Sacubitril-Valsartan Real-World Assessment of Total Cost of Care and Resource Utilization Pre/Post Initiation Among Commercially Insured Members with Reduced Ejection Fraction Heart Failure

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BACKGROUND

- Sacubitril-valsartan (sac-val) is FDA approved to treat heart failure from reduced ejection fraction (HFrEF).[1]
- In 2017, the American College of Cardiology (ACC), American Heart Association (AHA) and the Heart Failure Society of America (HFSA) jointly approved new treatment guidelines for systolic heart failure (SHF), aka HFrEF.[2] These guidelines recommend an angiotensin receptor-neprilysin inhibitor (ARNI), with the only available ARNI being sac-val as first line therapy for treatment of SHF in New York Heart Association (NYHA) stages II to IV. The new guidelines state: "In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality."
- Sac-val has been proven to reduce mortality and decrease HFrEF hospitalizations.[3]
- Sac-val costs approximately $6,000 per year and ICER has reported sac-val is cost effective at the $100,000 per QALY threshold.[4]
- At the time of initial drug approval, many insurers required a sac-val PA to ensure safe and appropriate use. If underutilization occurs and a PA exists, insurers should consider removing the PA, if the drug has been shown to be cost effective.
- Through collaborative pharmaceutical manufacturer value-based contracting (VBC), insurers and pharmacy benefit managers (PBMs) may be able to withdraw a PA and conduct analyses to ensure safe, appropriate, cost-effective pharmaceutical use.

OBJECTIVE

- Prime Therapeutics, a PBM representing 15 million commercially insured lives with integrated medical and pharmacy claims data, and Novartis, the manufacturer of sac-val, entered into a VBC with the removal of the sac-val PA. Prime Therapeutics sought to assess sac-val cost effectiveness among members newly initiating sac-val therapy and adherent to therapy for one year by:
  1. Determining the change in total cost of care (TCC) and events among members newly initiating sac-val for HFrEF: hospitalizations (hosp) and emergency room (ER) visits, using real-world data.
  2. Decomposing the TCC into pharmacy costs and medical costs: hospitalizations, ER, office visits, and all other.
  3. Assessing the HFrEF-only costs and decomposed HFrEF costs into pharmacy costs and medical costs: hospitalizations, ER, office visits, and all other.

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METHODS

- All analyses were conducted using integrated medical and pharmacy claims data from 15 million commercially insured members.

Identification of Commercial Members with Sacubitril-Valsartan

- Members newly initiating sac-val from Oct. 2017 to Sept. 2018 were identified, defined as no prior sac-val claims in the 365 days prior to first (index) sac-val claim during Oct. 2017 to Sept. 2018.
- Members must have been 18–65 years old as of their index sac-val claim (index date).
- A 365-day pre-index and post-index continuous enrollment was required.
- Members must have evidence of HFrEF in the pre-index period, defined as an ICD-10-CM code for HFrEF (I50.20, I50.21, I50.22, I50.23, I50.40, I50.41, I50.42, I50.43) on a medical claim in any position.
- Lastly, members must be adherent on sac-val, defined as a proportion of days covered (PDC) ≥80% in the 365-day post-index period.

Outcomes Measurements

- The primary outcome of the analyses was the change in TCC from the pre-index to post-index periods. There was a two-month wash-out period prior to and after the sac-val index date where medical costs and events were excluded. The wash-out was done because sac-val is generally initiated as a result of a HF-related hospitalization and would result in inflated pre-index costs. Therefore, the pre-index and post-index TCC and events comparison consisted of the 10 months prior to (days -61 to -365) and 10 months after (days 61 to 365) sac-val index date. TCC included all pharmacy and medical claims. Claims costs were inclusive of member-share and plan-allowed amounts with all sac-val discounts applied. Post-index medical costs were adjusted for inflation using the medical care consumer price index (CPI) change.
- An additional analysis was conducted where pre-index and post-index TCC was compared in members regardless of their sac-val adherence in the post-index period. This was conducted due to the concern that requiring members to be adherent would not be representative of the entire commercial population initiating sac-val and may over estimate the reduction in TCC in the real-world sample.
- Medical costs were further broken out by site-of-service (hospitalization, ER and office visits). The site-of-service was defined using place of service and revenue codes on the medical claims.
- Sac-val costs in the post-index period were also examined separately.
- The change in the proportion of members with a hospitalization, ER or office visit in the pre-index and post-index periods was examined.
- HF-related medical costs, defined as medical claims with a ICD-10-CM for HF (I11.0, I13.0, I13.2, I50.0xx) in any position, was also determined. HF-related pharmacy costs included HF medications, including sac-val, ACE/ARB, beta blockers, digoxin, aldosterone antagonists, hydralazine and isosorbide dinitrates, ivabradine, and loop diuretics.
- Age, gender and Quan-Charlson[5] comorbidity score were examined for descriptive purposes.

