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Health Technology Assessment (HTA) in Prescription Drug Coverage and Pricing Decisions: Examples from Other Countries

Guidance for State Prescription Drug Affordability Boards
October 22, 2024

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Executive Summary

Some state Prescription Drug Affordability Boards (PDABs) are tasked with setting upper payment limits for drugs that are deemed unaffordable. States may consider several factors when determining appropriate upper payment limits, including drug costs in other countries. States also may wish to replicate processes from other countries that use health technology assessment (HTA) to negotiate prices. However, a barrier to using such information is that some states are precluded from considering data derived from quality-adjusted life-years (QALYs), which some international HTA organizations use. To inform state PDABs, this memo summarizes how certain countries use HTA, often in tandem with other government agencies, to make coverage decisions and negotiate prices, including how each country uses QALYs or alternative measures to assess drugs compared to therapeutic alternatives. We also provide details on how to access health technology assessment and pricing information in each country to the extent such information is made public.

Background

Many high-income countries around the world routinely perform HTA for new drugs to inform coverage and prices. HTA includes multidisciplinary processes to assess and examine dimensions of value for new technologies, including prescription drugs. HTA can include a variety of considerations and methods, including clinical effectiveness, safety, costs and economic implications, ethical, social, cultural, and legal issues, organizational and environmental aspects, and consequences for patients, relatives and caregivers, and the broader population.[1] A formal HTA process examines the consequences (intended or not) of using a prescription drug compared to alternatives to inform decision-making.[2]

It is uncommon for countries to use HTA to unilaterally set maximum prices for prescription drugs. More commonly, HTA bodies evaluate a drug's cost-effectiveness or value for money based on the price set by the manufacturer and recommend whether the national health system should cover drugs at the current price or whether a discount is needed before coverage should be considered. Such analyses

[1] O'Rourke B, Oortwijn W, Schuller T, the International Join Task Group. The new definition of health technology assessment: A milestone in international collaboration. *International Journal of Technology Assessment in Health Care*. 2020;36(3):187-190.
[2] *Ibid.*

then inform subsequent price negotiation processes between the payer (e.g., the national health insurance plan) and the drug manufacturer.[3]

The country-specific HTA and pricing approaches described here were selected from high-income countries with well-documented procedures and guidance. We also selected countries that demonstrate a range of approaches. Of these countries, only Germany's HTA process does not use QALY-based analyses (**Table 2**). However, the variety of approaches employed (**Table 3**), even among countries that use QALYs as a component of HTA and pricing, include strategies that could be replicated by PDABs using alternative outcome measures.

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[3] Syversen ID, Schulman K, Kesselheim AS, Feldman WB. A Comparative Analysis of International Drug Price Negotiation Frameworks: An Interview Study of Key Stakeholders. *The Milbank Quarterly*. Published online September 17, 2024:1-28.

England (United Kingdom)

HTA Agency
National Institute for Health and Care Excellence (NICE)

HTA Authority
NICE determines whether the National Health Service (NHS) will cover a drug. Drugs that NICE does not review are either covered under the statutory scheme, a centralized price-setting process typically reserved for older medicines, or there is local discretion on coverage. If NICE recommends a drug, it must be covered by the national health system.

Primary Basis of Recommendation
Formal cost-effectiveness analysis, including QALYs, with a value-for-money threshold. According to guidelines, a cost-effectiveness threshold or incremental cost-effectiveness ratio (ICER) of less than £20,000-30,000 per QALY gained is considered cost-effective. There are modifiers that raise the threshold (e.g., drugs for ultra-rare or severe diseases), and in recent years, NICE has recommended some drugs even if the ICER exceeds this threshold.

Other Evaluation Methods, Outcomes, or Considerations
In addition to QALYs, NICE always considers analyses using life years gained for any drug that extends life. In some instances, modifiers can be applied that weight QALYs differently, including:[4]

1. Higher weighting of benefits for drugs that treat severe conditions, measured by the absolute QALY shortfall.[5,6]Absolute QALY shortfall is a measure of disease severity: the difference in total QALYs for the population assuming average life expectancy and health status minus the condition-specific population average life expectancy and health status. Conditions that shorten life expectancy (e.g., pediatric or young adult cancers) typically result in a large absolute QALY shortfall.

   A second measure of severity NICE considers is proportional QALY shortfall**:** The proportion of average life expectancy and health lost to the condition, which is determined by dividing general population lifetime QALYs by the condition-specific population QALYs.[7] NICE maps QALY shortfalls (absolute and proportional) to weightings for total QALYs gained from the treatment to modify the analysis of treatments for severe conditions.

2. Higher cost-effectiveness threshold (ICER up to £100,000 per QALY gained) for "highly specialized technologies." These technologies are defined in legislation and treat very rare diseases that have small numbers of patients (prevalence less than 1 per 50,000 people and no

[4] NICE. NICE Health Technology Evaluations: The Manual. October 2023. Tables 6.1 and 6.2.
[5] "Absolute QALY shortfall is the future health, including quality and length of life, that is lost by people living with a condition, compared with the expected future health without the condition over the remaining lifetime of the patients. Absolute QALY shortfall is calculated as the expected total QALYs that people living with a condition would be expected to have with current treatment over their remaining lifetime subtracted from the total QALYs that the general population with the same age and sex distribution would be expected to have." (NICE Health Technology Evaluations: The Manual, Section 6.2.14)
[6] Schneider P, McNamara S, Love-Koh J, Doran T, Gutacker N. QALY Shortfall Calculator. University of York. Published 2021.
[7] "Proportional QALY shortfall represents the proportion of future health, including quality and length of life, that is lost by people living with the condition. Proportional QALY shortfall is calculated by taking the absolute QALY shortfall and dividing it by the remaining QALYs that the general population with the same age and sex distribution would be expected to have over their remaining lifetime." (NICE Health Technology Evaluations: The Manual, Section 6.2.15)

more than 500 people in England eligible for the treatment across all indications), limited or no treatment options, and challenges in conducting research and collecting evidence because of the rarity or other features of the condition.[8,9,10]

Separately, NICE conducts a budget impact analysis, and if a drug's net budget impact is expected to exceed £20 million per year in any of the first three years of its introduction to the health system, then the government will engage in price negotiations. The government may implement a NICE recommendation to impose limitations on coverage, such as through a phased roll-out.[11]

Accessing HTA Information

Final guidance, advice, and quality standards issued by NICE are available in a public database searchable by disease/condition, generic drug name, and other filters.[12] These reviews include a summary of the evidence considered, stakeholder input, and whether a commercial arrangement exists for the drug to provide an additional price discount to the NHS.

Example: Semaglutide (Wegovy) for managing overweight and obesity. Published March 8, 2023.[13]

Party Responsible for Price Negotiation

NICE does not negotiate drug prices; that is the responsibility of the Department of Health and Social Care. The NICE cost-effectiveness evaluation is based on the manufacturer's proposal. If NICE determines that a drug is not cost-effective and should not be covered, the Department of Health and Social Care may negotiate a lower price. NICE may update recommendations based on the new negotiated price; in these cases, positive recommendations are often conditional on the manufacturer supplying the drug at the negotiated price. Negotiated prices or other discount schemes are usually confidential.

