of Trulicity (dulaglutide) and its therapeutic alternatives:

Added Therapeutic Benefit of Top-Selling Brand-Name Drugs in Medicare[1]
Egilman and colleagues examined the added therapeutic benefit of the 50 highest-selling drugs in Medicare in 2020 as assessed by the national health technology assessment agencies in France, Germany, or Canada. They found that 27 drugs (55%) had a low added therapeutic benefit rating by at least one country's HTA, representing $19.5 billion (35%) of estimated net Medicare spending in 2020 on the top 50 single-source drugs. Dulaglutide received a "low" added therapeutic benefit rating in Canada, France, and Germany, with an "Important" absolute therapeutic benefit rating in France.

Patent Portfolios Protecting 10 Top-Selling Prescription Drugs[2]
Horrow et al. examined the patent portfolios protecting the 10 highest-selling prescription drugs in the US in 2021, including dulaglutide. They found that nearly three-quarters of all patents and applications were filed after FDA approval, with post-approval patent filings more common for biologics than for small-molecule drugs (80% vs 58%). For biologics, patent thickets peaked around 13 years after FDA approval, at a median of 41 active patents. Visualizations of the patent thicket surrounding dulaglutide are presented in eFigure 1 and eFigure 2 in the study supplement.

[1] Egilman AC, Rome BN, Kesselheim AS. Added Therapeutic Benefit of Top-Selling Brand-name Drugs in Medicare. JAMA. 2023 Apr 18;329(15):1283. doi:10.1001/jama.2023.4034 PubMed PMID: 37071095; PubMed Central PMCID: PMC10114018.
[2] Horrow C, Gabriele SME, Tu SS, Sarpatwari A, Kesselheim AS. Patent Portfolios Protecting 10 Top-Selling Prescription Drugs. JAMA Intern Med. 2024 Jul 1;184(7):810. doi:10.1001/jamainternmed.2024.0836 PubMed PMID: 38739386; PubMed Central PMCID: PMC11091822.

Therapeutic Value of Drugs Frequently Marketed Using Direct-to-Consumer Television Advertising, 2015 to 2021[3]

Patel and colleagues assessed the therapeutic value of prescription drugs that were most frequently marketed through US direct-to-consumer (DTC) television advertising between 2015 and 2021. Among 73 heavily advertised drugs with at least one health technology assessment rating, 53 (73%), representing $15.9 billion in advertising spending, were rated as providing low added therapeutic value, suggesting that the majority of DTC advertising promotes drugs offering limited clinical advances over available alternatives. Dulaglutide was among the top-advertised drugs in the study cohort and was categorized as having "low" added therapeutic benefit by HTA agencies in Canada, France, and Germany.

Generic Liraglutide — Overlooked but Not Forgotten[4]

In this commentary, the authors discuss liraglutide, one of the earliest GLP-1 receptor agonists which is now available in generic form. Although liraglutide has been largely displaced in clinical practice by newer GLP-1 agents because of greater efficacy and more convenient weekly dosing, the authors emphasize that liraglutide should still be considered a clinically reasonable comparator when assessing the relative value and pricing of newer GLP-1 drugs such as dulaglutide.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Trulicity. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

PORTAL Program On Regulation, Therapeutics, And Law

[3] Patel NG, Hwang TJ, Woloshin S, Kesselheim AS. Therapeutic Value of Drugs Frequently Marketed Using Direct-to-Consumer Television Advertising, 2015 to 2021. JAMA Netw Open. 2023 Jan 13;6(1):e2250991. doi:10.1001/jamanetworkopen.2022.50991 PubMed PMID: 36637824; PubMed Central PMCID: PMC9857401.
[4] Gondi S, Kesselheim AS, Rome BN. Generic Liraglutide — Overlooked but Not Forgotten. N Engl J Med. 2026 Jan 8;394(2):107–10. doi:10.1056/NEJMp2515668 PubMed PMID: 41370797.

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Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Verzenio (abemaciclib)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Cancer Innovation and Regulation Initiative and the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

As detailed in prior comments on CMS' Draft Guidance on the Medicare Drug Price Negotiation Program,[1] we recommend that the agency use the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in assessing section 1194(e)(2) factors relating to the therapeutic value and comparative effectiveness of negotiation-eligible cancer products.

Background on the ESMO Magnitude of Clinical Benefit Scale

ESMO (European Society for Medical Oncology, representing >40,000 cancer specialists from 177 countries) developed the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) in 2015 to facilitate improved decision-making regarding the value of cancer therapies.[2] The ESMO-MCBS was developed in a rigorous and transparent process with peer review and feedback from patient representatives, clinicians, statisticians, and researchers. ESMO-MCBS scores for new drugs are incorporated into cancer guidelines, helping to provide patients and clinicians globally with the best care options for their conditions.

The ESMO-MCBS tool can be used to score cancer drugs using publicly available outcome data: overall survival, progression- and disease-free survival, quality of life, response rates, and toxicity. Separate

[1] Centers for Medicare and Medicaid Services. Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2028 and Manufacturer Effectuation of the Maximum Fair Price in 2026, 2027, and 2028. May 2025.
[2] The ESMO-MCBS Scorecards for approved cancer drugs and indications are available online at esmo.org; widely cited in the peer-reviewed scientific literature; and used as part of Health Technology Assessment (HTA) processes in >15 countries.

scoring forms are provided for the curative (scores range from A to C, with A representing the highest score) and non-curative (scores range from 5 to 1, with 5 indicating the highest score) settings. The ESMO-MCBS does not incorporate any cost-effectiveness or quality-adjusted life year information.