Statistical Analyses

- A paired T-test was used to compare costs in the pre-index and post-index periods.
- A McNemar test was used to compare the percentage change of members with a hospitalization or ER visit from the pre-index to post-index period.

RESULTS

Analytic Population Identification — Sacubitril-Valsartan Commercial Members (Table 1)

- A total of 6,547 commercial members with a sac-val pharmacy claim were identified from Oct. 1, 2017 to Sept. 30, 2018.
- After applying the age and continuous enrollment criteria, 2,827 commercial members met analysis criteria. A total of 1,500 members were new to sac-val and 1,036 were found to have HFrEF using medical claims.
- 658 (62.5%) of 1,036 members newly initiating sac-val and potentially analyzable met the criteria of continuous enrolled 365 days pre/post index date and having a sac-val PDC ≥ 80% during the 365-day post-index period.
  - The mean age of the population was 54.3 years, and 72.9% of members were male.
  - The mean Quan-Charlson comorbidity score was 3.1. Considering that heart failure is scored as a one, this indicates the population, on average, had multiple comorbid conditions.

Mean Costs Change Pre-index to Post-index (Table 2)

- TCC decreased $10,177 (22.0%), from $46,242 pre-index to $36,065 post-index ($p<0.01$).
- A comparison of the TCC in the 60 days prior to and after the index date, that were excluded from analyses, showed a significantly higher mean cost pre at $19,474 compared to post at $12,062.
- Medical costs decreased $15,724 (37.7%), from $41,677 pre-index to $25,953 post-index period ($p<0.01$).
- Pharmacy costs increased $5,547 (121.5%), from $4,565 pre-index to $10,112 post-index ($p<0.01$). The mean costs of sac-val in the post-index period was $4,010, which accounted for 72.3% of the increase in post-index pharmacy costs.

Medical Costs Change in Hospitalizations, ER and Office Visits (Table 2)

- Hospitalization costs decreased from a pre-index mean of $23,892 to post-index mean of $7,360, a 69.2% reduction ($p<0.01$).
- ER costs decreased from a pre-index mean of $541 to a post-index mean of $378, a 30.1% decrease ($p<0.01$).
- Office visit costs increased from a pre-index mean of $11,369 to a post-index mean of $12,876, a 13.3% increase ($p<0.01$).

Health Resource Utilization Pre-index to Post-index Change (Table 3)

- The proportion of members with a hospitalization decreased from 34.8% in the pre-index period to 12.8% in the post-index period, a reduction of 63.3% ($p<0.01$).
- The proportion of members with an ER visit decreased from 45.0% in the pre-index period to 25.2% in the post-index period, a 43.9% decrease ($p<0.01$).
- The proportion of members with an office visit increased from 94.2% in the pre-index period to 98.8% in the post-index period, a 4.8% increase ($p<0.05$).

Heart Failure (HF) Related Costs Change in Pre-index and Post-index Periods (Table 4)

- When examining HF-only related costs, the findings were similar to the TCC results. A 11.4% reduction in HF-only related TCC was identified, with a 61.6% reduction in HF-related hospitalization costs.

Inclusion of Non-adherent (N = 378) and Adherent (N = 658) Sac-val Members

- Total cost of care was 2.0% lower in the post-index period when including all members meeting analytic criteria initiating sac-val regardless of their post-index PDC (N = 1036). Comparing the 1,036 members findings to the adherent-only members (N = 658), there was a similar increase in pharmacy costs, but a much lower reduction in medical costs at 13.1% post-index compared to pre-index.