If NICE determines that the drug is not good value for money, the manufacturer must offer a discount for the drug to be covered by the national health insurance. NICE makes indication-specific recommendations and has the option—as do the other agencies in this memo—to recommend coverage for a more restricted population than the market authorization of the drug. For example, after regulators approve a drug for two different indications, NICE may recommend that the drug only be covered for one indication or at a certain treatment stage. In the case of pembrolizumab, NICE positively recommended it as an option for treating advanced (unresectable or metastatic) melanoma in adults who had not been previously treated with ipilimumab; NICE did not recommend it for treating relapsed or refractory classical Hodgkin lymphoma in adults who had autologous stem cell transplants and who had received brentuximab vedotin.[14,15] For indications for which NICE has recommended pembrolizumab, the recommendation is conditional on the manufacturer providing a confidential discount to the list

[8] For reference the estimated population of England in mid-year 2022 was 57,106,000. UK Office of National Statistics. Population estimates for the UK, England, Wales, Scotland, and Northern Ireland: mid-2022. Published March 2024.
[9] NICE. The Highly Specialised Technologies Programme. Published January 31, 2022.
[10] UK Statutory Instruments. 2012 No. 2996. National Health Service Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) Regulations 2012, Schedule 4.
[11] NICE Health Technology Evaluations: the Manual. Section 5.10 : Varying the funding requirement to take account of net budget impact (technology appraisals and highly specialised technologies). Published October 31, 2023.
[12] NICE. Published: Guidance, quality standards and advice. Accessed October 2024.
[13] NICE. Semaglutide for managing overweight and obesity. Updated September 4, 2023.
[14] NICE. Guidance - Pembrolizumab for advanced melanoma not previously treated with ipilimumab. Updated September 12. 2017.
[15] NICE. Recommendations - Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma. Updated May 1, 2024.

price. The UK is a leader in HTA, and many countries reference against its prices; therefore, manufacturers have an interest in not publicizing any list price reductions.

If a drug is deemed not cost-effective by NICE and is not recommended, it will not be covered for that indication through the National Health Service. A NICE recommendation does not affect market authorization, so patients may still access the drug through private insurance or on the private market if the manufacturer chooses to sell it in the UK.

This value assessment and negotiation process is called the "voluntary scheme for branded medicines pricing, access, and growth (VPAG)."[16] Once manufacturers agree to a negotiated price under this scheme, they cannot raise prices more than a fixed growth rate percent per year and must reimburse any costs exceeding those rates.[17] Under this scheme, manufacturers must cap spending growth on their drugs and pay rebates to the national health system at a rate renegotiated every four to five years.

UK Statutory Scheme—An Example of Unilateral Price Setting

Drug manufacturers that opt out of the voluntary negotiation scheme would instead be covered under a separate statutory scheme.[18] The statutory scheme is a maximum price-setting approach in which the government unilaterally determines the maximum price for a drug. This contrasts with the voluntary scheme described above, in which an HTA body determines coverage based on a manufacturer's price. Most manufacturers of new brand-name drugs opt into the voluntary scheme. Those that do not are subject to the statutory scheme. In 2023, AbbVie and Eli Lilly left the voluntary scheme, claiming the re-payment rates were too high and are now subject to the statutory scheme.[19]

Like the voluntary scheme, the statutory scheme includes a capped spending growth rate and re-payments of net sales in the UK to the national health service. The statutory scheme does not use HTA and sets a maximum price for drugs that suppliers or manufacturers may charge. The manufacturer may propose a list price, and the Secretary will decide if the price is acceptable, considering the factors listed below.[20] How these factors are combined and evaluated to determine a maximum price is not publicly explained.

- The clinical need for the new drug;
- The price and associated operational costs of therapeutically equivalent or comparable medicines;
- The price and associated operational costs of the new presentation in the European Economic Area and any other markets if it is available elsewhere in the world at the time that the maximum price is being considered;
- Whether the presentation contains a new active substance;
- The date on which the patent protection period for each indication of the new presentation expires; where there is more than one patent protection period, the patent protection period which expires on the latest date will apply;
- The total profit of the manufacturer or supplier before interest charges and taxes for their previous accounting reference period as set out in the manufacturer's or supplier's accounts;

[16] UK Department of Health and Social Care. 2024 Voluntary Scheme for Branded Medicines Pricing, Access and Growth. Published December 14, 2023.
[17] UK Statutory Instruments. 2018 No. 345. The Branded Health Service Medicines (Costs) Regulations 2018.
[18] UK Department of Health & Social Care. Review of the scheme to control the cost of branded health service medicines: consultation response. Updated December 4, 2023.
[19] Association of the British Pharmaceutical Industry (ABPI). Leading global pharma firms exit UK drug pricing agreement. Published January 16, 2023.
[20] UK Statutory Instruments. 2018 No. 345 The Branded Health Service Medicines (Costs) Regulations 2018, Section 9.

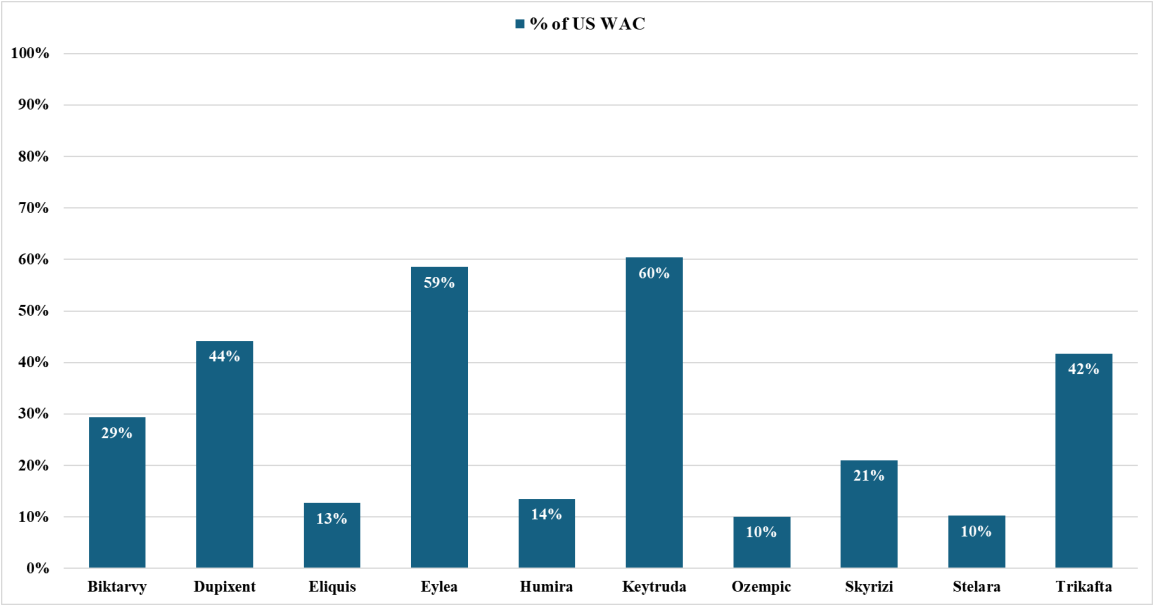
- The estimated total quantity to be supplied and estimated total net sales income of the new presentation over the period of the first five financial years of the manufacturer's or supplier's sales of the new presentation or where the patent protection period expires before the end of the first five financial years, the period until the date of the expiration of the patent protection period;
- The reasonableness of the estimated costs of the presentation over the period of the first five financial years of the manufacturer's or supplier's sales of the new presentation, or where the patent protection period expires before the end of the first five financial years, the period until the date of the expiration of the patent protection period, including—
    - manufacturing and supply costs,
    - research and development costs,
    - operational costs, and
    - any other costs; and
- The price at which the manufacturer's or supplier's reasonable costs for that presentation, as determined by the Secretary of State, would be met.

