Out-of-Pocket Costs and Prescription Reversals: the case of Oral Linezolid

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Abstract

Background: Linezolid is indicated in the treatment of vancomycin-resistant *Enterococcus faecium* infections, complicated and uncomplicated skin and soft tissue infections (SSTI), and nosocomial and community-acquired pneumonia. Among antibiotics used to treat SSTI and pneumonia, linezolid is available in both intravenous and oral forms. This availability of intravenous and oral forms may allow for a shortened length of hospital stay if treatment is continued orally post-discharge, resulting in lower total costs of treating the infection. However, coinsurance benefit design for oral linezolid generally results in higher patient out-of-pocket (OOP) costs compared to copay, which is associated with prescription reversals and subsequent treatment with alternative antibiotics or in some cases no antibiotic treatment altogether. If patients who reverse their prescriptions for oral linezolid have higher medical and total healthcare costs as a consequence of their reversals versus patients who filled their prescriptions for oral linezolid, then payers would be advised to improve patient access to this important medication.

Objective: To determine the relationship between benefit design, OOP costs, and prescription reversals among Medicare members prescribed oral linezolid, post-discharge from a hospital stay for an SSTI or pneumonia. In addition, to investigate the impact of reversals on re-hospitalizations and total healthcare costs among these patients.

Methods: Medicare members from a national health plan prescribed oral linezolid post-hospitalization for SSTI or pneumonia were evaluated retrospectively. Members were identified by an oral linezolid prescription, 6/1/2007-4/30/2011, where the index event was a prescription fill or reversal, ≤ 2 days before or ≥ 10 days after discharge from a hospitalization for SSTI or pneumonia. The association between OOP costs and reversal, and between reversal and re-hospitalization 30 days post-index, were compared for members with a prescription fill versus reversal. A generalized linear model calculated adjusted total healthcare costs per member controlling for age, gender, geographic region, and clinical characteristics.

Results: A final sample of 1,062 Medicare members was available for analysis; 16.5% of members reversed their prescriptions for oral linezolid. Demographic and clinical characteristics by fill versus reversal groups indicated there were no statistical differences in age, gender, or geographic region. However, a higher percentage of members filling their linezolid prescription had low income subsidy/dual eligibility status compared to members reversing their linezolid prescription ($P < 0.001$). Mean OOP costs were higher for members with coinsurance ($466.52) versus copay ($7.05) benefits ($P < 0.001$), and reversal rates rose progressively from 2% for members with OOP costs of $0 to 27% for members with OOP costs >$100 ($P < 0.001$). Infection-related re-hospitalizations were 23% versus 9% for members with a prescription reversal versus fill ($P < 0.001$). While post-discharge prescription drug costs were $1,229 lower ($P < 0.001$), adjusted mean medical costs were $2,062 higher ($P = 0.003$) and total healthcare costs were $1,281 higher ($P = 0.035$) for reversal versus fill members.

Conclusions: Higher OOP costs, and coinsurance rather than copay, were associated with higher rates of reversal, and reversals were associated with higher rates of re-hospitalization and adjusted total healthcare costs among Medicare members prescribed oral linezolid post-hospitalization for SSTI or pneumonia.

Introduction

Among antibiotics used to treat SSTI and pneumonia, linezolid is available in both intravenous and oral forms.[1] Bioavailability is approximately 100%,[1] allowing for sequential intravenous to oral administration without changing the drug or dosing regimen. The availability of intravenous and oral forms may allow for a shortened length of hospital stay if treatment is continued orally post-discharge, resulting in lower total costs of treating the infection.[2] However, coinsurance benefit design for oral linezolid generally results in higher patient out-of-pocket (OOP) costs compared to copay, and this is associated with prescription reversals and subsequent treatment with alternative antibiotics or in some cases no antibiotic treatment altogether.[3] If patients who reverse their prescriptions for oral linezolid have higher medical and total healthcare costs as a consequence of their reversals versus patients who filled their prescriptions for oral linezolid, then payers would be advised to improve patient access to this important medication.