TABLE 1

Sacubitril-Valsartan (sac-val) Utilizing Members and Study Population Identification

15 Million Commercially Insured Members	N (%)
Unique Members with a claim for sac-val 10/1/2017–9/30/2018	6,547
Age 18 to 65 years	5,336 (81.5%)
Continuous Enrollment for 365 Days in Pre-index Period	3,631 (68.0%)
Continuous Enrollment for 365 Days in Post-index Period	2,827 (77.9%)
No sac-val In Pre-index Period (newly initiating sac-val)	1,500 (53.1%)
HFrEF claim during Pre-index Period	1,036 (69.1%)
Sac-val PDC ≥ 80% in Post-index Period	658 (63.5%)

HFrEF = heart failure with reduced ejection fraction, PDC = proportion of days covered adherence measure.
Pre-index period is the 365 days prior to sac-val index date (i.e., date newly initiating sac-val therapy).
Post-index period is the 365 days after sac-val index date.

TABLE 2

Total Cost of Care Pre to Post Change after Starting Sacubitril-Valsartan among 658 Commercially Insured Members

	Pre-index		Post-Index		Pre/Post Change in Mean Costs
	Mean (SD)	Median (5^{th}, 95^{th} Percentile)	Mean (SD)	Median (5^{th}, 95^{th} Percentile)	
Medical costs	$41,677 ($87,644)	$12,917 ($62, $152,345)	$25,953 (64,013)	$6,455 ($467, $115,243)	-$15,724
Hospitalization	$23,892 ($72,204)	- (-, $109,829)	$7,360 ($35,453)	- (-, $35,343)	-$16,532
ER	$541 ($1,852)	- (-, $2,929)	$378 ($1,258)	- (-, $2,324)	-$163
Office visit	$11,369 ($25,655)	$2,892 (-, $60,068)	$12,876 (24,736)	$3,546 ($291, $69,179)	$1,507
Other	$5,876 ($37,217)	$751 (-, $16,064)	$5,338 ($39,213)	$704 (-, $12,731)	-$538
Pharmacy costs	$4,565 ($13,117)	$1,101 (-, $17,052)	$10,112 ($13,612)	$6,974 ($3,699, $25,883)	$5,547
Total	$46,242 ($89,058)	$18,973 ($151, $160,221)	$36,065 ($66,006)	$15,787 ($4,786, $128,851)	-$10,177

ER = emergency room.
Pre-index period is the 365 days prior to sac-val index date (i.e., date newly initiating sac-val therapy).
Post-index period is the 365 days after sac-val index date
There was a two-month wash-out period prior to and after the sac-val index date where events and costs were excluded. The wash-out was done because sac-val is generally initiated as a result of a HF-related hospitalization and would result in inflated pre-index costs. The pre-index and post-index TCC and events comparison consisted of the 10 months prior to (days -61 to -365) and 10 months after (days 61 to 365) sac-val index date.
*Health care consumer price index (CPI) adjusted costs.
†Sacubitril-valsartan costs after adjustment for formulary access rebate and administrative fees; all other pharmacy costs unadjusted.

TABLE 3

Health Care Utilization Pre to Post Change after Starting Sacubitril-Valsartan among 658 Commercially Insured Members

Health Care Utilization	Pre-Index N (%)	Post-Index N (%)	Pre/Post Change in Health Care Utilization
Hospitalization	229 (34.8%)	84 (12.8%)	-63.2%
ER	296 (45.0%)	166 (25.2%)	-44.0%
Office visit	620 (94.2%)	650 (98.8%)	4.9%

ER = emergency room
Pre-index period is the 365 days prior to sac-val index date (i.e., date newly initiating sac-val therapy).
Post-index period is the 365 days after sac-val index date.
There was a two-month wash-out period prior to and after the sac-val index date where events were excluded. The wash-out was done because sac-val is generally initiated as a result of a HF-related hospitalization and would result in inflated pre-index events. The pre-index and post-index TCC and events comparison consisted of the 10 months prior to (days -61 to -365) and 10 months after (days 61 to 365) sac-val index date.