Accessing Price Information

Prices of drugs negotiated under either the voluntary or statutory price schemes are listed in the NHS Dictionary of Medicines & Devices, which is searchable by product and ingredient name.[21] Prices are listed at the package level and reflect the NHS Indicative Price, which is the manufacturer list price, or the price NHS pays for the centralized purchase of the drug. The NHS also issues the monthly Drug Tariff, which details the prices pharmacies pay for NHS prescriptions and other pharmacy services (e.g., dispensing fees).[22] Prices for individual drugs are listed under Part VIIIA.

Price Comparison: US vs. UK

Below are the current NHS prices as a percent of US list prices for ten drugs with the highest US spending in 2023. For additional information, see Appendix 1.



[21] NHS. Dictionary of Medicines & Devices. Updated September 26, 2024.
[22] NHS. Drug Tariff. Updated October 1, 2024.

Canada

HTA Agency
Canada's Drug Agency (CDA), formerly called the Canadian Agency for Drugs and Technologies in Health (CADTH)

HTA Authority
HTA reports are non-binding and are used to inform provincial and territorial payers (except Quebec), who are responsible for establishing formularies and negotiating prices.

Primary Basis of Recommendation
Formal cost-effectiveness analysis using QALYs with a value-for-money threshold. Reports use a cost-effectiveness threshold of $50,000 (CAD) per QALY to recommend whether a drug should be covered or how much a drug should be discounted to be covered.

Other Evaluation Methods, Outcomes, or Considerations
Any outcomes presented must be reported in natural units (such as life years gained or clinical outcomes, like events prevented) in addition to their translation into composite units, like the QALY. A cost-minimization analysis may be accepted if the drug has similar clinical effects to therapeutic alternatives; this type of analysis assumes equal outcomes for the selected drug and its comparator and evaluates which option is the least costly, accounting for the cost of the drug and management of the condition with the different options.

In addition to clinical benefit and economic evidence, which inform the cost-effectiveness analysis, CDA recommendations consider patient and clinician expert input, existing treatment options, the sponsor's proposed price, and implementation considerations. When there is uncertainty about the evidence, substantial unmet clinical need may justify a recommendation to reimburse a drug with certain conditions, for example, a time-limited reimbursement that will be reviewed after more evidence is available.[23]

Accessing HTA Information
CDA publishes its reimbursement reviews, including clinical and cost-effectiveness information, in a public database of Reimbursement Review Reports searchable by generic drug name and indication.[24] Each review page includes a primary "Recommendation and Reasons" report and files outlining the clinical and pharmacoeconomic evidence evaluated during the review.

> Example: Reimbursement Review - Semaglutide (Ozempic) for diabetes mellitus, type 2. Final recommendation issued May 15, 2019.[25]

CDA may also conduct custom Health Technology Reviews, which include a broader assessment of a particular technology's clinical, economic, social, and policy implications but are not directly tied to

[23] Canada's Drug Agency (CDA). Procedures for Reimbursement Reviews. Updated May 30, 2024.
[24] CDA. Reimbursement Review Reports. Updated October 3, 2024.
[25] CDA. Semaglutide Reimbursement Review. Published May 15, 2019.

reimbursement decision-making.[26] These reviews may be specific to one drug or indication or can be broader in scope.

Example: Rapid Review - Semaglutide 2 mg for Type 2 Diabetes. Published October 19, 2023.[27]

Party Responsible for Price Negotiation

If CDA issues a positive reimbursement recommendation for a drug, public plans (e.g., provincial and territorial payers, excluding Quebec) initiate price negotiation with the manufacturer as a block via the pan-Canadian Pharmaceutical Alliance (pCPA).[28] The final negotiated price is available to all public plans, each of which has the final decision on whether to include the drug in its formulary. Private plans individually negotiate prices and set formularies.

Separately, the Patented Medicines Price Review Board (PMPRB) is a consumer protection agency that will determine if a price for a branded drug is excessive and impose a binding maximum price that the drug may be sold for in Canada. Prices are reviewed if the list price increases more than the consumer price index and the list price is below the maximum non-excessive price, calculated as the median list price of the drug in 11 countries.[29,30] If the median price is unavailable, then the highest Canadian prices of drugs in the same therapeutic class or with the same approved indication determine the maximum. If there is no domestic therapeutic class comparator, international comparator therapies and prices are used.[31]

The courts prevented a 2019 reform effort to include CDA reports and economic value into PMPRB considerations, which found that the body was only authorized to act on excessive pricing, not to make decisions about reasonable pricing.[32] The PMPRB is currently developing new guidance in response.[33] The HTA activities of the CDA and the price caps of the PMPRB remain separate regulatory activities and powers.

Accessing Pricing Information

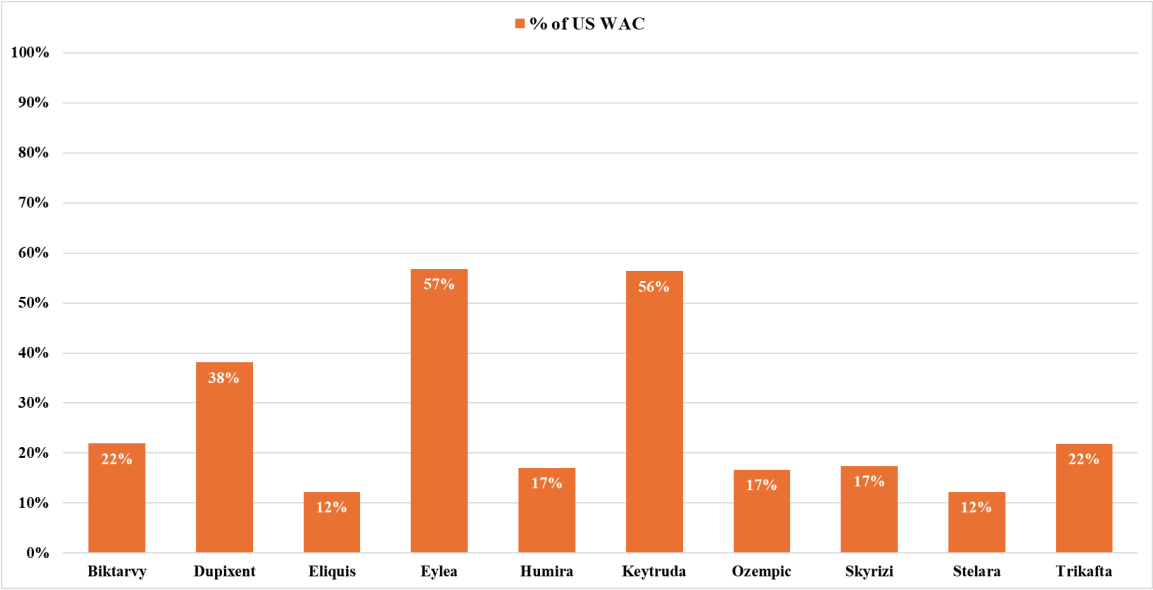
Pricing for drugs covered by public plans is available via the standard formularies of each province and territory.[34] A database of formulary coverage information for public drug plans, excluding price, is provided by the Canadian Institute for Health Information.[35]

