Oregon Prescription Drug
Affordability Board

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Entresto®
(*sacubitril/valsartan*)[1]

Version 4.2

[1] Image source: https://mms.mckesson.com/product/1017676/Novartis-00078077720

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Document version history

Version	Date	Description
v1.0	7/9/2025	Original Release
v2.0	7/11/2025	Updated gross spend amounts in the “Cost to the healthcare system” section; added a “Cost to payers” section; updated table 3 to reflect costs to the healthcare system; added table 4 for payer paid amounts; updated sections referencing patients to reference enrollees; added the drug name to the footer; Table 2 removed Total for paid/enrollee & claims and indicated the number as an average.
v2.1	7/17/2025	Added to the appendix table the public comment from the 7/16/2025 board meeting.
v3.0	9/12/2025	Added new tables, formatting changes throughout the document.
v4.0	10/21/2025	WAC data and 30 day supply data updated. New patent and exclusivity data added. Formatting changes.
v4.1	12/17/2025	Generic information added.
V4.2	12/23/2025	Updated scoring rubric information for patent expiration from “Yes” to “No”.

Review summary

Therapeutic alternatives[2,3,4]

Entresto® (*sacubitril/valsartan*) does not have any therapeutic alternative:

Proprietary name	Non-proprietary name	Manufacturer	Number of patents	Patent date range	Exclusivity expiration	On the CMS drug Maximum Fair Price (MFP) list
Entresto	*sacubitril/ valsartan*	Novartis Pharmaceuticals Corp.	10	2025-2036	2025[5]	Yes

Price history[6,7]

Entresto® (*sacubitril/valsartan*) rose at an average annual rate of 6 percent.

Additionally, the average annual rate exceeded inflation in 2020, 2023, and 2024. Pharmacy acquisition costs (AAAC) for **Medicaid also increased by 27 percent** over the same period, reflecting broader trends in pricing escalation.

Price concessions[8]

Based on data received from healthcare carriers, Entresto in 2023 had the **gross spend of $1,126 per claim**, while the **spend net of discount was $996 per claim**. Price concession per claim was reported to be **$130**.

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[2] Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book. U.S. Food & Drug Administration, Aug. 8, 2025. https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book.

[3] Frequently Asked Questions on Patents and Exclusivity, U.S. Food & Drug Administration, Feb. 5, 2020. https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity#What_is_the_difference_between_patents_a.

[4] Selected Drugs and Negotiated Prices. Centers for Medicare & Medicaid Services, May 23, 2025. https://www.cms.gov/priorities/medicare-prescription-drug-affordability/overview/medicare-drug-price-negotiation-program/selected-drugs-and-negotiated-prices.

[5] Generic sacubitril / valsartan commercially launched in the U.S. in July 2025. GoodRx, November 21, 2025. https://www.goodrx.com/entresto/entresto-generic-faqs

[6] Medi-Span. Wolters Kluwer, 2025. https://www.wolterskluwer.com/en/solutions/medi-span/medi-span

[7] Consumer Price Index. U.S. Bureau of Labor Statistics. https://www.bls.gov/cpi/tables/supplemental-files/.

[8] Based on data submitted to the Department of Consumer and Business Services (DCBS) by Oregon's commercial insurance carriers. Cost information from the data call is the cost of the drug after price concessions.

Cost to payers[9]

Table 1 2023 APAC gross annual payer total expenditure, utilization, and cost per enrollee

Proprietary name	Total expenditure	Utilization	Cost per enrollee	Cost per enrollee, median
Entresto	$47,032,152	53,866	$5,179	$684

Cost to enrollees[10]

Table 2 2023 APAC gross annual enrollee out-of-pocket (OOP) cost

Proprietary name	OOP cost per enrollee	OOP cost per enrollee median	OOP cost per claim	OOP cost per claim median
Entresto	$535	$45	$103	$30

Rubric considerations

Domain	Consideration
Utilization	53,866
Price evaluation	Avg change in WAC > 5%, outpaces inflation for 4 years
Price concessions	High percent of claims discounted (82%)
System & payer costs	Total gross spend $15M-$50M, total net spend $3M-$10M
Enrollee burden	Total APAC OOP annual cost $200-$700
Equity impact	Yes
Access restrictions	No
Therapeutic alternative fail to reduce system spending	Yes
Stakeholder input identify access or financial hardship?	No
Patent expirations more than 18 months from time of review?	No
Excluded from CMS Maximum Fair Price List (MFP)	No

[9] Based on Oregon's 2023 All Payer All Claims (APAC) data across commercial insurers, Medicaid, and Medicare. APAC cost information are prior to any price concessions such as discounts or coupons. For more information regarding APAC data visit: https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx.
[10] Ibid

Review background

This review incorporates supporting information from Medi-Span, FDA databases (e.g., Orange Book, Purple Book), and other publicly available data where applicable.

Two primary data sources inform this review: the Oregon All Payers All Claims (APAC) database and the commercial carrier data call. APAC aggregates utilization data across all payer types in Oregon, including Medicaid, Medicare, and commercial plans, and presents gross cost estimates. In contrast, the data call reflects submissions from 11 commercial health insurers and reports primarily net costs after manufacturer rebates, PBM discounts, and other price concessions. As a result, APAC generally reflects larger total utilization and cost figures due to broader reporting, while the data call offers insight into actual expenditures from private payers in the commercial market.

This review addresses the affordability review criteria to the extent practicable. Due to limitations in scope and resources, some criteria receive minimal or no consideration.

In accordance with OAR 925-200-0020, PDAB conducts affordability reviews on prioritized prescription drugs selected under OAR 925-200-0010. In 2023, the selection process for affordability review included multiple criteria: orphan-designated drugs were removed, drug; were reviewed based on payer-paid cost data from the data call submissions; and drugs reported to the APAC program across Medicare, Medicaid, and commercial lines of business were included. To ensure broader public impact, drugs with fewer than 1,000 enrollees reported in APAC reports were excluded from consideration.

Senate Bill 844 (2021) created the Prescription Drug Affordability Board (PDAB) to evaluate the cost of prescription drugs and protect residents of this state, state and local governments, commercial health plans, health care providers, pharmacies licensed in Oregon and other stakeholders within the health care system from the high costs of prescription drugs.

Drug information[11]

Drug proprietary name(s):	Entresto®	
Non-proprietary name (active ingredients)	*sacubitril and valsartan*	
Manufacturer	Novartis Pharmaceuticals Corp.	
Therapy class	Cardiovascular agents – misc.	
Treatment	• To reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.	
	• For the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. Entresto reduces NT-proBNP, an established biomarker used to assess the severity and determine the prognosis of heart failure and is expected to improve cardiovascular outcomes.[12]	
Dosage and strength		
	• Tablets: 24/26 mg; 49/51 mg; 97/103 mg	
	• Capsule, sprinkles: 6/6 mg; 15/16 mg	
Indication	Titration step dose (twice daily)	
	Starting	**Final**
• **Adult Heart Failure**	49/51 mg	97/103 mg
• **Pediatric Heart Failure Patients less than 40 kg**	1.6 mg/kg*	72/78 mg
• **Pediatric Heart Failure Patients at least 40 kg, less than 50 kg**	24/26 mg	72/78 mg

[11] U.S. Food & Drug Administration. Entresto (sacubitril and valsartan) Prescribing Information. Novartis Pharmaceuticals Corp., Revised 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207620s018lbl.pdf.

[12] "New Novartis study supports Entresto as foundational HFrEF therapy and in-hospital initiation in appropriate stabilized heart failure patients." Novartis, Nov 11, 2018. https://www.novartis.com/us-en/news/media-releases/new-novartis-study-supports-entresto-foundational-hfref-therapy-and-hospital-initiation-appropriate-stabilized-heart-failure-patients.