Objectives

- To determine the relationship between benefit design, OOP costs, and prescription reversals among Medicare members prescribed oral linezolid post-discharge from a hospitalization for SSTI or pneumonia.
- To examine the impact of linezolid reversals on re-hospitalizations and total healthcare costs among Medicare members prescribed oral linezolid post-discharge.

Methods

- Fully insured Medicare Advantage members from a national health plan were identified by an oral linezolid prescription, 6/1/2007 – 4/30/2011, where the index event was a prescription fill or reversal, ≤ 2 days before or ≥ 10 days after discharge from a hospitalization for SSTI or pneumonia.
- Members were required to be continuously enrolled for 120 days pre- and 30 days post-index.
- The association between benefit design, out-of-pocket costs, and reversal, and between reversal and re-hospitalization 30 days post-index, were compared for members with a prescription fill versus reversal.
- The impact of reversal on total healthcare costs (plan payment plus member medical costs) was modeled using a generalized linear model (GLM) with a gamma distribution as its probability distribution and log-link as its link function.[4] Covariates included in the model were OOP cost per member, age, gender, geographic region, low income subsidy/dual eligible status, baseline RxRisk-V score,[5,6,7,8,9] a surgical procedure or ICU stay during the initial hospitalization, and pre-index healthcare costs (per $1,000).

Results

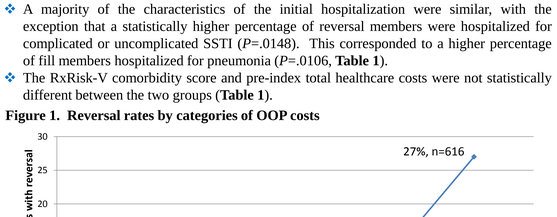
Table 1. Demographic and clinical characteristics by prescription fill versus reversal

	Prescription Fill	Prescription Reversal	*P* value
Sample size	887	175	-
Age (mean, SD)	66.5 (±12.4)	66.3 (±10.4)	.8395
Female (n, %)	441 (50.0)	78 (45.0)	.2132
Geographic region (n, %)			
Northeast	15 (2.0)	0 (0.0)	.0804
Midwest	161 (18.0)	32 (18.0)	
South	621 (70.0)	133 (76.0)	
West	90 (10.0)	10 (6.0)	
Low income subsidy/dual eligible status (n, %)	374 (42.0)	17 (10.0)	<.0001
Initial hospitalization (n, %)			
Surgery	405 (46.0)	77 (44.0)	.6870
ICU stay	237 (27.0)	43 (25.0)	.5556
SSTI	748 (84.0)	160 (91.0)	.0148
Complicated SSTI	215 (24.0)	52 (30.0)	.1270
Pneumonia	149 (17.0)	16 (9.0)	.0106
RxRisk-V score (mean, SD)	6.7 (±3.2)	6.4 (±2.7)	.2725
Pre-index healthcare costs (mean, SD)	$16,728 (±$13,280)	$15,146 (±11,426)	.1313

Note: SD = Standard Deviation

- A final sample size of 1,062 members was available for analysis. Among the total sample, 16.5% of the members reversed their prescription for oral linezolid (**Table 1**).
- Demographic and clinical characteristics by fill versus reversal groups indicated there were no statistical differences in age, gender, or geographic region. However, a higher percentage of the members filling their linezolid prescription had low income subsidy/dual eligibility status compared to members reversing their linezolid prescription ($P<.0001$, **Table 1**).
- A majority of the characteristics of the initial hospitalization were similar, with the exception that a statistically higher percentage of reversal members were hospitalized for complicated or uncomplicated SSTI ($P=.0148$). This corresponded to a higher percentage of fill members hospitalized for pneumonia ($P=.0106$, **Table 1**).
- The RxRisk-V comorbidity score and pre-index total healthcare costs were not statistically different between the two groups (**Table 1**).