TABLE 4

Heart Failure-related Costs Pre to Post Change after Starting Sacubitril-Valsartan among 658 Commercially Insured Members

	Pre-index		Post-Index		Pre/Post Change in Mean Costs
	Mean (SD)	Median (5^{th}, 95^{th} Percentile))	Mean (SD)	Median (5^{th}, 95^{th} Percentile)	
HFrEF Medical costs*	$18,243 ($58,732)	$785 (-, $90,564)	$11,974 ($37,606)	$1,045 (-, $67,790)	-$6,269
Hospitalization	$11,541 ($52,097)	- (-, $63,690)	$4,435 ($28,958)	- (-, $17,875)	-$7,106
ER	$187 ($1,060)	- (-, $1,026)	$127 ($795)	- (-, $797)	-$60
Office visit	$4,480 ($19,616)	$178 (-, $22,220)	$5,747 ($18,434)	$595 (-, $37,649)	$1,267
Other	$2,036 ($17,549)	- (-, $4,545)	$1,665 ($9,747)	$13 (-, $4,528)	-$371
HFrEF Pharmacy costs†	$205 ($451)	$83 (-, $687)	$4,375 ($1,008)	$4,208 ($3,295, $6,367)	$4,170
HFrEF Total	$18,448 ($58,745)	$1,026 (-, $90,657)	$16,348 ($37,615)	$5,602 ($3,651, $72,167)	-$2,100

HFrEF = heart failure with reduced ejection fraction; SD = standard deviation; ER = emergency room
Pre-index period is the 365 days prior to sac-val index date (i.e., date newly initiating sac-val therapy).
Post-index period is the 365 days after sac-val index date.
There was a two-month wash-out period prior to and after the sac-val index date where events and costs were excluded. The wash-out was done because sac-val is generally initiated as a result of a HF-related hospitalization and would result in inflated pre-index costs. The pre-index and post-index TCC and events comparison consisted of the 10 months prior to (days -61 to -365) and 10 months after (days 61 to 365) sac-val index date.
*Health care consumer price index (CPI) adjusted costs
†Sacubitril-valsartan costs after adjustment for formulary access rebate and administrative fees; all other pharmacy costs unadjusted

LIMITATIONS

- Pharmacy claims include assumptions of members' actual drug use and diagnoses.
- The data used in this study was limited to a commercial population and results may not be generalizable to Medicare or Medicaid populations. Other real-world evidence (RWE) studies have found sac-val use to be associated with lower rates of all-cause hospitalizations and lower TCC for HFrEF patients in Medicare patient sample(s) including Medicare lives.[6]
- Adherence is assessed using claims data and may inaccurately identify a member as adherent or non-adherent. In addition, the adherence cut point of 80% or greater PDC is an arbitrary adherence determinate, although it is used commonly in health services research.
- Costs in this analysis are limited to health care claim expenses. However, HFrEF also results in significant indirect and societal costs.
- Mortality data is unavailable, potentially influencing our findings as members who died during the 365-day post period would have been excluded due to the 365-day continuous enrollment requirement.

CONCLUSIONS

- 658 commercially insured members newly initiating and adherent to sacubitril-valsartan for a year were found to have a cumulative associated $6.7 million lower total cost of care post sacubitril-valsartan initiation compared to prior to initiation.
- Members newly initiating sacubitril-valsartan and adherent to their therapy for one year were found to have an associated significant 22% reduction in their total cost of care and a 2.7-fold hospitalization decrease, in this real-world study.
- Although pharmacy costs increased 122%, due primarily to sacubitril-valsartan, these costs were offset by lower medical care costs.
- A secondary analysis of all members initiating sacubitril-valsartan, both those adherent and non-adherent during the year follow-up, demonstrated cost neutrality.
- These significant real-world findings, along with a pharmaceutical manufacturer value-based contract, clinical trial data and clinical guidelines, resulted in the removal of the sacubitril-valsartan prior authorization.
- Integrated medical and pharmacy benefits provide the ability to execute value-based contracts, the feasibility to assess medication value and the data to influence insurers' management decisions.

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