• **Pediatric Heart Failure Patients at least 50 kg**	49/51 mg	97/103 mg
***the mg/kg dose is for the oral suspension that has to be compounded from tablets.**		
Different dosing for sprinkle capsules.	• Adjust adult doses every two to four weeks and pediatric doses every two weeks to the target maintenance dose, as tolerated by the patient. • Reduce starting dose to half the usually recommended starting dosage for: ○ patients not currently taking an angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents ○ patients with severe renal impairment ○ patients with moderate hepatic impairment	
Rout of administration	By mouth	
Physician administered	No	

FDA approval

Entresto (*sacubitril and valsartan)* was first approved by the FDA on July 7, 2015.[13]

The drug qualified for the following expedited forms of approval: Priority

At time of the review, the drug had no approved designations under the Orphan Drug Act.

Health inequities

ORS 646A.694(1)(a) and OAR 925-200-0020 (1)(a) & (2)(a)(A-B). Limitations in scope and resources available for this statute requirement. Possible data source through APAC.

Entresto is recognized as a recommended therapy for heart failure. A study utilizing Optum de-identified Clinformatics Data Mart, which included over 135,000 Medicare and commercially insured patients, revealed that individuals in the lowest income bracket (< $40,000/year) had a 30 percent lower likelihood of receiving Entresto within six months of diagnosis compared to higher-income counterparts (odds ratio (OR) 0.70; adjusted OR 0.83), even after adjusting for clinical factors.[14] Additionally, adherence—defined as covering ≥80 percent of days—was

[13] FDA approval date based on the earliest occurring approval dates in the FDA Orange/Purple Book. For drugs with multiple forms/applications, the earliest approval date across all related FDA applications was used.
[14] Johnson AE, et al. "Relation of Household Income to Access and Adherence to Combination Sacubitril/Valsartan in Heart Failure: A Retrospective Analysis of Commercially Insured Patients." Circ Cardiovasc Qual Outcomes, 2022 Jul;15(7):e009179. https://pubmed.ncbi.nlm.nih.gov/35549378/.

markedly lower among Black (OR 0.64) and Hispanic patients (OR 0.62), compared with white patients.[15]

Cost-related barriers also impact patients' ability to initiate or continue using Entresto. In a study, while 92 percent of heart failure patients expressed willingness to switch to Entresto if their copay increased by just five dollars per month, that number dropped dramatically to 43 percent when faced with a $100 increase.[16] Notably, the impact of cost was not limited to low-income individuals; even among higher-income groups, around 40 percent were unwilling to switch when confronted with the higher copay threshold.[17]

During a CMS forum in Nov. 2023[18] for Entresto, speakers addressed the pressing concerns related to patients access to the essential medication through appropriate formulary positioning and spoke out against the high cost of a life-saving cardiac medication. They specifically highlighted how marginalized groups, particularly Black and Indigenous communities—who suffer disproportionately from heart failure—would face further burdens in terms of mortality and hospitalization risk factors if the cost of the drug continues to rise.[19]

Residents prescribed

ORS 646A.694(1)(b) and OAR 925-200-0020(1)(b) & (2)(b). Data source from APAC. Data sources: Oregon All Payers All Claims (APAC) database and commercial carrier data call.

Based on APAC claims, **9,081** Oregonians filled a prescription for Entresto in 2023.[20]

Price for the drug

ORS 646A.694(1)(c) and OAR 925-200-0020(1)(c) & (2)(e), (f), & (g). Data source from Medi-Span, APAC, and carrier data call.

This section examines the pricing dynamics of Entresto, drawing on multiple data sources to characterize its historical cost trends and implications for affordability. It includes an analysis of the wholesale acquisition cost (WAC) and the Oregon Actual Average Acquisition Cost (AAAC), as well as the impact of negotiated price concessions which include discounts, rebates, and

[15] Johnson AE, et al. "Relation of Household Income to Access and Adherence to Combination Sacubitril/Valsartan in Heart Failure: A Retrospective Analysis of Commercially Insured Patients." Circ Cardiovasc Qual Outcomes, 2022 Jul;15(7):e009179. https://pubmed.ncbi.nlm.nih.gov/35549378/.
[16] Smith, G. H., et al. (2019). Discussing Out-of-Pocket Costs With Patients: Shared Decision Making for Sacubitril-Valsartan in Heart Failure. Journal of the American Heart Association, 8(1), e010635. https://doi.org/10.1161/JAHA.118.010635.
[17] Rao, B. R., et al. (2020). Heart Failure and Shared Decision-Making: Patients Open to Medication-Related Cost Discussions. *Circulation. Heart failure*, *13*(11), e007094. https://doi.org/10.1161/CIRCHEARTFAILURE.120.007094.
[18] Transcript: Entresto, November 1, 2023 Medicare Drug Price Negotiation Program Patient-Focused Listening Session. Centers for Medicare & Medicaid Services (CMS), Nov. 1, 2023. https://www.cms.gov/files/document/entresto-transcript-110123.pdf
[19] Ibid.
[20] Number of 2023 enrollees in APAC database across commercial insurers, Medicaid, and Medicare. For more information regarding APAC data visit: https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx.

other price reduction negotiations. Together, the data provides a comprehensive view of Entresto's list price trajectory, pharmacy acquisition costs, and the degree to which price reductions are realized in practice by payers in Oregon.

Price history

WAC per 30-day supply was calculated with unit WAC from Medi-Span and was reviewed as an indication of historic price trends for the drug. However, WAC does not account for discounts, rebates, or other changes to the drug's cost throughout the supply chain.

Table 3 30-day supply for review drug

	Entresto
30-day supply	60 units (60 pills)

Table 4 2018 through 2024 WAC per 30-day supply[21]

Year	Entresto
2018	$463
2019	$503
2020	$533
2021	$566
2022	$611
2023	$639
2024	$656
Avg. Annual % Change	6.0%
% change 2018 and 2024	41.6%

The WAC of Entresto, averaged across seven NDCs reported, was approximately **$11 per unit** at the end of 2024.[22] Between 2018-2024, the unit WAC increased at an average annual rate of **6.0 percent**, exceeding the general consumer price index (CPI-U) inflation rate in 2018-2019, 2019-2020, 2020-2021, and 2022–2023 (see Table 5 and Figure 2).[23]

[21] Medi-Span. Wolters Kluwer, 2025. https://www.wolterskluwer.com/en/solutions/medi-span/medi-span.
[22] Ibid
[23] Consumer Price Index. U.S. Bureau of Labor Statistics. https://www.bls.gov/cpi/tables/supplemental-files/.

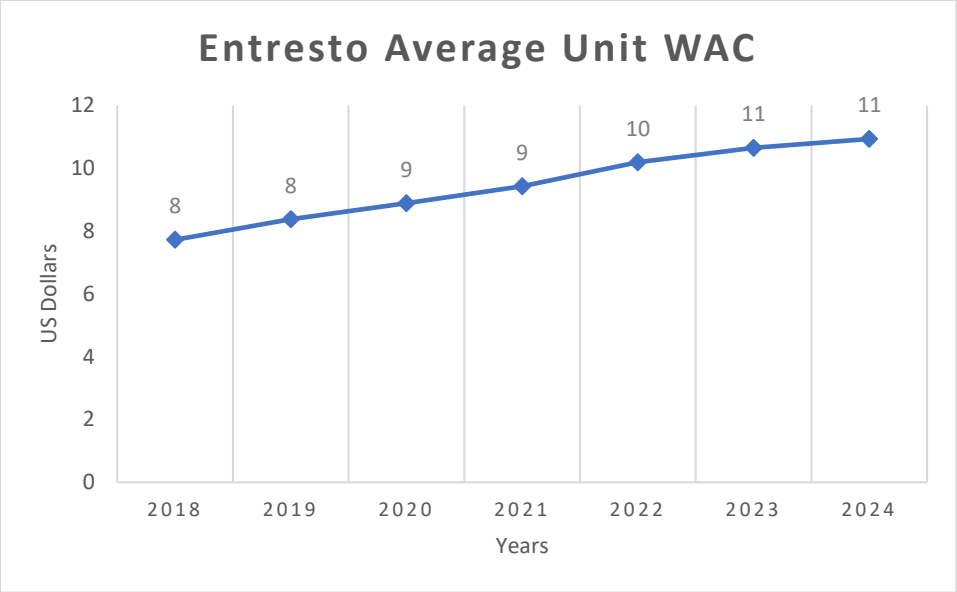

Figure 1 Entresto WAC from 2018-2024

Table 5 Percent change of WAC of drug with CPI comparison[24]

Year	Entresto	CPI-U
2018-2019	8.5%	1.7%
2019-2020	6.1%	0.7%
2020-2021	6.1%	5.3%
2021-2022	8.1%	9.0%
2022-2023	4.5%	3.1%
2023-2024	2.7%	3.0%

[24] Percentages might differ from Table 4 as Table 5 percentages are based on unit WAC only.