The PMPRB releases an annual report of the patented drugs referred for PMPRB review, sorted by manufacturer, including details on whether the drug's price is within pricing guidelines.[36]

[26] CDA. Health Technology Review. Updated October 3, 2024.
[27] CDA. Semaglutide 2 mg for Type 2 Diabetes. Published October 19, 2023.
[28] Pan-Canadian Pharmaceutical Alliance. About pCPA. Accessed October 2024.
[29] Patented Medicine Prices Review Board (PMPRB). Interim Guidance. Amended September 27, 2023.
[30] PMPRB. Potential Sources for Foreign Prices: PMPRB11. Updated June 5, 2024.
[31] PMPRB. PMPRB Guidelines, Section 5. Updated January 1, 2022.
[32] Fasken. Quebec Court of Appeal Renders Major Decision on the PMPRB. Published February 21, 2022.
[33] PMPRB. Patented Medicine Prices Review Board 2024-25 Departmental Plan. Published March 3, 2024.
[34] Canadian Institute for Health Information (CIHI). Pan-Canadian Prescription Drug Data Landscape. Published March 2024.
[35] CIHI. Formulary coverage. Updated July 31, 2024.
[36] PMPRB. Annual Reports. Updated December 2023.

Price Comparison: US v. Canada

Below are the current Ontario public plan prices as a percent of the US list price for ten drugs with the highest net US spending in 2023. For additional information, see Appendix 1.



Australia

HTA Agency
Pharmaceutical Benefits Advisory Committee (PBAC)

HTA Authority
Determines whether drugs will be covered by the national health system under the Pharmaceutical Benefits Scheme (PBS). A positive recommendation from the PBAC is necessary for a drug to be included in the national formulary.

Primary Basis of Coverage Recommendation
Formal cost-effectiveness analysis using QALYs to evaluate cost-effectiveness and an incremental cost-effectiveness ratio (ICER). There is no formal threshold for cost-effectiveness. Some research suggests that the likelihood that PBAC recommends a drug decreases if the cost is more than $50,000 (AUD) per QALY gained. However, there is no definitive threshold for cost-effectiveness. By law, the PBAC is tasked with considering both the effectiveness of a therapy and its cost to the national prescription benefit.[37]

Other Evaluation Methods, Outcomes, or Considerations
Life years gained is measured for drugs that extend life, and a cost-effectiveness analysis is conducted with life years gained as the outcome. Special consideration is given if drugs fill an unmet clinical need or if effective treatments are unavailable. Another less-quantifiable consideration is equity, or the fair distribution of health technologies and resources among various groups, such as age, socioeconomic status, and geography (rural vs urban). [38,39] Because there is no formal threshold or weighting scheme for these less-quantifiable factors, the approach allows for more flexible, qualitative decision-making on drugs that treat conditions with high unmet clinical need.[40,41] The PBAC also considers patient affordability, as cost per patient per course of therapy or per year, or the ability of patients to pay for the drug if it is not covered by national insurance.

Accessing HTA Information
PBAC maintains a list of summary documents of its evidence assessments by generic product name or by PBAC meeting date.[42] These reviews are conducted by indication but are titled by date, which means it may be necessary to review all reports for an associated drug to find the desired indication.

> Example: Semaglutide (Ozempic) solution for injection 2 mg in 1.5 mL pre-filled pen, Solution for injection 4 mg in 3 mL pre-filled pen. Published July 2, 2021.[43]

Party Responsible for Price Negotiation

[37] Senate Community Affairs References Committee. Availability of new, innovative and specialist cancer drugs in Australia. Published September 17, 2015.
[38] Pharmaceutical Benefits Advisory Committee. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee. Updated September 2016.
[39] Sellars M, Carter SM, Lancsar E, Howard K, Coast J. Making recommendations to subsidize new health technologies in Australia: A qualitative study of decision-makers' perspectives on committee processes. *Health Policy*. 2024;139:104963.
[40] Manipis K, Viney R, De Abreu Lourenço R, et al. HTA Methods: Economic Evaluation. University of Technology Sydney Centre for Health Economics Research and Evaluation. Published April 2024.
[41] Senate Community Affairs References Committee. Availability of new, innovative and specialist cancer drugs in Australia. Published September 17, 2015.
[42] PBAC. Public Summary Documents. Updated August 30, 2024.
[43] PBAC. Public Summary Document – Semaglutide (Ozempic) solution for injection 2 mg in 1.5 mL pre-filled pen, Solution for injection 4 mg in 3 mL pre-filled pen. Published July 2, 2021.

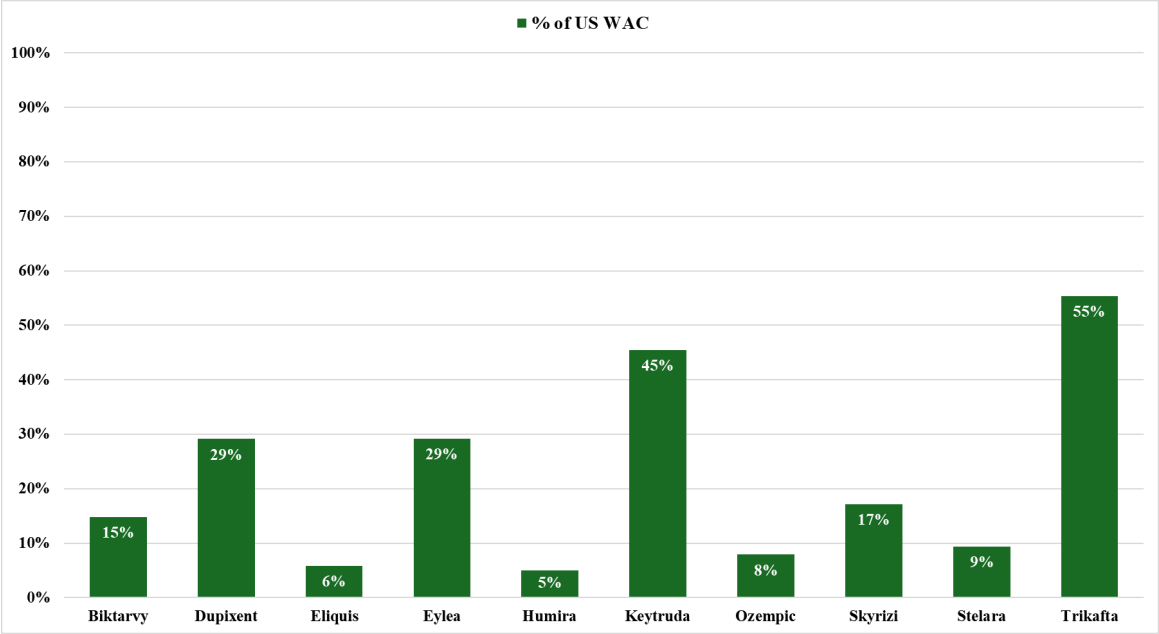
If PBAC finds a drug cost-effective, the Australian Ministry of Health will directly negotiate the price with the manufacturer to list the product on the Pharmaceutical Benefits Scheme. In some circumstances, PBAC may withhold a recommendation until a price is negotiated and agreed on. It will then re-review the drug and determine whether it should be recommended at the new, negotiated price. Drugs listed on the PBS are subject to statutory price reductions at specific time points after initial listing (5% at 5 and 10 years, 26.1% at 15 years) and upon generic or biosimilar entry.[44][45] Drugs not listed on the PBS are not subsidized by the government, meaning patients face the total market-established price.[46]

Accessing Price Information

PBS lists all medicines included on the general PBS schedule and other specialized drug schedules, indicated as the dispensed price for maximum quantity or amount (DPMQ/A).[47] The typical patient price share is also listed. PBS listings are sorted by generic or brand name and are listed at the product level.