Figure 1. Reversal rates by categories of OOP costs



- **Figure 1** shows that as OOP costs increased the percentage of members reversing their prescriptions also increased, with OOP costs above $100 resulting in a reversal rate as high as 27% ($P<.0001$).
- Assuming that patients with OOP costs >$100 were subject to a coinsurance benefit versus a copay for most patients with OOP <$100, mean (±standard deviation) OOP costs for members with copay were $7.05 (±$14.89), and for members with coinsurance were $466.52 (±$574.67).

Table 2. Re-hospitalization rates by prescription fill versus reversal

	Prescription Fill (n, %)	Prescription Reversal (n, %)	*P* value
All cause re-hospitalizations	172 (20.0)	55 (30.0)	.0027
Infection-related re-hospitalizations	83 (9.0)	42 (23.0)	<.0001
SSTI	74 (89.0)	37 (88.0)	.5052
Pneumonia	7 (8.0)	5 (12.0)	
SSTI and Pneumonia	2 (2.0)	0 (0.0)	
SSTI initial and re-hospitalization	76 (9.0)	37 (20.0)	<.0001
Pneumonia initial and re-hospitalization	7 (1.0)	5 (3.0)	.0268

- As shown in **Table 2**, infection-related (complicated or uncomplicated SSTI or pneumonia) re-hospitalizations were 14 percentage points higher ($P<.0001$), and all-cause re-hospitalizations were 10 percentage points higher ($P=.0027$), in the reversal versus fill group.
- For each type of infection (complicated or uncomplicated SSTI, pneumonia, or both SSTI and pneumonia), no significant difference was detected between the fill and reversal groups (**Table 2**).
- When grouping prescription fill versus reversal groups by percentage re-admitted for the same infection as the initial hospitalization diagnosis, a higher percentage of the reversal group was hospitalized for the same infection than the fill group – 20% reversal group versus 9% fill group ($P<.0001$) for complicated or uncomplicated SSTI, and 3% reversal group versus 1% fill group ($P=.0268$) for pneumonia, respectively (**Table 2**).

Table 3. Unadjusted and adjusted post-index healthcare costs, by prescription fill versus reversal

	Unadjusted healthcare costs*			Adjusted healthcare costs**		
Outcome measure	Prescription Fill	Prescription Reversal	*P* value	Prescription Fill	Prescription Reversal	*P* value
Rx costs	$1,826.80 (± $1,476.10)	$552.05 (± $745.98)	<.0001	$2,044.28 [$1,834.06-$2,278.59]	$815.50 [$702.07-$947.26]	<.0001
Medical costs	$4,061.10 (± $7,726.20)	$6,257.00 (± $11,149.00)	.0013	$4,495.07 [$3,530.03-$5,723.92]	$6,556.76 [$4,660.62-$9,224.33]	.0033
Total Costs	$5,888.00 (± $7,917.50)	$6,809.00 (± $11,311.00)	.1853	$6,617.07 [$5,650.61-$7,748.83]	$7,898.00 [$6,319.84-$9,870.24]	.0349

Notes: *mean, SD; **mean, 95% confidence interval.

- Unadjusted post-index prescription drug, medical, and total healthcare costs are reported in **Table 3**. Whereas post-index prescription drug costs were significantly lower for members with a reversal ($P<.0001$), post-index medical costs were significantly higher for these members ($P=.0013$) compared to members with a fill. The combined total unadjusted healthcare costs were not statistically different between the two groups ($P=.1853$, **Table 3**).
- After adjusting for demographic and clinical characteristics, differences in the prescription drug and medical costs remained statistically significant between the fill and reversal groups (**Table 3**). Notably, with adjustment, the difference in total healthcare costs between the fill and reversal groups became statistically significant ($P=.0349$), with mean healthcare costs for the reversal group of $1,280.93 more than the fill group (Table 3).