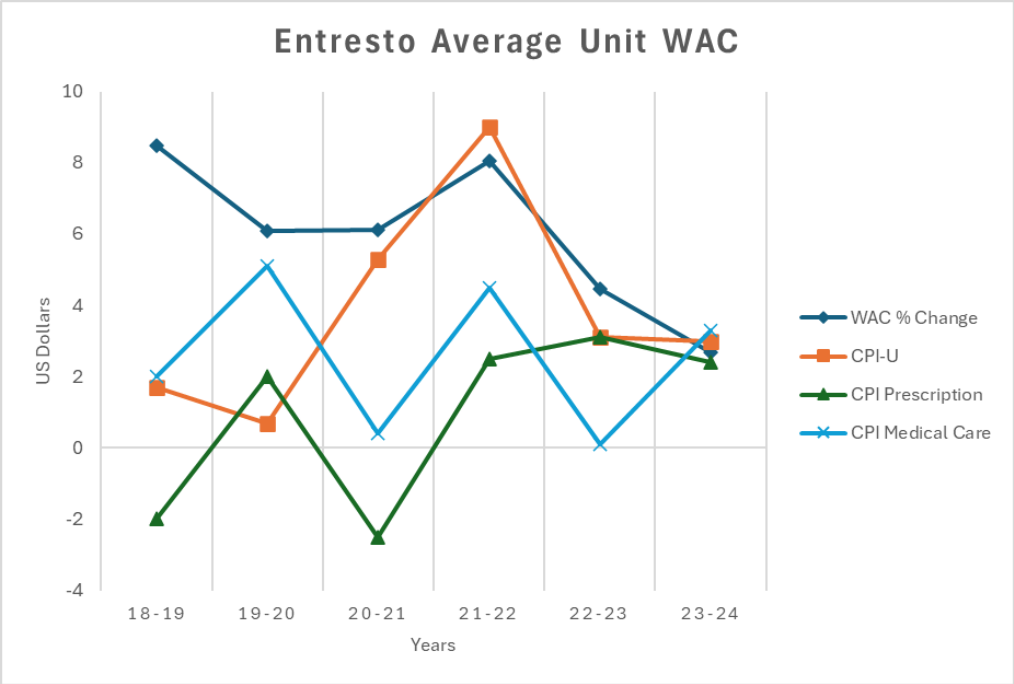

Figure 2 Year over year change in WAC compared to inflation rates[25]

Pharmacy acquisition costs

The AAAC, which reflects pharmacies' actual purchase prices for Medicaid fee-for-service claims, rose from **$8.65 per unit in Q1 2020 to $10.99 per unit in Q4 2024**, an approximate **27 percent increase** over the period (see Table 6).[26] Relative to the **$10.93 WAC** in end-of-year 2024, an **AAAC increase of 0.55 percent** is indicated.

While WAC provides a standardized benchmark of list price, it does not account for negotiated price concessions. In contrast, the AAAC offers a more representative estimate of the net price incurred by Medicaid payers in Oregon, derived from regular pharmacy surveys conducted by the Oregon Health Authority. Monitoring these trends over time contextualizes Entresto's price trajectory relative to inflation and informs the assessment of its affordability for public and private payers.

[25] Consumer Price Index. U.S. Bureau of Labor Statistics. https://www.bls.gov/cpi/tables/supplemental-files/.
[26] Average Actual Acquisition Cost (AAAC) Rate Listing for Brand Drugs. Pharmacy Prescription Volume Survey, January 2020 to December 2024. AAAC Rate Review. Myers and Stauffer and Oregon Health Authority. https://myersandstauffer.com/client-portal/oregon/.

Table 6 2020-2024 AAAC Medicaid FFS quarterly purchase prices

Year	Quarter 1	Quarter 2	Quarter 3	Quarter 4	Average AAAC	Average WAC
2020	$9	$9	$9	$9	$9	$9
2021	$9	$9	$9	$9	$9	$9
2022	$10	$10	$10	$10	$10	$10
2023	$11	$11	$11	$11	$11	$11
2024	$11	$11	$11	$11	$11	$11

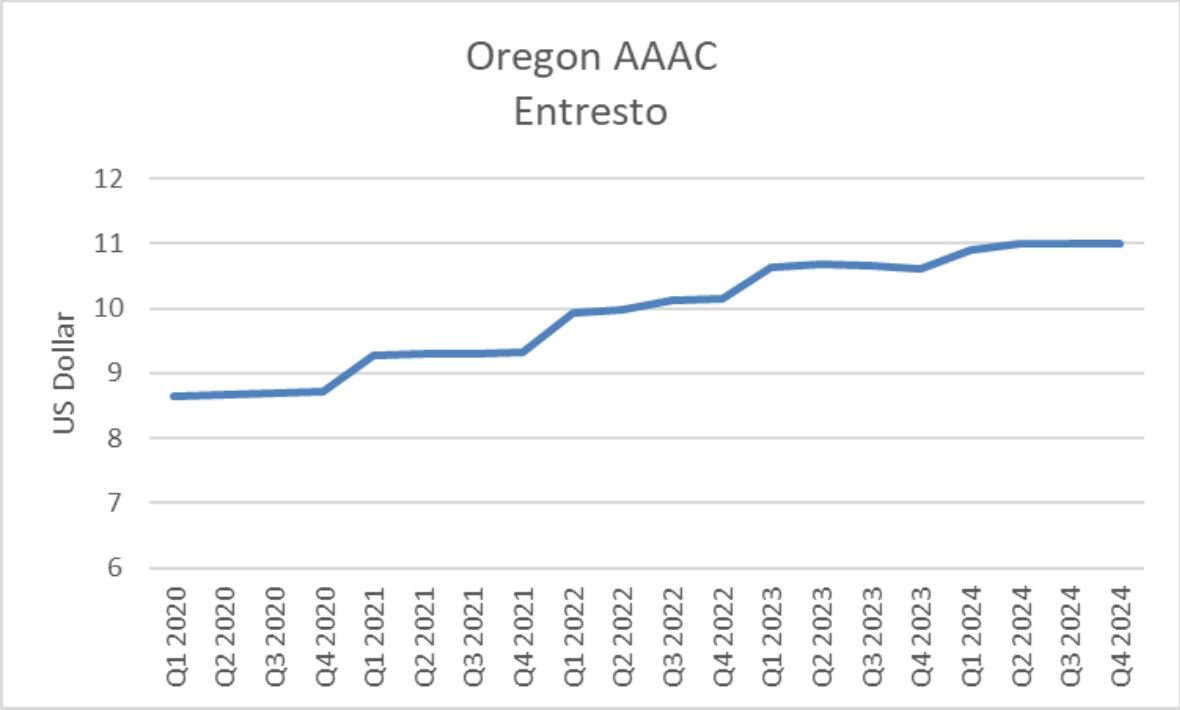

Figure 3 AAAC for Entresto from Q1 2020 to Q4 2024

Estimated average monetary price concession

ORS 646A.694(1)(d) and OAR 925-200-0020(1)(d) & (2)(d) & (2)(L)(A-B). Data source information provided from data call.

