American Journal of Preventive Cardiology 21 (2025) 100940

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

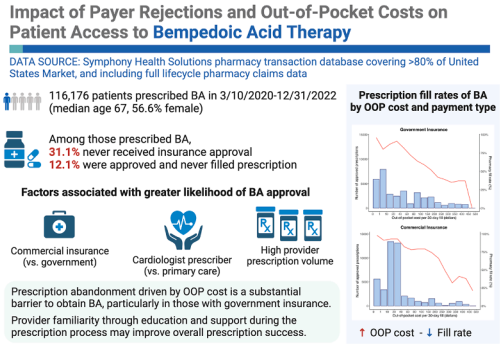
Original Research

Impact of payer rejections and out-of-pocket costs on patient access to bempedoic acid therapy

Jimin Hwang [a], Eric Peterson [a], Anand Gupta [a], Evelyn Sarnes [b], Kristin Gillard [b,1], Ann Marie Navar [a,*]

[a] University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd. E5.722, Dallas, TX 75390, United States
[b] Esperion Therapeutics, Ann Arbor, MI, United States

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Novel lipid-lowering therapies
Bempedoic acid
Access to therapy
Pharmacoequity
Utilization management

ABSTRACT

Background: Early uptake of novel cholesterol-lowering therapies was limited by extensive utilization management practices and high cost. Whether similar challenges affected access to bempedoic acid (BA) is unknown.
Methods: For all patients prescribed BA from the date of FDA approval (February 2020) through 12/31/2022 identified using nationwide pharmacy transaction data, we assessed whether their first prescription was approved or rejected. Multivariable logistic regression was performed to assess factors associated with approval. Among those approved, prescription fill rates were evaluated by out-of-pocket cost. For those with rejected prescriptions, changes in lipid-lowering therapy after rejection were described.
Results: Of 116,176 patients (median age 67 years; 56.6 % women) initially prescribed BA, 80,056 (68.9 %) received approval. Factors associated with approval included: commercial insurance (odds ratio [OR] 1.62 [95 % confidence interval (CI) 1.56, 1.68] vs. government insurance, $P < 0.001$), cardiology specialty prescriber (OR 1.39 [1.34, 1.44] vs. primary care physicians, $P < 0.001$), and prescriber volume (OR 1.44 [1.38, 1.51] for fourth [highest] quartile vs. first [lowest] quartile prescribers, $P < 0.001$). Of those who received approval, 82.4 % ($n = 65,969$) filled the prescription, while 17.3 % ($n = 14,087$) abandoned the prescription. Abandonment rates increased with increasing patient OOP costs. Escalation in an alternative lipid-lowering therapy over the

* Corresponding author.
E-mail address: Ann.Navar@UTSouthwestern.edu (A.M. Navar).
[1] At the time of the study.

https://doi.org/10.1016/j.ajpc.2025.100940
Received 7 January 2025; Received in revised form 5 February 2025; Accepted 7 February 2025
Available online 8 February 2025

subsequent year was observed in 36.2 % and 33.3 % of patients with rejected and abandoned prescriptions, respectively.
Conclusion: Nearly half of patients prescribed BA failed to receive therapy due to a combination of payer rejections and prescription abandonment. Arduous utilization management criteria or high OOP costs put patients at high risk for failure of therapy initiation.

1. Introduction

On February 21, 2020, the United States Food and Drug Administration (FDA) approved bempedoic acid (BA) for the reduction of low-density lipoprotein cholesterol (LDL-C) [1–5]. However, the uptake of BA since the initial indication has been low [6].

Similar to other novel lipid-lowering therapies, the cost of BA is up to $400 per 30-day fill [7]. In response to high prices, payers often apply utilization-management practices, including prior authorization and/or high patient copays [8,9]. As a result, the uptake of novel therapies is often limited. Earlier research demonstrated that initial uptake of proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) was markedly limited by high rates of payer rejections and by high out-of-pocket (OOP) costs resulting in prescription abandonment even when approved [9].