Section 1194(e)(2) of the Inflation Reduction Act directs CMS to consider evidence about alternative treatments to the selected drug, including the extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the comparative effectiveness of the selected drug and its therapeutic alternative(s). **In general, cancer medicines with ESMO-MCBS scores of A or B (for therapies with curative intent) and 4 or 5 (for those with non-curative intent) should be highlighted for high therapeutic value.**

ESMO-MCBS Scores for Selected Drugs for Price Applicability Year 2028

Please see below ESMO-MCBS scoring for abemaciclib (Verzenio) for all approved indications as of February 2026. This benefit scoring information could be relevant for CMS in adjusting the starting point for these selected cancer medicines (as well as comparison of scoring for therapeutic alternatives). ESMO-MCBS is a potentially useful tool for informing section 1194(e)(2) adjustment moving forward.

Drug	Indication	ESMO-MCBS Score
Abemaciclib (Verzenio)	Adjuvant treatment of HR+, HER2-, node-positive early breast cancer at high risk of recurrence, in combination with endocrine therapy	**A (High Benefit)**
	HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine therapy	1
	HR+, HER2- advanced or metastatic breast cancer with fulvestrant in patients with disease progression after endocrine therapy	3
	HR+, HER2- advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting	3

Please also see below ESMO-MCBS scoring for potential therapeutic alternatives for abemaciclib based on the relevant National Comprehensive Cancer Network (NCCN) practice guidelines.

Drug	Indication	ESMO-MCBS Score	Therapeutic Alternative	ESMO-MCBS Score for Alternative
Abemaciclib (Verzenio)	Adjuvant treatment of HR+, HER2-, node-positive early breast cancer at high risk of recurrence, in combination with endocrine therapy	**A (High Benefit)**	Ribociclib (Kisqali)	**A (High Benefit)**
	HR+, HER2- advanced metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine therapy	1	Ribociclib (Kisqali)	**4 (High Benefit)**
			Palbociclib (Ibrance)	2
	HR+, HER2- advanced or metastatic breast cancer with fulvestrant in patients with disease progression after endocrine therapy	3	Ribociclib (Kisqali)	**4 (High Benefit)**
			Palbociclib (Ibrance)	**4 (High Benefit)**
	HR+, HER2- advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting	3	Megestrol, estradiol, targeted therapy	—

CONCLUSION

We thank CMS for the opportunity to provide comment on the selected drugs for Initial Price Applicability Year 2028. PORTAL is available to discuss these issues at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

These comments were prepared with input from: Thomas Hwang, M.D.; Ariadna Tibau, M.D.; and Aaron S. Kesselheim, M.D., J.D., M.P.H.

PORTAL Program On Regulation, Therapeutics, And Law

PORTAL Program On Regulation, Therapeutics, And Law
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March 1, 2026

Dr. Mehmet Oz, Administrator
Chris Klomp, Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation for Initial Price Applicability Year 2028 (CMS-10849)
Selected Drug: Xeljanz; Xeljanz XR (tofacitinib)

Dear Administrator Oz and Deputy Administrator Klomp:

On behalf of the Program On Regulation, Therapeutics, And Law (PORTAL), we appreciate the opportunity to submit comments to the Centers for Medicare and Medicaid Services (CMS) on the selected drugs for Medicare Drug Price Negotiation for Initial Price Applicability Year 2028.

Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, PORTAL is one of the largest academic research centers in the United States dedicated to investigating the regulation, use, evidence, and cost of prescription drugs. Our research program is independent of the pharmaceutical industry.

Below, we have included a summary of a peer-reviewed publication from our group that we think may be valuable to CMS' evidence-based assessment of Xeljanz (tofacitinib) and its therapeutic alternatives:

Therapeutic Value of Drugs Frequently Marketed Using Direct-to-Consumer Television Advertising, 2015 to 2021[1]
Patel and colleagues assessed the therapeutic value of prescription drugs that were most frequently marketed through US direct-to-consumer (DTC) television advertising between 2015 and 2021. Among 73 heavily advertised drugs with at least one health technology assessment (HTA) rating, 53 (73%), representing $15.9 billion in advertising spending, were rated as providing low added therapeutic value, suggesting that the majority of DTC advertising promotes drugs offering limited clinical advances over available alternatives. Tofacitinib was among the top-advertised drugs in the study cohort and was categorized as having "low" added therapeutic benefit by HTA agencies in Canada, France, and Germany for the treatment of rheumatoid arthritis.

We thank CMS for the opportunity to submit our research for consideration during the price negotiation of Xeljanz. PORTAL is available to discuss our research at any time, and we welcome further engagement with CMS to deliver lower drug prices for Medicare beneficiaries.

This submission was prepared with input from Matthew J. Martin, M.A. and Aaron S. Kesselheim, M.D., J.D., M.P.H.

[1] Patel NG, Hwang TJ, Woloshin S, Kesselheim AS. Therapeutic Value of Drugs Frequently Marketed Using Direct-to-Consumer Television Advertising, 2015 to 2021. JAMA Netw Open. 2023 Jan 13;6(1):e2250991. doi:10.1001/jamanetworkopen.2022.50991 PubMed PMID: 36637824; PubMed Central PMCID: PMC9857401.