This section provides an analysis of the average monetary discounts, rebates, and other price concessions applied to Entresto claims in the commercial market. Drawing on 2023 data submitted through the carrier data call, it evaluates the extent to which these concessions reduced gross drug costs and estimates the average net costs to payers after adjustments. The analysis includes claim-level data on the proportion of claims with applied discounts and the breakdown of the total concession amounts by type, offering insight into the reduced costs provided through manufacturers, PBM, and other negotiated price reductions.

Based on carrier-submitted data for 2023, the **average gross cost of Entresto per enrollee in the commercial market was approximately $3,544**. After accounting for manufacturer rebates, pharmacy benefit manager (PBM) discounts, and other price concessions, the **average net cost per enrollee declined to approximately $3,136**, reflecting an **estimated mean discount of 11.5 percent** relative to gross costs.

Across all reporting carriers and market segments, the total cost of Entresto before concessions was **$6,063,238**, with total reported price concessions amounting to approximately **$698,205**, as detailed in Table 7. Notably, **81.9 percent of claims benefited from some form of price concession**, **leaving 18.1% at full gross cost**.

Table 7 Net cost estimate based on carrier submitted 2023 data

Total number of enrollees	1,711
Total number of claims	5,387
Total number of claims with price concessions applied	4,412
Percentage of claims with price concessions applied	81.9%
Percentage of cost remaining after concessions	88.5%
Percentage of discount	11.5%
Manufacturer price concessions for all market types	$619,355
PBM price concessions for all market types	$70,097
Other price reductions for all market types	$8,754
Cost before price concessions across all market types	$6,063,238
Total price concessions across all market types	$698,205
Cost of after price concessions across all market types	$5,365,033
Avg. payer spend per enrollee without price concessions	$3,544
Avg. payer spend per enrollee with price concessions	$3,136

Including all market segments, the **gross spend of Entresto per claim for commercial carriers was $1,126** before any discounts, rebates, or other price concessions. The net cost per enrollee discounts, rebates, and other price concessions was **$996**, meaning that insurers reported a price concession of **$130** per claim on the initial drug cost as shown in Table 8.

Table 8 The average price concessions across market types provided from Data Call[27]

	Average	Individual market	Large market	Small market
Spend per claim, gross	$1,126	$1,161	$1,090	$1,207
Spend per claim, net	$996	$1,003	$973	$1,067
Price concessions per claim	$130	$158	$116	$141

Figure 4 shows manufacturer concessions comprised the largest share, supplemented by PBM discounted price arrangements and other adjustments across the payer types.

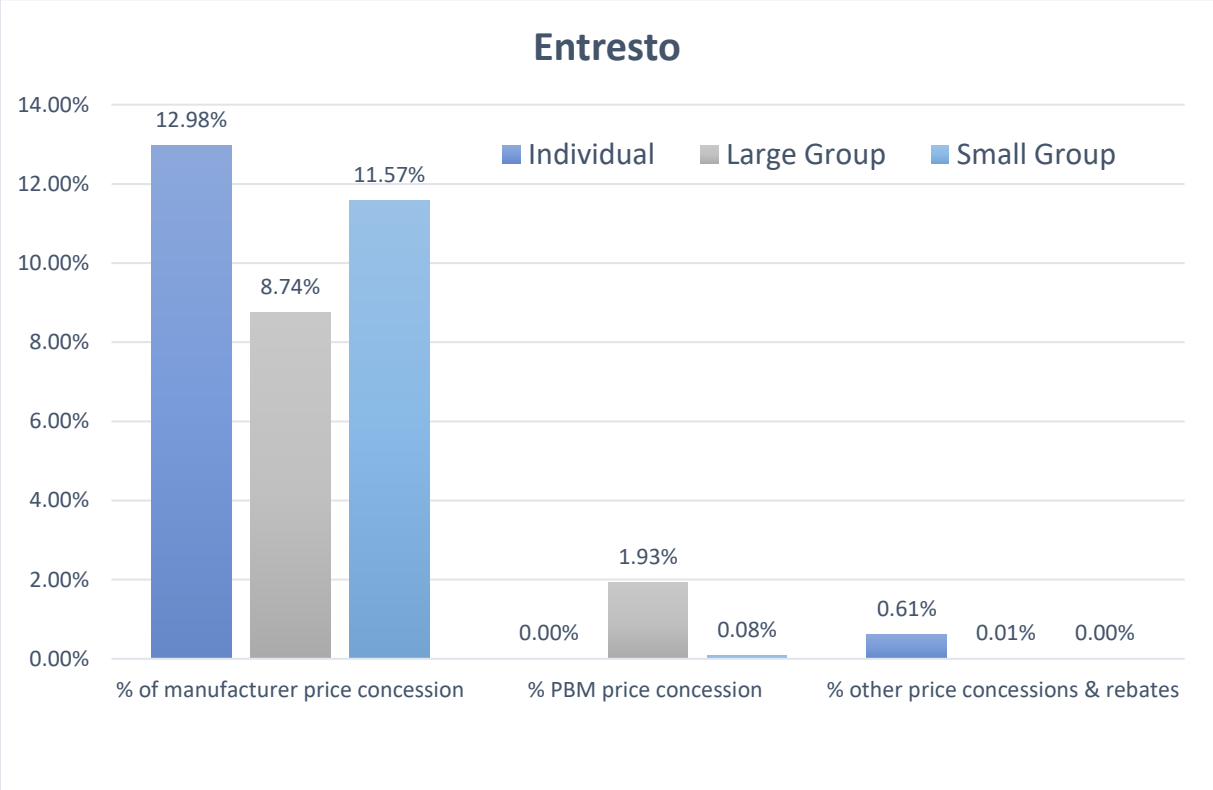

Figure 4 Percent of price concession in each market type[28,29]

[27] Based on data submitted to the Department of Consumer and Business Services (DCBS) by Oregon's commercial insurance carriers.

[28] Price concession refers to any form of discount, directed or indirect subsidy, or rebate received by the carriers or its intermediary contracting organization from any source that serves to decrease the costs incurred under the health plan by the carriers. Examples of price concessions include but are not limited to: Discounts, chargebacks, rebates, cash discounts, free goods contingent on purchase agreement, coupons, free or reduced-price services, and goods in kind. Definition adapted from Code of Federal Regulations, Title 42, Chapter IV, Subchapter B, Part 423, Subpart C. See more at: CFR-2024-title42-vol3-sec423-100.pdf.

[29] Rebate refers to a discount that occurs after drugs are purchased from a pharmaceutical manufacturer and involves the manufacturer returning some of the purchase price of the purchaser. When drugs are purchased by a managed care organization, a rebate is based on volume, market share, and other factors. Academy of Managed Care Pharmacy. https://www.amcp.org/about/managed-care-pharmacy-101/managed-care-glossary.

Estimated total amount of the price concession

ORS 646A.694(1)(e) and OAR 925-200-0020(1)(e) & (2)(d) & (2)(L)(A-B). Limitations in scope and resources available for this statute requirement. Possible data source carrier data call.

This section is intended to quantify the total discounts, rebates, or other price concessions provided by the manufacturer of Entresto to each pharmacy benefit managers, expressed as a percentage of the drug's price. At the time of this review, there was no specific data available to PDAB to determine the total amount of such price concessions in the Oregon market.