Our study sought to evaluate whether such payer policies were similarly limiting use of BA in community practice. Utilizing a nationwide pharmacy transaction database, we analyzed the fate of prescriptions of BA and the factors associated with its uptake in the first years after FDA approval for LDL-C reduction. Specifically, we (1) evaluated what proportion of patients prescribed BA ultimately received therapy and assessed patient and provider characteristics associated with insurance approval; (2) examined the association between patient OOP costs and prescription abandonment for those who did receive approval; and (3) assessed lipid-lowering therapy changes at 1 year in patients who never received BA due to either prescription rejection or prescription abandonment.

2. Methods

2.1. Description of data source

Using US national pharmacy transaction data from the Symphony Health Solutions claims database (Symphony Health, Blue Bell, Pennsylvania, PA, USA), we evaluated new prescriptions of BA (including BA monotherapy and the fixed-dose combination with ezetimibe) from March 10, 2020 through December 31, 2022. The Symphony Health Solutions database includes pharmacy transaction data for approximately 80 % of the United States pharmacy market [11,12], and captures the full life cycle of prescriptions from initial submission to final disposition. Each prescription claim was date- and time-stamped, and included whether the claim was approved or rejected, and whether the patient filled (dispensed) the prescription or did not pick it up after it was approved (abandoned). For each prescription, the dataset also includes payer type; total OOP cost for the patient after coinsurance, discounts, or copay assistance programs; de-identified patient information (age, gender, race, ethnicity); and prescriber information (including taxonomy code and prescriber specialty). Race and ethnicity data were collected through Symphony Health Solutions' proprietary methods and entered into the database. Payer type was categorized into government (Medicare, Medicaid, Medicare Managed), commercial, cash, and patient-assistance programs. Given that this analysis sought to evaluate the impact of utilization-management processes on outcomes, those paying cash or who had patient-assistance programs only were excluded from the analysis. Prescriber specialty was derived based the provider National Provider Identifier linked to the National Plan and Provider Enumeration System database and included cardiologist, endocrinologist, primary care provider, advance practice providers (physician assistants or nurse practitioners), and other/unknown.

2.2. Patient identification

We identified all adult patients (age at or above 18 years) with at least one prescription claim for BA from March 10, 2020 (the date of the first BA prescription in the dataset) through December 31, 2022. The first BA claim was defined as the index date. Individual prescription claims in this timeframe were first collapsed into prescription episodes to account for administrative prescription resubmissions and duplicate initial submissions. For each patient, prescription claims data for other lipid-lowering therapies (statins, ezetimibe, and PCSK9i) dating back to January 1, 2018 were also linked to data for each patient. Current lipid-lowering therapy was defined as a prescription of lipid-lowering therapy with estimated refill date (ie, days-supply of prescription added to prescription date) between 30 days before and 30 days after the first BA prescription. Prior lipid-lowering therapy was defined as any prescription for statin, ezetimibe, or PCSK9i prior to the date of the BA prescription. Statin therapy was categorized as high, moderate, or low intensity (Supplementary Table S1).

2.3. Approvals, rejections, and prescription abandonment

For each individual, we identified the first prescription episode for BA and determined whether the prescription was initially approved or rejected by the payer, whether it was appealed, and whether it was ultimately approved or rejected. For approved prescriptions, we further assessed whether the medication was filled, or abandoned (never filled by the patient at the pharmacy).

Patient and prescriber characteristics were compared between approved and rejected BA prescriptions, including demographic information (age, sex, race and ethnicity), payer type, initial patient OOP cost per 30-day supply, prior or concurrent statin or other lipid-lowering therapy use, and prescriber information (specialty, prescriber volume). Univariable and multivariable logistic regression was used to evaluate factors associated with ever receiving approval for BA, with covariates including age, sex, race and ethnicity, payer type, provider specialty, provider volume of prescriptions, and current lipid-lowering therapy (statin, ezetimibe, and PCSK9i). Prescriber volume was classified into quartiles according to the total number of patients for whom each physician had prescribed BA between March 10, 2020 and December 31, 2022 in the database.