Price Comparison: US v. Australia

Below are the current PBS prices as a percent of the US list price for ten drugs with the highest net US spending in 2023. For additional information, see Appendix 1.



[44] PBS. Anniversary Price Reductions. Updated August 14, 2024.
[45] PBS. First New Brand Price Reductions. Updated October 1, 2024.
[46] Australian Department of Health and Aged Care. Cost of medicines. Updated June 23, 2023.
[47] PBS. A-Z Medicine Listing by Brand. Updated October 2024.

France

HTA Agency
National Health Authority (Haute Autorité de Santé, HAS)

HTA Authority
Assessments are conducted by the HAS Transparency Committee (TC) and, though non-binding, inform decisions on whether the National Health Insurance Fund will cover the drug, how much of the cost patients will pay out of pocket, and whether a higher price than therapeutic alternatives is justified.[48]

Primary Basis of Recommendation
Coverage is determined by *the absolute medical benefit of the drug* relative to no treatment. Absolute medical benefit is determined by considering the following factors: efficacy and adverse events; place in therapeutic strategy, the seriousness of the disease indicated; whether the drug is preventive, curative, or symptom-treating; and public health benefit of the drug.[49] Public health benefits include reducing resource use, the seriousness of the condition, or the effect on morbidity and mortality of the population. Drugs with no absolute benefit are excluded from the national formulary. The amount of absolute benefit also determines what share of a drug's costs will be covered by the national insurance, ranging from 15% for drugs with minor benefit (i.e., the patient is responsible for 85%) to 65% for those with substantial benefit (i.e., patient responsible for 35%).

HAS also ranks the amount of *additional* benefit the drug provides compared to therapeutic alternatives, ranging from no to major improvement based on evidence quality, the magnitude of effect size on clinical efficacy, quality of life, and safety, and the need for this therapy relative to a comparator.[50] For example, a rating of major additional benefit would be warranted if a drug had a new mechanism of action, robust evidence demonstrating its superiority to comparators, and clinically relevant effects on mortality and morbidity for a serious disease with unmet need. By contrast, substantial or moderate benefit is determined when a drug has demonstrated superiority of morbidity and mortality effects, and there is unmet medical need; upward adjustment would be warranted for substantial improvements in quality of life or safety. For no improvement, which is determined if there is no therapeutic improvement relative to comparators, the drug's price cannot exceed the cost of therapeutic alternatives. Drugs with any added benefit are allowed a premium over the prices of therapeutic alternatives.

A health economic analysis is done if a drug is rated as providing moderate to major additional benefit over existing therapies, is an advanced therapy medicinal product, or is expected to have sales of greater than €20 million by its second year on the market.[51,52] A cost-effectiveness analysis with life-years as the outcome is always conducted. If health-related quality of life is a primary clinical outcome, then a cost-utility analysis is conducted with QALYs. An efficiency frontier approach is used to determine if the price is reasonable relative to therapeutic alternatives.

[48] Haute Autorité de Santé (HAS) Commission de la Transparence. Pricing & Reimbursement of drugs and HTA policies in France. Updated March 6, 2024.
[49] HAS TC. Methods and criteria for assessing medicinal products. Published October 29, 2015.
[50] *Ibid.*
[51] HAS. Economic and Public Health Evaluation Committee. Published March 6, 2024.
[52] HAS. Choices in Methods for Economic Evaluation. Updated November 6, 2020.

Other Evaluation Methods, Outcomes, or Considerations

The choice must be justified to use any other outcome in CEA besides life years and QALYs. When outcomes for the drug and its comparator are similar, a cost-minimization analysis can be conducted.

Accessing HTA Information

HAS assessments are available via a database of "drugs, devices and medical acts."[53] Results are searchable by brand name or therapeutic area and can be limited to only products for which English summaries are available. For each drug, a timeline of HAS review of each indication and Transparency Committee scoring of the drug's added clinical value (CAV) are presented.

> Example: Reevaluation of semaglutide (Ozempic) indicated in the treatment of type 2 diabetes mellitus.[54]

Party Responsible for Price Negotiation

The Economic Committee for Health Products (CEPS) is an inter-ministerial body tasked with setting prices for medicines covered by the Health Insurance Fund.[55] CEPS uses HAS evaluations of absolute and additional value to inform pricing.[56] List prices negotiated by CEPS are referenced to those in the UK, Germany, Italy, and Spain for drugs found to demonstrate at least moderate improvement over comparators in HAS' assessment. CEPS may also negotiate additional rebates from the manufacturer below the list price, though rebate amounts are confidential at the product level.

Accessing Price Information

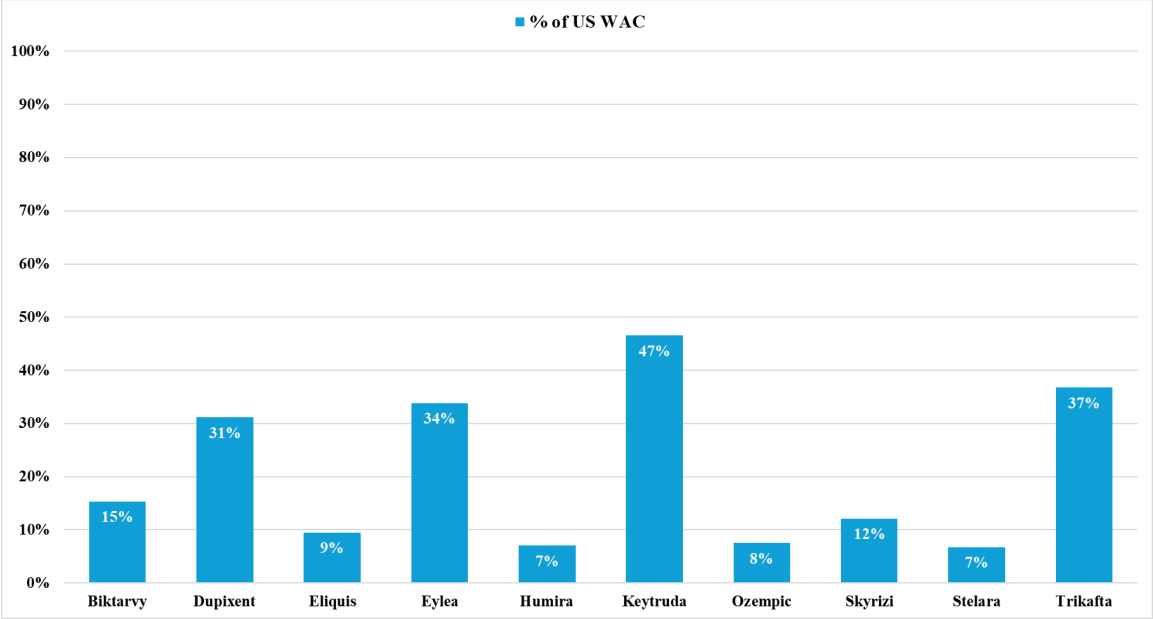
List prices set by CEPS are available by product via the Database of Medicines and Tariff Information (BdM IT) maintained by France's public health insurance system (l'assurance maladie).[57] This database includes both the manufacturer price ("Prix Fabricant HT") and the price plus relevant taxes ("Prix Public TTC"). Information on the reimbursement level of each product is also available.