The statutory and regulatory criteria call for consideration of such information to the extent practicable; however, due to limitations in available evidence and reporting, this analysis was not performed. Future reviews may incorporate these data as they become available through improved reporting or additional disclosures from manufacturers, PBMs, and payers.

Estimated price for therapeutic alternatives[30]

ORS 646A.694(1)(f) and OAR 925-200-0020(1)(f), (2)(c) & (2)(m). Data source information provided from APAC.

No therapeutic alternatives were identified for Entresto based on clinical equivalence. Therefore, no estimated pricing information for therapeutic alternatives is applicable for this section.

Estimated average price concession for therapeutic alternatives

ORS 646A.694(1)(g) and OAR 925-200-0020(1)(g) & (2)(d) & (2)(L)(A-B). Limitations in scope and resources available for this statute requirement.

This section addresses the estimated average of discounts, rebates, or other price concessions associated with therapeutic alternatives to Entresto, as compared to the subject drug itself. At the time of this review, there was no quantifiable data available to PDAB to assess the average price concessions for the identified therapeutic alternatives in the Oregon market.

The statutory and regulatory criteria call for consideration of such information to the extent practicable. However, due to limitations in available evidence and reporting, this analysis was not performed. Future reviews may incorporate this information as additional data become available through carrier reporting, manufacturer disclosures, or other sources.

[30] Therapeutic alternative means a drug product that contains a different therapeutic agent than the drug in question, but is FDA-approved, compendia-recognized as off-label use for the same indication, or has been recommended as consistent with standard medical practice by medical professional association guidelines to have similar therapeutic effects, safety profile, and expected outcome when administered to patients in a therapeutically equivalent dose. ORS 925-200-0020(2)(c).

Estimated costs to health insurance plans

ORS 646A.694(1)(h) and OAR 925-200-0020(1)(h) & (2)(h) & (m). Data source information provided from APAC and data call.

This section quantifies the financial impact of Entresto on health insurance plans in Oregon, based on claims and expenditure data from APAC and the carrier data call. Costs are delineated by payer type—including commercial, Medicaid, and Medicare—as well as by market segment within the commercial population. These estimates highlight the distribution of expenditures across different health coverage lines and inform assessments of the drug's budgetary implications for public and private payers.

In 2023, the Oregon APAC database recorded **53,866 claims for Entresto among 10,016 enrollees**, corresponding to a **total gross expenditure of $47.0 million**.

Table 10 provides gross cost estimates by payer line of business:

- **Medicare** accounted for the largest share of utilization, with 28,432 claims from 5,833 enrollees and a total spend of **$38.4 million**.
- **Medicaid** and **commercial** payers reported smaller but notable expenditures of approximately **$8.8 million** and **$9.8 million**, respectively.

Table 9 Estimated 2023 APAC total annual gross payers' expenditure for total enrollees and total claims[31]

Payer line of business	Total enrollees	Total claims	Total payer paid	Average cost amount per enrollee	Average cost amount per claim
Commercial	2,181	12,094	$9,762,540	$4,476	$807
Medicaid	2,002	13,340	$8,842,935	$4,417	$663
Medicare	5,833	28,432	$28,426,676	$4,873	$1000
TOTAL	**10,016**	**53,866**	**$47,032,151**		

Table 11 compares the overall payer cost per enrollee of Entresto, distinguished by lines of business. The total cost per enrollee for Entresto is $5,179, with Medicare being the highest line of business at $4,873. The median cost per enrollee of Entresto is $684. The cost per enrollee ranges widely and is represented by the IQR of $1,222.

[31] Based on 2023 Oregon APAC data across commercial insurers, Medicaid, and Medicare. APAC cost information is prior to any price concessions such as discounts or coupons.

Table 10 Estimated 2023 APAC payer annual gross cost per enrollee of the review drug[32]

Proprietary name	Commercial cost/ enrollee	Medicaid cost/ enrollee	Medicare cost/ enrollee	Total[33] cost per enrollee	Cost per enrollee, median	IQR	Cost per enrollee, 75th percentile	Cost per enrollee, 95th percentile
Entresto	$4,476	$4,417	$4,873	$5,179	$684	$1,222	$1,766	$2,155

Data submitted via the carrier data call further stratifies commercial expenditures by market segment. The collected **total net cost to the healthcare system was around $6 million**, with payer paying $5.4 million, and enrollees our-of-pocket estimating to be $698,148. Table 12 includes the average plan costs per enrollee in the commercial market ranged from **$3,456 (large group)** to **$3,710 (individual)** annually.

Table 11.a Estimated 2023 total net costs to the healthcare system, payers and OOP/enrollee[34]

Market	Number of claims	Number of enrollees	Total annual spending	Payer Paid	Enrollee out-of-pocket cost
Individual	1,166	362	$1,343,077	$1,075,318	$267,759
Large Group	3,287	1,052	$3,636,186	$3,312,565	$323,621
Small Group	934	297	$1,101,632	$994,863	$106,768
Total	**5,387**	**1,711**	**$6,080,895**	**$5,382,746**	**$698,148**

Table 11.b Estimated 2023 total net costs to the healthcare system, payers and OOP/enrollee

Market	Avg. plans spend/ claim	Avg. payer paid/ claim	Avg. enrollee paid/ claim	Avg. plans spend/ enrollee	Avg. payer paid/ enrollee	Avg. OOP/ enrollee
Individual	$1,152	$922	$230	$3,710	$2,970	$740
Large Group	$1,106	$1,008	$98	$3,456	$3,149	$308
Small Group	$1,179	$1,065	$114	$3,709	$3,350	$359

As shown in Figure 5, the **large group market segment** represented the majority of commercial spending (73% of total), followed by individual and small group markets.

[32] Based on 2023 Oregon APAC data across commercial insurers, Medicaid, and Medicare. APAC cost information is prior to any price concessions such as discounts or coupons.
[33] The total is the overall cost per enrollee across commercial insurers, Medicaid, and Medicare.
[34] Cost information from the data call is the net cost of the drug after price concessions.

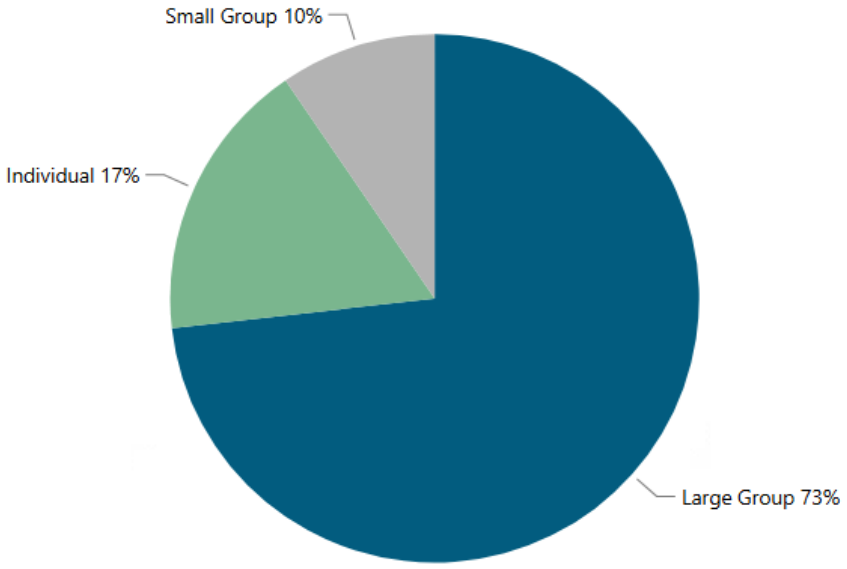

Figure 5 Data call total annual spend (payer paid)

Table 13 indicates CCOs reported Entresto as having an annual greatest increase from 2022-2023 (rebates not included) with a $2,860,102 year-over-year total cost growth.