2.4. Prescription abandonment and time to therapy

The association between patient OOP cost and prescription abandonment was evaluated among patients with approved prescriptions. For patients who filled their prescription, the time to therapy, including time to first approval and time to first dispense, were assessed, and compared across payer characteristics.

2.5. Change in lipid-lowering therapy at 1 year

For patients who failed to initiate bempedoic acid, prescription information at 1 year following the index date was utilized to assess for subsequent escalation in lipid lowering therapy. Therapy escalation was defined as the initiation of statin, ezetimibe, or a PCSK9i in patients not receiving the therapy, or, in patients already on a statin, increase in

statin intensity.

All statistical analyses were performed with Oracle SQL (Structured Query Language) Developer version 23.1.0 (Oracle Corporations, California, United States of America) and R version 4.0.2 (R Core Team, Vienna, Austria). The study was considered exempt from review by the University of Texas Southwestern institutional review board given the use of de-identified data.

3. Results

Of 127,929 adult patients prescribed BA for the first time from March 10, 2020 to December 31, 2022 in the database, 1.1 % ($n = 1456$) had only cash and 8.0 % ($n = 10,297$) had only patient-assistance programs listed as payer type, and these were excluded from the analysis. Of the sample of patients with government or commercial insurance ($n = 116,176$), 58.2 % of prescriptions were initially approved (Fig. 1). Of the 41.8 % that were initially rejected, only 44.8 % were appealed, of which 57.4 % ($n = 12,486$) were ultimately approved, for an overall approval rate of 68.9 %. Of those approved, 82.4 % ($n = 65,969$) were filled; the remaining – 17.6 % of those approved and 12.1 % of all prescribed – were abandoned.

The characteristics of patients who were prescribed BA overall and stratified by final approved vs. rejected status are shown in Table 1. Overall, 57.4 % of patients prescribed with BA were aged 65 years or older (mean age 66, median 67 years), and 56.6 % were female. Compared with patients whose prescriptions for BA were approved, patients whose prescriptions were rejected tended to be older (median age 67 for those rejected vs. 66 for those approved, $P < 0.001$), female (58.9 % of those rejected vs. 55.5 % approved, $P < 0.001$), and included more Black persons (9.0 % of those rejected vs. 8.3 % approved, $P < 0.001$). Differences were more pronounced by insurance type: fewer patients with rejected prescriptions had commercial insurance than had those with approved prescriptions (45.8 % vs. 56.0 %, $P < 0.001$).

The use of concurrent lipid-lowering therapy at the time of BA prescription was low overall, with only 29.5 % on any statin, 22.5 % on ezetimibe, and 6.6 % on PCSK9i. More patients with rejected prescriptions were on ezetimibe (25.1 % vs. 21.3 %, $P < 0.001$), but fewer were on a PCSK9i (5.1 % vs. 7.2 %, $P < 0.001$).

3.1. Factors associated with approval

In multivariable logistic regression modeling, we identified several demographic, clinical, and payer factors associated with likelihood of approval of BA prescription (Table 2). Women were less likely than men to receive approval (odds ratio [OR], 0.94 [95 % confidence interval (CI) 0.91, 0.97], $P < 0.001$) adjusting for age, ethnicity, payment type, provider specialty, provider volume of prescriptions, and current LLT use. Hispanic and Black persons were less likely than White persons to receive approval (OR 0.85 [0.81, 0.90], $P < 0.001$ for Hispanic; 0.93 [0.88, 0.97], $P < 0.001$ for Black individuals), whereas Asian persons were more likely to receive approval (OR 1.12 [0.99, 1.26], $P = 0.06$). Patients with commercial insurance had 62 % higher odds of ultimately receiving approval for BA (OR 1.62 [1.56, 1.68] vs. government insurance, $P < 0.001$). Prescriptions written by cardiologists had the highest chances of success compared with those written by primary care physicians (OR 1.39 [1.34, 1.44], $P < 0.001$), followed by endocrinologists (OR 1.08 [1.01, 1.16], $P = 0.03$). Increasing provider volume of prescriptions was also associated with higher chances of success in a dose–response manner (OR 1.44 [1.38, 1.51] for fourth [highest] quartile vs. first [lowest] quartile, $P < 0.001$). Current statin use or intensity was not significantly associated with approval in the multivariable model. Those receiving ezetimibe were less likely to receive approval (OR 0.86 [0.83, 0.89], $P < 0.001$), whereas those receiving PCSK9i were more likely (OR 1.40 [1.31, 1.50], $P < 0.001$).