The Public Database of Medicinal Products also provides a centralized platform with regulatory and pricing information for drugs marketed within the previous three years.[58]

[53] HAS. All Publications.
[54] HAS. Ozempic. Published August 26, 2021.
[55] French Ministry of Labor and Health. Economic Committee for Health Products (CEPS). Published March 3, 2023.
[56] Valencia J. Pricing & Reimbursement Laws and Regulations 2024 – France. Global Legal Insights. Published May 9, 2024.
[57] l'assurance maladie. Base des médicaments et informations tarifaires.
[58] Base de données publique des medicaments.

Price Comparison: US v. France

Below are the current CEPS prices as a percent of the US list price for ten drugs with the highest net US spending in 2023. For additional information, see Appendix 1.



Germany

HTA Agencies
Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG); Federal Joint Committee (G-BA)

HTA Authority
IQWiG reports are non-binding and are commissioned by the Federal Joint Committee (G-BA), the major decision-making body in the German health insurance system, to inform decisions on whether a service will be reimbursed by Germany's highly regulated, private "statutory health insurers." All approved drugs are included in insurance during the first year of market approval while IQWiG and G-BA review the product.

Following completion of IQWiG's assessment, G-BA issues a resolution outlining the reimbursement requirements for the drug and initiating price negotiations.[59] IQWiG has no authority to negotiate or set prices, so the advisory role of HTA reports has led to some conclusions in the literature that IQWiG is more conservative in its evaluations (i.e., less likely to determine that drugs offer major benefits and are cost-effective) compared to HTA agencies like NICE or the PBAC that make binding recommendations.[60]

Primary Basis of Recommendation
Drugs are rated as providing no, minor, considerable, or major additional benefit or unproven benefit. Drugs determined to offer no added benefit are reference priced to therapeutic alternatives, i.e., should be priced the same. Drugs with added benefit should be priced in line with the amount of benefit relative to therapeutic alternatives, using an efficiency frontier comparing net health benefit (see other evaluation methods below) and costs of the drug and therapeutic alternatives.

Other Evaluation Methods, Outcomes, or Considerations
Patient-relevant and condition-specific outcomes are used in the primary analysis: improvements in length of life/mortality, serious symptoms and adverse effects, health-related quality of life, and non-serious symptoms and adverse effects. Outcomes may be aggregated together into a judgment of net health benefit. IQWiG sets standards for translating the magnitude of effect for some outcomes into an assessment of benefit (not proven, less added benefit, no, minor, considerable, or major added benefit benefit).[61] The process of determining net benefit does not use quantified standards. Multiple outcomes can be analyzed separately if a single benefit measure is not used. IQWiG does not use the QALY in its assessment.

Accessing HTA Information
IQWiG publishes English extracts of its health technology assessments in an online database that is searchable by generic drug name, therapeutic area, review status, and year.[62] Press releases summarizing the results of each assessment are often available in English. Each extract typically includes a "key

[59] Federal Joint Committee. Resolutions. Updated July 2024
[60] Klingler C, Shah SM, Barron AJ, Wright JS. Regulatory space and the contextual mediation of common functional pressures: analyzing the factors that led to the German Efficiency Frontier approach. *Health Policy*. 2013;109(3):270-80.
[61] Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG). General Methods. Published September 19, 2023.
[62] IQWiG. Projects and results. https://www.iqwig.de/en/projects/projects-results/

statement" section outlining the conclusions on a drug's added therapeutic benefit over its comparator(s).

> Example: Benefit assessment of biotechnologically produced drugs for the treatment of rheumatoid arthritis. Published September 17, 2019.[63]

G-BA reimbursement resolutions are available in German, with English versions and justifications available for some products.[64] The database includes a filter only to show resolutions with English translations.

> Example: Pharmaceutical Directive/Annex XII: Upadacitinib [Rinvoq] for Rheumatoid Arthritis. Published July 16, 2020.[65]

Party Responsible for Price Negotiation

The National Association of Statutory Health Insurance Funds (GKV-Spitzenverband, GKV), a coalition representing statutory health insurers, is tasked with negotiating the maximum price for drugs approved for reimbursement by the G-BA.[66] For drugs found to have no additional therapeutic benefit over their comparators, the GKV sets a fixed reference price based on a basket of therapeutic alternatives set by G-BA.[67,68] If the manufacturer decides not to sell the drug at the fixed reference price, patients must pay the difference between reference and list prices out of pocket.

If the drug has an added benefit over its comparator, GKV negotiates a premium price that aligns with the additional benefit. The agreed price is the maximum for all participating insurers, though individual insurers may negotiate further discounts with manufacturers. The negotiation will move to an arbitration proceeding if neither the manufacturer nor GKV can reach an agreement. If a manufacturer disagrees with the price offer, it may withdraw from the German market instead of accepting the German price. It is rare for a manufacturer to exit the market, and when this has happened, it has usually been for drugs found by IQWiG and the G-BA to provide no added benefit over comparators.[69,70]

Accessing Pricing Information

Current and historical reference prices are publicly available in German and updated biweekly.[71] This reference price list is organized by product name and includes the reference price group ("Festbetragsgruppe") in which a given drug is included.

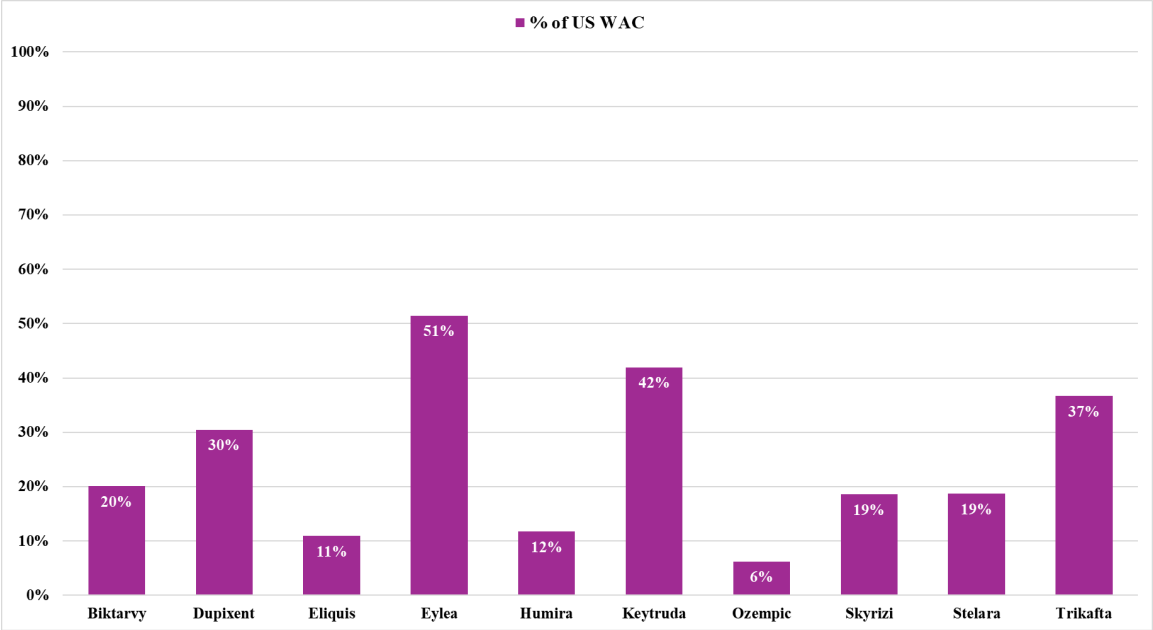
Maximum reimbursement prices for drugs with added therapeutic benefit are accessible via the Lauer-Taxe database, which requires a paid license to access.[72] Germany is one of the few countries that makes