Table 12 Medicaid CCOs greatest increase in share to total cost from 2022-2023 (rebates not included)[35]

Medicaid CCOs			
2022	**2023**	**YoY change in spending**	**Percent of total CCO cost 2023**
$5,387,651	$8,247,753	$2,860,102	0.2%

CCO Pharmacy spend provided by Oregon State University drug use research and management program.

Impact on enrollee access to the drug

ORS 646A.694(1)(i) and OAR 925-200-0020(1)(i). Data source information provided from carrier data call.

This section summarizes information reported by carriers regarding plan design features that relate to coverage of Entresto, including prior authorization requirements, step therapy protocols, and formulary placement. These data describe how the drug is positioned within

[35] CCO pharmacy spend provided by: Oregon State University Drug Use and Research Management DUR utilization reports 2023. College of Pharmacy, Oregon State University. https://pharmacy.oregonstate.edu/research/pharmacy-practice/drug-use-research-management/dur-reports.

insurance benefit designs and the extent to which utilization management processes were applied during the reporting period.

Based on information reported through the carrier data call, the follow plan design features were observed for Entresto. In 2023, approximately **40.3 percent of reporting plans required prior authorization (PA)** for coverage of the drug, and **no plans requiring step therapy** before approving its use.

For formulary placement, **6.1 percent of plans categorized Entresto as a non-preferred drug** and **no plans excluded it entirely from the formulary**.

Table 13 Plan design analysis from 2023 data

Percentage of Plan	
Required prior authorization	40.3%
Required step therapy	0.0%
On a non-preferred formulary	6.1%
Not covered	0.0%

Note: percentages can equal over 100 percent as some carrier and market combos may have multiple plans that fall under different designs. For example: Carrier A may have three plans in the small group market that require prior authorization but two other plans in the small group market that do not require prior authorization.

Relative financial impacts to health, medical or social services costs

ORS 646A.694(1)(j) and OAR 925-200-0020(1)(j) & (2)(i)(A-B). Limitations in scope and resources available for this statute requirement.

This section addresses the extent to which the use of Entresto may affect broader health, medical, or social service costs, as compared to alternative treatments or no treatment. At the time of this review, there was no quantifiable data available to PDAB assess these relative financial impacts in the Oregon population.

The statutory and regulatory criteria contemplate consideration of such impacts to the extent practicable. However, due to limitations in available evidence, data systems, and the challenges inherent in isolating the indirect effects of a single drug on broader healthcare or social service costs, this analysis was not performed.

Future reviews may incorporate findings from real-world evidence, health technology assessments, or economic modeling as such data become available.

Estimated average enrollee copayment or other cost-sharing

ORS 646A.694(1)(k) and OAR 925-200-0020(1)(k) & (2)(j)(A-D). Data source information provided from APAC and carrier data call. Data limitations with patient assistance programs

This section summarizes the average annual enrollee out-of-pocket (OOP) costs for Entresto in Oregon, as reported in 2023 by the two data sources: the Oregon All Payers All Claims (APAC) database and the carrier data call.[36] These costs include enrollee copayments, coinsurance, and deductible contributions for the drug and are presented by insurance type and commercial market segment.

Table 15 and 16 presents the average annual enrollee cost-sharing amounts derived from APAC and carrier-submitted data. The APAC data, which includes claims from commercial, Medicaid, and Medicare enrollees, showed average per-claim and per-enrollee OOP gross costs that varied by payer line of business. For example, **Medicare insured enrollees recorded higher average annual OOP costs** than commercial enrollees. Due to the absence of Medicaid OOP costs, the insurance type has been omitted entirely from the following tables.

Table 14 APAC annual out-of-pocket gross cost per enrollee [37]

Proprietary name	Annual Medicare OOP cost/ enrollee	Annual Commercial OOP cost/ enrollee	Total[38]	Median	IQR	75th percentile	95th percentile
Entresto	$531	$501	$535	$45	$184	$184	$848

Table 15 APAC out-of-pocket gross cost per claim[39]

Proprietary name	Medicare OOP cost/ claim	Commercial OOP cost/ claim	Total[40]	Median	IQR	75th percentile	95th percentile
Entresto	$109	$90	$103	$30	$109	$109	$500

[36] Gross costs from the APAC database are prior to any price concessions such as discounts or coupons. Net cost information from the data call is the cost of the drug after price concessions.
[37] Based on 2023 Oregon APAC data across commercial insurers, Medicaid, and Medicare. APAC cost information is prior to any price concessions such as discounts or coupons.
[38] The total is the overall cost per enrollee across commercial insurers, Medicaid, and Medicare.
[39] Based on 2023 Oregon APAC data across commercial insurers, Medicaid, and Medicare. APAC cost information is prior to any price concessions such as discounts or coupons.
[40] The total is the overall cost per claim across commercial insurers, Medicaid, and Medicare.

Clinical information based on manufacturer material[41]

ORS 646A.694(1)(L) and OAR 925-200-0020(1)(L). Information provided from manufacturers and information with sources from contractor(s).

Drug indications

- FDA Approved:
    - *Sacubitril and valsartan* is indicated:
        - to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.
        - for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. *Sacubitril and valsartan* reduces NT-proBNP, an established biomarker used to assess the severity and determine the prognosis of heart failure and is expected to improve cardiovascular outcomes.[42]

- Off Label Uses: Lowering blood pressure: Studies conducted showed using Entresto to lower blood pressure was well tolerated.[43,44]

Clinical efficacy[45]

Sacubitril and valsartan is a combination of neprilysin inhibitor (sacubitril) and an angiotensin II receptor blocker (valsartan) that is for the treatment of chronic heart failure in adults and pediatric patients aged one and older. Its clinical efficacy in adults with heart failure has been demonstrated in two randomized controlled trials: PARASDGM-HF (vs enalapril) and PARAGON-HF (vs valsartan). The trial supporting pediatric use comes from the PANORAMA-HF study.

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[41] U.S. Food & Drug Administration. Entresto (sacubitril and valsartan) Prescribing Information. Novartis Pharmaceuticals Corp., Revised 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207620s018lbl.pdf

[42] "New Novartis study supports Entresto as foundational HFrEF therapy and in-hospital initiation in appropriate stabilized heart failure patients." Novartis, Nov 11, 2018. https://www.novartis.com/us-en/news/media-releases/new-novartis-study-supports-entresto-foundational-hfref-therapy-and-hospital-initiation-appropriate-stabilized-heart-failure-patients.

[43] Xuelin Wang, Feier Song, Lujing Jiang, Ziling Huang, Songyuan Luo, Xin Li, Xuyu He, Efficacy and Safety of Sacubitril/Valsartan in Chronic Type B Aortic Dissection Combined With Mild Hypertension, *American Journal of Hypertension*, Volume 37, Issue 8, August 2024, Pages 612–620, https://doi.org/10.1093/ajh/hpae038.

[44] Rakugi, H., Kario, K., Yamaguchi, M. *et al.* Efficacy of sacubitril/valsartan versus olmesartan in Japanese patients with essential hypertension: a randomized, double-blind, multicenter study. Hypertens Res 45, 824–833 (2022). https://doi.org/10.1038/s41440-021-00819-7.

[45] U.S. Food & Drug Administration. Entresto (sacubitril and valsartan) Prescribing Information. Novartis Pharmaceuticals Corp., Revised 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207620s018lbl.pdf.