3.2. Prescription fill rate and time to therapy after approval

Among those with approved prescriptions, 82.4 % ($n = 65,969$) of patients filled their medications. The remaining 17.6 % never collected their prescription at the pharmacy. Patients who abandoned bempedoic acid tended to be older, more women, and substantially more likely to have government insurance than commercial insurance (Supplementary Table S2). Fill rates were negatively associated with OOP cost (Fig. 2). Ninety-seven percent of patients with no OOP cost for BA filled their medications. In contrast, among patients who had OOP cost above $200, fill rates never exceeded 50 %. At $350, the fill rate dropped to as low as 34 %. Overall, 14.3 % of patients with approved prescriptions had no OOP cost ($0). Close to 70 % had an OOP cost under $40 per month. On the other end, 16.5 %, 8.3 %, and 1.3 % of patients had a monthly OOP cost of above $100, $200, and $400, respectively.

Stratified by insurance, fill rates declined steeply with increasing OOP costs in patients with government insurance, dropping below 50 % at a threshold of $200 (Supplementary Fig. 1A). Notably, fill rates were 0 % for those who had to pay above $450 monthly. For patients with commercial insurance, the decline in fill rate was more gradual, remaining at 66 % at an OOP range of $200–250, compared with a steep drop to 42 % for those with government insurance (Supplementary Fig. 1B). Overall, patients had high fill rates surpassing 90 % when monthly cost was below $40. Many more patients with commercial insurance (79.2 %) fell into this range than those with government

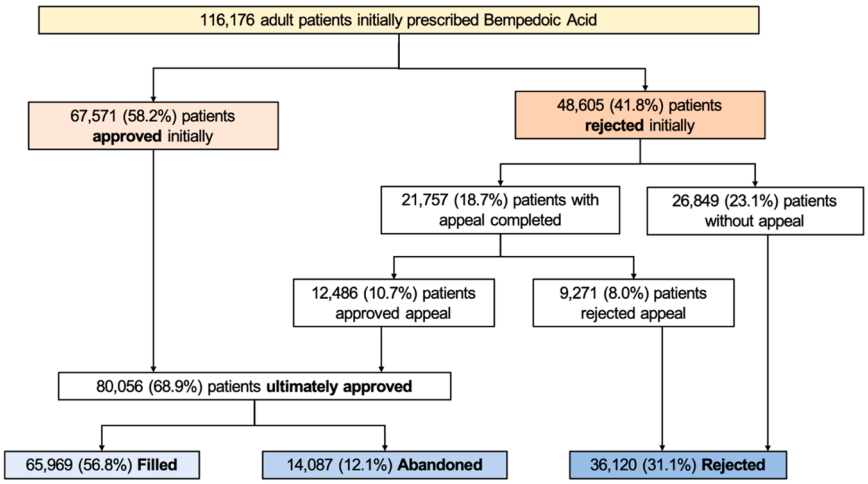


Fig. 1. Approval, dispense, rejection, and abandonment rates of patients prescribed bempedoic acid.

Table 1
Demographics and baseline characteristics of patients prescribed bempedoic acid, by approval status.