Table 4. Parameter estimates from GLM model for post-index healthcare costs

Variable	Parameter estimate	Exp (parameter estimate)	P value
Reversal	0.177	1.194	.0349
Age	0.001	1.001	.6132
Gender (Male versus Female)	0.183	1.201	.0027
RxRisk-V Score	0.047	1.048	<.0001
ICU stay during initial hospitalization	-0.103	0.902	.1529
Surgery during initial hospitalization	0.051	1.052	.4194
Pre-Index healthcare costs	0.000	1.000	<.0001
OOP costs (> $100 vs. $0)	-0.470	0.625	.0080
OOP costs (> $25 - $100 vs. $0)	-0.239	0.788	.2654
OOP costs (> $0 -$25 vs. $0)	-0.149	0.861	.3166
Low income subsidy (Dual eligible)	-0.145	0.865	.2622

- Parameter estimates (including exponentiated estimates for ease of interpretation) from the GLM for adjusted costs are reported in **Table 5**.
- Notably, the parameter estimate for the reversal variable was statistically significant, indicating that adjusted costs for members with a reversal were 19.4% higher than those with a fill ($P=.0349$, **Table 5**).
- Male gender was associated with higher adjusted costs (by 20.1%, $P=.0027$), and an incremental point increase in the RxRisk-V score was associated with a 4.8% increase in adjusted costs ($P<.0001$). The parameter estimate on pre-index healthcare costs was statistically significant, but indicated minimal magnitude. The parameter estimate for members with >$100 OOP costs was associated with lower adjusted total healthcare costs ($P=.0080$, **Table 5**).
- Parameter estimates for the remaining variables reported in **Table 5**, as well as for geographic regions (not shown) were not statistically significant.

Discussion

- The current study found that Medicare members who had an oral linezolid fill had fewer infection-related and 30 day all-cause hospital re-admissions than members who reversed their prescriptions and either did not receive any antibiotic or received a different antibiotic following their reversal.
- A higher re-admission rate, combined with all other types of medical encounters, resulted in higher medical costs during the 30 days post-discharge from the initial hospitalization for SSTI or pneumonia.
- Whereas treatment with oral linezolid was associated with higher prescription drug costs post-index, higher prescription drug costs were offset by lower medical costs for the fill group resulting in total healthcare costs that were $1,280.93 lower for the fill versus reversal groups (**Table 3**). This clearly highlights the need to examine prescription drug costs in the context of total healthcare costs.
- The fill and reversal groups were similar for the vast majority of their demographic and clinical characteristics, suggesting an economic perspective may have factored in the decision to fill or reverse the linezolid prescription. Consistent with this interpretation is the significantly higher distribution of low income subsidy/dual eligibility status among members with a fill versus members with a reversal (42% versus 10% respectively, **Table 1**). Low income subsidy/dual eligible members are more likely to fill the prescription for oral linezolid as it is probable they will have low or no OOP costs.
- If the decision to fill or reverse did indeed include economic reasons, then strategies to reduce member OOP costs (e.g. benefit design) for all health plan members could enable better member access, and in turn, reduce total healthcare costs.
- Given the cost savings, payers may wish to ensure the patient cost of oral linezolid is below $100.

Limitations

- One limitation of this study was its focus on members with an inpatient stay, which may not be generalizable to those prescribed oral linezolid in an ambulatory setting. In addition, the length of treatment for oral linezolid or other antibiotic therapies was not evaluated in this study and may have an impact on post-discharge outcomes.
- The distinction between copay and coinsurance was performed via visual inspection due to the fact that the pharmacy claims did not contain an indicator for copay or coinsurance. Future work will need to more accurately reflect the distinction between copay and coinsurance.
- Additionally, limitations common to studies using administrative claims data apply. These include lack of certain information in the database (eg, lab results, weight, and health behavior information) and errors in claims coding.
- No causal inference can be ascertained from this study, as it is an observational study using retrospective claims data. Although multivariate regression modeling was used to reduce selection bias and strengthen the causal inference, this approach can only reduce bias caused by measured covariates.

Conclusion

This study found coinsurance benefit design was linked to higher OOP costs which were associated with increased rates of reversals. In addition, reversals were associated with higher rates of re-hospitalization and adjusted total healthcare costs among Medicare members prescribed oral linezolid post-hospital discharge for skin or respiratory infections.

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Disclosures

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