- The PARADIGM-HF trial enrolled 8,442 adults with symptomatic chronic heart failure with reduced ejection fraction (HFrEF, LVEF ≤ 40%) and compared sacubitril/valsartan 97/103 mg twice daily to enalapril 10 mg daily. Key findings include:
    - *sacubitril and valsartan* reduced the risk of cardiovascular death or heart failure hospitalization by 20% compared to enalapril (21.8% vs. 26.5%, respectively, hazard ratio [HR] 0.80; 95% CI, 0.73–0.87; $p < 0.0001$) with an absolute risk reduction (ARR) of 4.7% and a number needed to treat (NNT) of 22.
    - *sacubitril and valsartan* also reduced the risk of all-cause mortality compared to enalapril (17% vs. 19.8%; HR 0.84; 95% CI, 0.76–0.93; $p = 0.0009$; ARR 2.8%)).
    - Symptomatic hypotension also occurred more frequently with sacubitril/valsarta n (14.0% vs. 9.2%; p<0.001).

These results support *sacubitril and valsartan*'s superiority over ACE inhibitors in reducing morbidity and mortality in HFrEF.

- The PARAGON-HF trial compared sacubitril/valsartan 97/103 mg twice daily to valsartan valsartan 160 mg twice daily in 4,796 patients with heart failure and LVEF ≥ 45%, including both heart failure with preserved ejection fraction (HFpEF) and heart failure with mildly reduced EF (HFmrEF). Key findings include:
    - There was a numerical reduction with sacubitril/valsartan, but no significant difference in the primary outcome of total HF hospitalizations and CV death with 12.8 events per 100 patient-yr in the sacubitril/valsartan group and 14.6 per 100 patient-year in the valsartan group (RR 0.87; 95% CI 0.75 to 1.01).
    - The effect was driven by fewer total HF hospitalizations (RR 0.85; 95% CI, 0.72–1.00).
    - Subgroup analyses suggested a possible benefit in patients with LVEF ≤ 57% compared to those with higher baseline LVEF. Benefits are more evident in patients with LVEF before normal.

- The expanded FDA approval in pediatric patients age one year and older was based on the PANORAMA-HF study, a randomized, double-blind study in 110 children aged 1-17 years with chronic HF and LVEF ≤ 40% previously on an ACE or ARB. Sacubitril/valsartan target dose of 3.1 mg/kg BID was compared to enalapril (target dose 0.2 mg/kg) and the primary outcome was reduction in NT-proBNP reduction over 12 weeks:
    - At week 12, sacubitril/valsartan (n=54) resulted in a 15.6% greater reduction than enalapril (n=54) (mean ratio 0.84; 95% CI 0.67-1.06) but did not reach superiority over enalapril.
    - While the between-group difference was not statistically significant, the reduction in NT-proBNP was considered clinically meaningful, supporting FDA approval.

Comparative effectiveness

- While there is no therapeutic alternative that includes a neprilysin inhibitor like sacubitril, data supports early and significant absolute risk reduction in all-cause mortality with ACE-inhibitors and substituted ARBs in patients with HFrEF.
- Data from meta-analysis suggests that sacubitril/valsartan is not superior to ACEI and ARB therapy when equivalent doses are utilized in patients with HFrEF and are superior to enalapril at sub-equivalent doses (10 mg daily).
- In patients who cannot tolerate sacubitril/valsartan due to hypotension or cannot access it, therapy with an ACE inhibitor or ARB is recommended.

Clinical safety

- FDA safety warnings and precautions:
    - Fetal toxicity
    - Angioedema
    - Hypotension
    - Impaired renal function
    - Hyperkalemia
- Contraindications:
    - Hypersensitivity to any component.
    - History of angioedema related to previous ACEi or ARB therapy.
    - Concomitant use with ACE inhibitors (and within 36 hours of ACE inhibitor use)
    - Concomitant use with aliskiren in patients with diabetes.
- Common adverse reactions:
    - Serious allergic reactions causing swelling of face, lips, tongue, and throat (angioedema) that may cause trouble breathing and death.
    - People who are Black and take *sacubitril and valsartan* may have a higher risk of having angioedema than people who are not Black and take *sacubitril and valsartan*.
    - People who have had angioedema before taking *sacubitril and valsartan* may have a higher risk of having angioedema than people who have not had angioedema before taking *sacubitril and valsartan*.
    - Low blood pressure (hypotension): 18%
    - Kidney problem (acute kidney injury): 15%
    - Increased amount of potassium in the blood (hyperkalemia): 12%

Input from specified stakeholders

ORS 646A.694(3) and OAR 925-200-0020(2)(k)(A-D)

See appendix page for all stakeholder feedback.

Patients and caregivers:

Note: The information presented is based on self-reported survey responses from individuals prescribed certain medications. Participation in the survey was voluntary, and the responses reflect the individual's personal understanding and interpretation of the question asked. As such, the data may contain inconsistencies or inaccuracies due to varying levels of comprehension, recall bias, or misinterpretation of question intent. These limitations should be considered when interpreting the responses.

Survey information was received from two individuals taking or having an association with Entresto. For both respondents, their insurance plan covered Entresto.

Zero patients were on Medicaid, two patients were on Medicare, and zero patients had private health insurance. No patient reported that their prescription was not covered. Zero patients reported being on patient assistance programs.

Below are written answers from Oregon patients who responded to the PDAB survey in April 2025. Survey responses have been edited for readability, length and to protect patient privacy.

"Entresto"

- I take Entresto 24/26mg 2X daily for heart problems and have been taking it since January 2021. The Veterans Administration pays for my medications. Entresto provides better heart function. It is a very expensive med and I'm happy that the VA covers the cost!

- For the past six months, I have been taking Entresto 24-26mg twice a day. My most recent, monthly, out-of-pocket cost was $181.14. In the past, I used losartan to treat the condition.

Individuals with scientific or medical training

This section summarizes information reported by individuals with scientific and medical training. There were no reports for Entresto to determine the impact of the disease, benefits or disadvantages, drug utilization, or input regarding off label usage.

Safety net providers

This section summarizes information reported by safety net providers regarding their experience dispensing Entresto, particularly in relation to the federal 340B Drug Pricing

Program. The survey collected information on utilization of the drug, the extent to which it was eligible for 340B discounts, dispensing arrangements, and payment and reimbursement levels.

A total of **11 safety net clinics** responded to the survey. Among respondents, **nine clinics indicated that Entresto was covered as a 340B-eligible prescription** within their programs. Most clinics (91%) reported operating an internal pharmacy for dispensing 340B-eligible medications, and 64 percent reported using one or more contract pharmacies for this purpose.

Additionally, **82 percent of clinics reported having a prescription savings program**, and all respondents (100%) reported employing a staff member dedicated to 340B compliance.

Regarding expenditures under the 340B program, respondents reported a range of total amounts paid for Entresto: 27% reported paying between **$0–$100,000**, 18% reported between **$100,001–$300,000**, while **55% declined to report citing trade secret protections**.

Reported reimbursement for dispensing Entresto under 340B also varied: 18 percent of respondents reported reimbursement between **$0–$100,000**, 9 percent between **$100,001–$500,000**, and 18 percent between **$500,000–$10,000,000**.

Without additional detail on the volume of patients treated or the per-claim costs, it is difficult to interpret these figures in terms of clinic financial risk or access outcomes. The wide range may reflect differing clinic sizes, patient populations, or inventory management practices. Notably, the absence of full reporting by 55 percent of clinics makes it challenging to assess how Entresto's cost affects long-term affordability or sustainability for safety-net providers.

These results suggest that while Entresto is incorporated into many safety-net programs, further data would be necessary to understand how reimbursement aligns with acquisition cost and whether 340B discounts adequately mitigate financial exposure for patients and the healthcare system.