Parameter	Overall, N = 116,176[1]	Reject, N = 36,120[1]	Approved, N = 80,056[1]	p-value[2]
Age, median years (IQR)	67 (59, 74)	67 (59, 75)	66 (59, 74)	<0.001
Range	19, 81	19, 81	19, 81	
Age (categorical)				<0.001
<55	17,062 (14.7 %)	5290 (14.6 %)	11,772 (14.7 %)	
55–64	32,460 (27.9 %)	9443 (26.1 %)	23,017 (28.8 %)	
65–74	39,051 (33.6 %)	12,181 (33.7 %)	26,870 (33.6 %)	
At or above 75	27,603 (23.8 %)	9206 (25.5 %)	18,397 (23.0 %)	
Gender				<0.001
Men	50,473 (43.4 %)	14,855 (41.1 %)	35,618 (44.5 %)	
Women	65,701 (56.6 %)	21,263 (58.9 %)	44,438 (55.5 %)	
Unknown	2	2	0	
Ethnicity				
Asian	1540 (1.3 %)	434 (1.2 %)	1106 (1.4 %)	0.013
Black/African American	9892 (8.5 %)	3243 (9.0 %)	6649 (8.3 %)	<0.001
Hispanic	7284 (6.3 %)	2433 (6.7 %)	4851 (6.1 %)	<0.001
Other	1685 (1.5 %)	444 (1.2 %)	1241 (1.6 %)	<0.001
White/Caucasian	63,763 (54.9 %)	19,385 (53.7 %)	44,378 (55.4 %)	<0.001
Unknown	32,012 (27.6 %)	10,181 (28.2 %)	21,831 (27.3 %)	0.001
Payment type				
Commercial	61,420 (52.9 %)	16,560 (45.8 %)	44,860 (56.0 %)	<0.001
Government	54,756 (47.1 %)	19,560 (54.2 %)	35,196 (44.0 %)	<0.001
Out-of-pocket cost, median $[*] (IQR)	25 (10.0, 85)	NA (NA, NA)	25 (10.0, 85)	
$0	11,482 (14.4 %)	NA (NA, NA)	11,482 (14.4 %)	
< $20	39,011 (48.8 %)	NA (NA, NA)	39,011 (48.8 %)	
< $40	54,576 (68.2 %)	NA (NA, NA)	54,576 (68.2 %)	
Statin use				
Current Statin	34,304 (29.5 %)	10,735 (29.7 %)	23,569 (29.4 %)	0.3
Prior Statin	49,929 (43.0 %)	15,388 (42.6 %)	34,541 (43.1 %)	0.083
Unknown/Never Statin	31,943 (27.5 %)	9997 (27.7 %)	21,946 (27.4 %)	0.4
Statin Current				<0.001
High intensity	16,662 (14.3 %)	5076 (14.1 %)	11,586 (14.5 %)	0.059
Medium intensity	14,785 (12.7 %)	4689 (13.0 %)	10,096 (12.6 %)	0.079
Low intensity	2857 (2.5 %)	970 (2.7 %)	1887 (2.4 %)	<0.001
No statin	81,872 (70.5 %)	25,385 (70.3 %)	56,487 (70.6 %)	0.3
Non-statin LLT[#]	44,236 (38.1 %)	14,728 (40.8 %)	29,508 (36.9 %)	<0.001
Ezetimibe	26,125 (22.5 %)	9055 (25.1 %)	17,070 (21.3 %)	<0.001
PCSK9i	7638 (6.6 %)	1839 (5.1 %)	5799 (7.2 %)	<0.001
Provider specialty				<0.001
Advanced Practice Provider	9389 (8.1 %)	3121 (8.7 %)	6268 (7.9 %)	<0.001
Cardiology	42,684 (36.9 %)	11,310 (31.4 %)	31,374 (39.3 %)	<0.001
Endocrinology	5755 (5.0 %)	1739 (4.8 %)	4016 (5.0 %)	0.15
Other specialty/ Unspecified	6313 (5.5 %)	2142 (6.0 %)	4171 (5.2 %)	<0.001
Primary Care	51,623 (44.6 %)	17,670 (49.1 %)	33,953 (42.6 %)	<0.001
Unknown	412	138	274	
Provider volume of prescriptions				<0.001
(1st quartile)	24,273 (22.0 %)	8527 (25.5 %)	15,746 (20.5 %)	
(2nd quartile)	29,128 (26.5 %)	9199 (27.5 %)	19,929 (26.0 %)	
(3rd quartile)	28,107 (25.5 %)	8262 (24.7 %)	19,845 (25.9 %)	
(4th quartile)	28,582 (26.0 %)	7409 (22.2 %)	21,173 (27.6 %)	
Unknown	6086	2723	3363	