[63] IQWiG. Benefit assessment of biotechnologically produced drugs for the treatment of rheumatoid arthritis. Published September 17, 2019.
[64] G-BA. Benefit assessment of medicines. Updated October 2024.
[65] G-BA. Nutzenbewertungsverfahren zum Wirkstoff Upadacitinib (Rheumatoide Arthritis). Published July 16, 2020.
[66] GKV-Spitzenverband. About Us. Accessed October 2024.
[67] G-BA. Festbetragsgruppenbildung. Updated February 2024.
[68] Federal Institute for Drugs and Medical Devices. List of Reference Prices for Medicinal Products. Accessed October 2024.
[69] Staab TR, Walter M, Mariotti Nesurini S, Dintsios CM, Graf von der Schulenburg JM, Amelung VE, et al. "Market withdrawals" of medicines in Germany after AMNOG: a comparison of HTA ratings and clinical guideline recommendations. Health Econ Rev. 2018;8(1):23.
[70] Stern AD, Pietrulla F, Herr A, Kesselheim AS, Sarpatwari A. The Impact Of Price Regulation On The Availability Of New Drugs In Germany. *Health Aff (Millwood)*. 2019;38(7):1182-1187.
[71] Federal Institute for Drugs and Medical Devices. Arzneimittel-Festbeträge. Updated September 15, 2024.
[72] CompuGroup Medical. Lauer-Taxe.

these negotiated rates publicly available. However, legislation passed in July 2024 creates a pathway for manufacturers to request that these prices remain confidential, which may affect future access.[73]

Price Comparison: US v. Germany

Below are the current GKV prices as a percent of the US list price for ten drugs with the highest net US spending in 2023. For additional information, see Appendix 1.



[73] Koyuncu A, Aretz M. Germany amends drug pricing and reimbursement laws with "Medical Research Act" – Drug pricing becomes intertwined with local clinical research expectations. Covington Global Policy Watch. Published July 12, 2024.

Appendix 1. Comparisons to US Prices

The top 10 drugs with the highest US net spending in 2023 were selected as examples throughout this memo, as identified using SSR Health.[74] For each drug, the most common dosage form used in the US was identified using the estimated number of prescriptions filled in the US in 2023 from the IQVIA National Prescription Audit. Dosage forms were matched with equivalent forms in the selected jurisdictions (UK, Australia, Canada, France, and Germany). Package descriptions for each drug are listed below.

Table 1. Package Description Information for International Price Comparisons

Drug	Package Description (US NDC)
Biktarvy	Biktarvy Tablets 1 Pack 30 Tabs 25 mg/50 mg/200 mg (61958250101)
Dupixent	Dupixent Injection 2 Prefilled Pen 2 ml 300 mg (00024591502)
Eliquis	Eliquis Tablets 1 Pack 60 Tabs 5 mg (00003089421)
Eylea	Eylea Intravitreal Injection 1 Prefilled Syringe 0.05 ml 2 mg (61755000501)
Humira	Humira Injection 2 Prefilled Pen 0.4 ml 40 mg (00074055402)
Keytruda	Keytruda Infusion 1 Vial 4 Ml 100 mg (00006302602)
Ozempic	Ozempic Injection 1 Prefilled Pen 3 ml 4 mg (00169413013)
Skyrizi	Skyrizi Injection 1 Prefilled Pen 1 ml 150 mg (00074210001)
Stelara	Stelara Injection 1 Prefilled Syringe 1 ml 90 mg (57894006103)
Trikafta/Kaftrio*	Trikafta Tablets 1 Pack 28 Tabs 600 mg (51167033101)

*Trikafta is marked under the brand name Kaftrio in the UK and Europe.

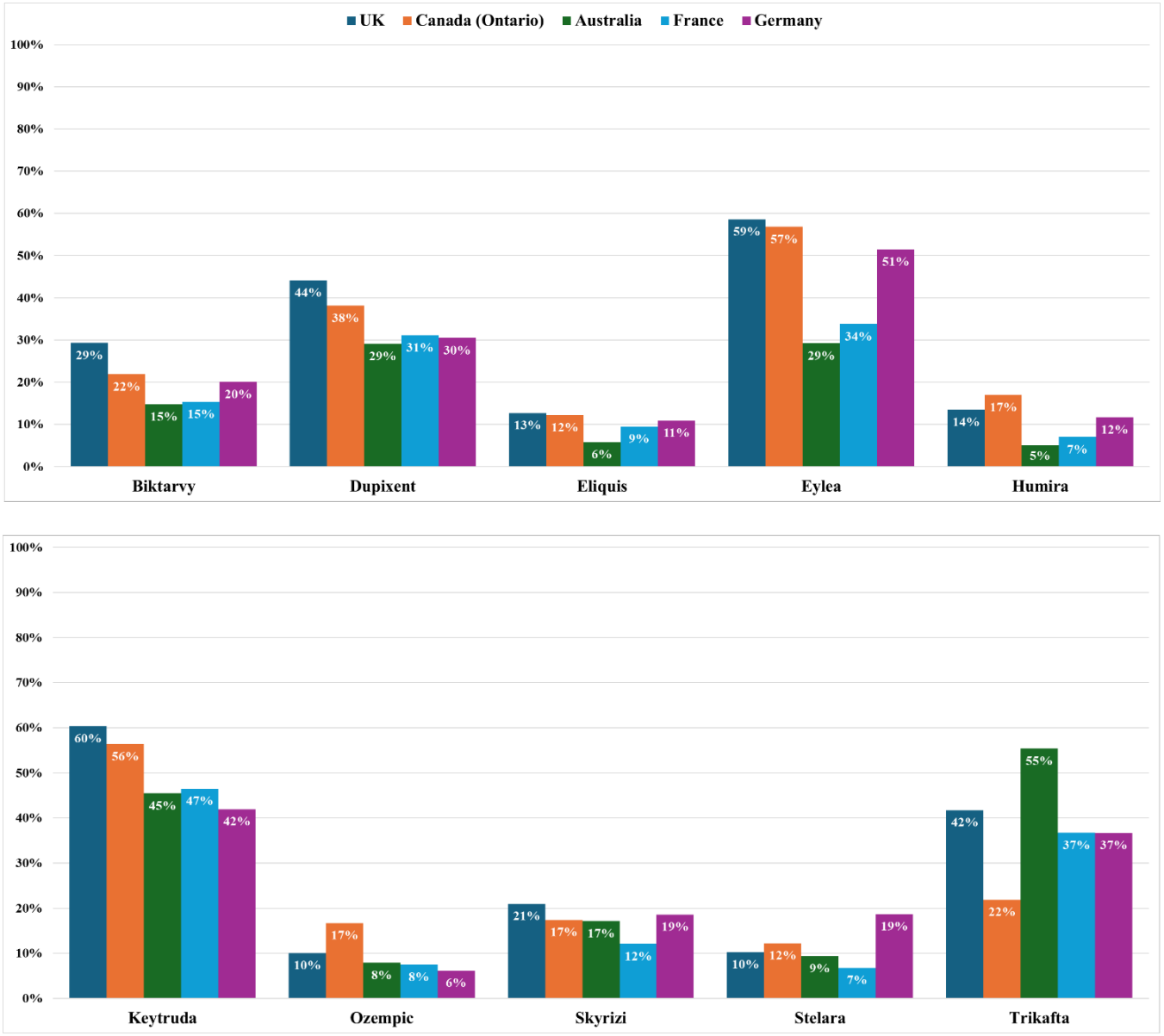
Current manufacturer list price data was obtained for each country from NAVLIN, a drug price and access platform that aggregates pricing, reimbursement, and HTA data across countries.[75] Prices were converted to US dollars. Pricing is presented as a percent of the current US wholesale acquisition cost (**Figure 1**).