Table 16 Safety net provider survey responses

Survey information	Response
Clinics responded	11
The drug is covered as a 340B eligible prescription in their program	9
Reported having an internal pharmacy they use to dispense 340B eligible prescriptions.	91%
Reported having one or more contract pharmacies from which 340b eligible prescriptions are dispensed.	64%
Reported having a prescription savings program to improve patient access to prescription medications	82%
Reported having a staff person dedicated to 340b compliance requirements	100%
Reported total amount paid for drug under 340B was between $0-$100,000	27%

Survey information	Response
Reported total amount paid for drug under 340B was between $100,001-$300-000	18%
Reported total amount paid for drug under 340B was between this was trade secret and did not provide an amount	55%
Reported total reimbursement for drugs dispensed under 340B was between $0-$100,000	18%
Reported total reimbursement for drugs dispensed under 340B was between $100-001-$500,000	9%
Reported total reimbursement for drugs dispensed under 340B was between $500,000-$10,000,000	18%

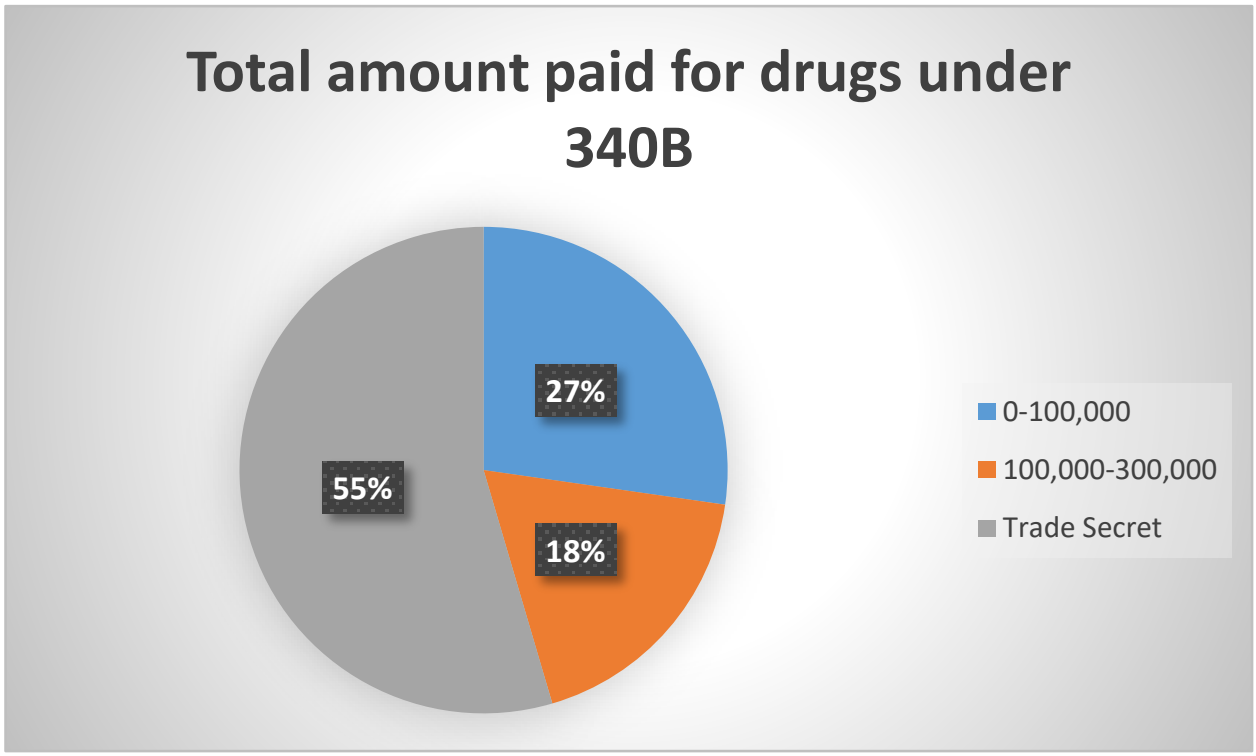

Figure 6 Amounts paid for drug under 340B discount program

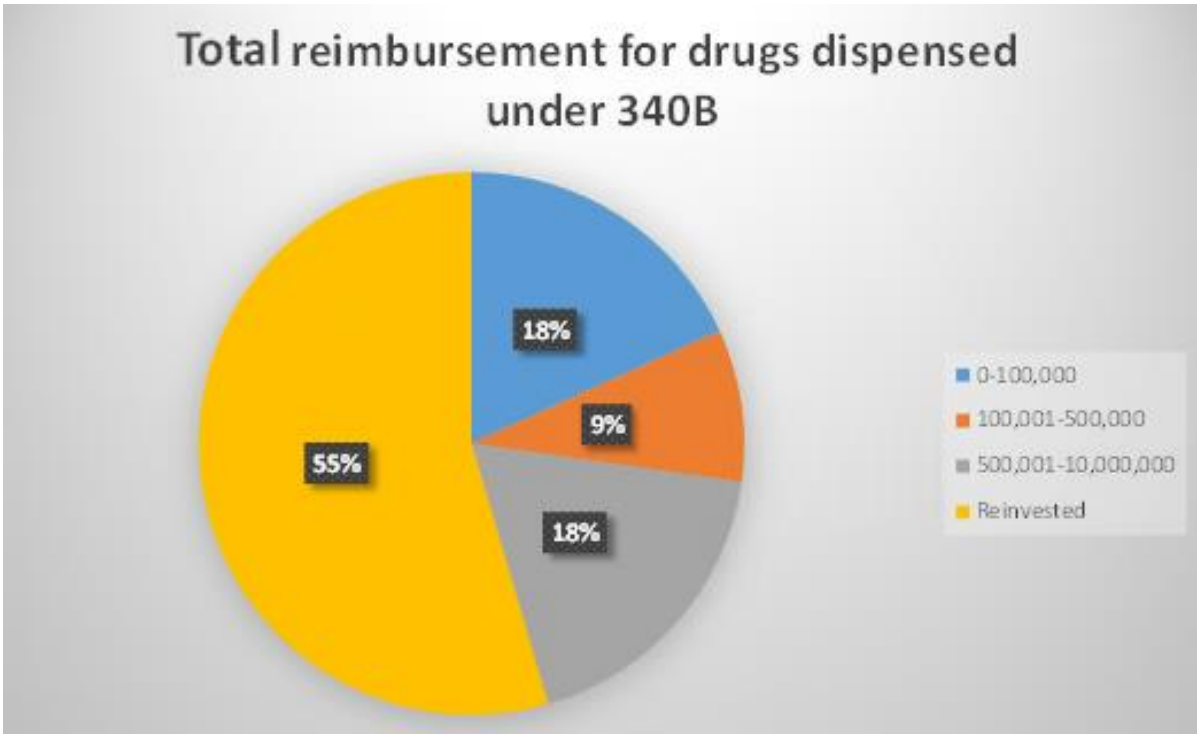

Figure 7 Estimated reimbursement ranges in dollars for potential reimbursement with drugs dispensed under 340B program

Payers

Relevant information from payers is incorporated throughout the material packed based on the data submitted through the formal data call process. This includes details on the total cost of care for the disease, the cost and utilization of the prescription drug, the availability and formulary placement, therapeutic alternatives, as well as reported impacts to member costs.

The data provided through the carrier data call serves as a comprehensive source of payer input and reflects aggregate insights across participating organizations. No separate qualitative feedback or narrative statements were requested or received from individual payers for inclusion in the section.

Appendix

Stakeholder feedback:

Name of speaker	Association to drug under review	Drug	Format	Date	Exhibit website link
Courtney Piron	Novartis	Entresto	Letter	5/1/2025	Exhibit A
Sarah Hoffman	Partnership to Advance Cardiovascular Health	Entresto	Letter	5/19/2025	Exhibit B
Courtney Piron	Novartis	Entresto	Letter	7/11/2025	Exhibit C
Sarah Hoffman	Partnership to Advance Cardiovascular Health	Entresto	Letter	7/14/2025	Exhibit D
Sue Koob	Preventive Cardiovascular Nurses Association	Entresto	Letter	7/14/2025	Exhibit E