For additional reading on drug price comparisons between the US and other countries, please see a recent analysis from the RAND Corporation by Mulcahy et al.[76]

To learn more about the accessibility of drug pricing data in countries beyond those selected in this memo, the World Health Organization maintains a database of information sources for drug prices and other market data, though not all sources may be publicly available.[77] The International Network of Agencies for Health Technology Assessment (INAHTA) also maintains a database of HTA reports from participating countries, as does the regional Health Technology Assessment Network of the Americas (RedETSA).[78,79]

[74] SSR Health.
[75] Eversana. NAVLIN Price & Access Data.
[76] Mulcahy AW, Schwam D, Lovejoy SL. *International Prescription Drug Price Comparisons: Estimates Using 2022 Data*. RAND Corporation; 2024.
[77] WHO. Medicine Prices and Other Market Information Sources. Updated June 27, 2024.
[78] INAHTA. International HTA Database. Accessed October 2024.
[79] RedETSA. Regional Base of Health Technology Assessment Reports of the Americas. Accessed October 2024.

Figure 1. Negotiated List Prices of Top Spending Drugs in Other Countries as a Percent of US Wholesale Acquisition Cost



Appendix 2. European Approaches to HTA

An EU directive has established a joint clinical assessment process to conduct HTA applicable across member states to promote access and harmonize criteria for HTA. A consortium of countries formed the European Network for Health Technology Assessment (EUnetHTA) project, which has been developing methods for joint assessments. The following two tables come from preparatory work that surveyed countries' methods of HTA. As a part of the EU-wide HTA development process, a mapping of pre-existing HTA methodologies was also conducted.[80]

Table 2. Use of QALYs and non-QALY as preferred outcome measures in HTA across European countries.[81]

Country	Preferred outcome measure/s
Austria	QALYs
Belgium	QALYs and LYG
Croatia	Both QALYs and natural units are possible.
Czech Republic	QALYs are preferred, then LYG and validated surrogates.
Denmark	QALYs or LYG, but also response rate, number of successful treatments, measure of time without symptoms, pains etc.
England	Technology Appraisals and Diagnostics Assessment Programme: QALYs Medical Technologies Evaluation Programme: clinical benefits for individual patients and its impact on clinical and system outcomes
Estonia and Latvia	Prevention of death, reduced incidence of complications, reduced incidence of side-effects, incidence of well controlled therapy symptoms, etc. QALYs only presented in additional analyses.
Finland	Primarily QALYs
France	QALYs or LYG
Germany	Primarily mortality, morbidity, HRQoL and validated surrogates
Hungary	CUA: QALYs Effectiveness: appropriate outcome for the selected condition, and final (long-term) outcome (morbidity, mortality) and changes in QoL
Ireland	QALYs
Italy	QALYs
The Netherlands	QALYs or life years gained
Norway	QALYs
Poland	Depends on type of economic analysis In CUA: QALY (preferred outcome) In CEA: LYG In CCA: costs and health consequences.
Portugal	The following are generally used: (1) Measurements related to the disease (2) Measurements related to the patient (e.g. reduction in the number of cardiovascular events or life years gained) (3) Measurements of the QoL (4) Monetary units.
Russia	QALY, LYG, serious complications, hospital admissions etc.
Scotland	QALYs. This should include adverse effects.
Slovakia	Chronic conditions: QALYs or LYG. Acute conditions: other relevant outcome variables, as in the clinical file
Slovenia	QALYs
Spain	QALYs (Spanish recommendations, CATSALUT and OSTEBA. Separate data on changes in both quantity and QoL (Spanish recommendations, CATSALUT, and OSTEBA).
Sweden	QALYs. In treatments that mostly affect survival: both QALYs and LYG
Switzerland	No specifications of preferred outcome, but CUA ratios are explicitly mentioned as not so important

CCA: cost-consequence analysis, CEA: cost-effectiveness analysis, CUA: cost-utility analysis, HRQoL: health-related quality of life, LYG: life years gained, QALY: Quality-adjusted life years, QoL: quality of life

[80] European Commission Directorate-General for Health and Food Safety. Mapping of HTA methodologies in EU and Norway. Published June 2017.
[81] EUnet HTA. Methods for Health Economic Evaluations – A Guideline Based on Current Practices in Europe. Published May 2015.

Table 3. Preferred type of health economic analysis across European countries.

Country	Preferred type of analysis
Austria	No preferred type
Belgium	CUA, CEA or CMA.
Croatia	CUA or CEA
Czech Republic	CUA
Denmark	Not explicitly stated. CEA and CUA seem to be accepted.
England	CUA (Technology Appraisals and NICE Diagnostics Assessment Programme) CCA (NICE Medical Technologies Evaluation Programme Methods Guide)
Estonia and Latvia	CEA or CMA
Finland	CUA, CEA, CMA or CBA
France	CUA and CEA
Germany	CEA (several endpoints= several efficiency frontiers)
Hungary	CUA, CEA or CMA,
Ireland	CUA or CEA
Italy	CUA or CEA
The Netherlands	CUA, CEA or CMA
Norway	CUA, CEA or CMA.
Poland	CUA (preferred according to the regulation), CEA or CMA and a CCA. CBA is possible only as an additional analysis (according to the guidelines).
Portugal	CUA, CEA, CMA or CBA (CUA is preferred)
Russia	CEA or CMA (Ministry of health) CMA, CEA, CUA or CBA (ISPOR Russian HTA Chapter)
Scotland	CUA or CMA
Slovakia	CUA, CEA or CMA
Slovenia	CUA, CEA or CMA and Cost Analysis.
Spain	CUA, CEA, CMA or CBA. CUA is preferred. (Spanish recommendations, Osteba) CUA, CEA or CMA (AETSA) CUA or CMA (CEA only if a CUA cannot be conducted) (CatSalut)
Sweden	CUA, CEA, CMA or CBA
Switzerland	CEA

CBA: Cost-benefit analysis, CCA: Cost-consequence analysis, CEA: Cost-effectiveness analysis, CUA: Cost-utility analysis, CMA: Cost-minimization analysis.