[1] n (%) unless otherwise stated.
[2] Wilcoxon rank sum test; Pearson's Chi-squared test, Chi-squared Test for Trend in Proportions.
[*] OOP cost per 30-day fill.
[#] Non-statin LLT (lipid-lowering therapy) includes ezetimibe, PCSK9 inhibitors, fibrates, niacin (Niacin), omega 3 derivatives, and fish oil.

insurance (54.2 %).

Among the 65,969 patients who were able to dispense BA, 72.1 % had prescriptions approved within 1 day of first prescription submission, and 87.8 % had approval within 2 weeks (Supplementary Table S3).

3.3. Change in therapy after failure to receive BA treatment

Table 3 shows changes in lipid-lowering therapy 1 year after initial prescription attempt for BA among those who were unable to receive therapy (those with rejected or abandoned prescriptions). After 1 year, initiation of ezetimibe monotherapy was most common (17.8 % and 15.0 % for rejection and abandonment, respectively), followed by initiation of or increase in intensity of statin therapy (15.9 % for rejection, 15.7 % for abandonment), and initiation of PCSK9i (6.5 % for rejection, 6.2 % for abandonment). Overall, only 36.2 % and 33.3 % of patients with rejected and abandoned prescriptions, respectively, underwent evidence of guideline-based intensification of their lipid-lowering therapy.

4. Discussion

Our data confirms the ongoing challenges in obtaining BA in community practice. Up to one-third of patients prescribed BA from March 2020 through December 2022 never received insurance approval, and nearly 20 % of those who did receive approval failed to fill their prescription. Fill rates dropped as OOP cost increased. Ultimately, even among patients with insurance, only about half of the patients who were prescribed BA actually received this therapy.

While this study was not designed to capture the proportion of eligible patients who were prescribed BA, our database captures approximately 80 % of the US pharmacy market, and through the end of 2022, only 116,176 new prescriptions of BA were identified among insured patients. This raises concern that prescribers may be prescribing narrowly to those who are more likely to receive approval or afford the high cost. Temporal factors may have been at play, given that BA was FDA-approved in February 2020, immediately before the COVID-19 lockdowns in the United States. The concurrent public health crisis may have reduced provider awareness of the availability of BA. A decline in preventive health visits during this period could also have led

Table 2
Univariable and multivariable logistic regression for ever receiving approval of bempedoic acid prescription.

	Unadjusted OR (95 % CI)	p-value	Fully adjusted OR (95 % CI)	p-value
Age categories				
65–74	Ref	Ref	Ref	Ref
<55	1.01 (0.97, 1.05)	0.89	0.84 (0.79, 0.88)	<0.001
55–64	1.10 (1.07, 1.14)	0.01	0.94 (0.89, 0.98)	<0.001
75 and over	0.91 (0.88, 0.94)	<0.001	0.96 (0.92, 1.001)	0.06
Female gender	0.87 (0.85, 0.89)	<0.001	0.94 (0.91, 0.97)	<0.001
Ethnicity				
White/Caucasian	Ref	Ref	Ref	Ref
Asian	1.11 (0.99, 1.25)	0.06	1.12 (0.99, 1.26)	0.06
Black/African American	0.90 (0.86, 0.94)	<0.001	0.93 (0.88, 0.97)	<0.001
Hispanic	0.87 (0.83, 0.92)	<0.001	0.85 (0.81, 0.90)	<0.001
Other	1.22 (1.09, 1.36)	<0.001	1.17 (1.04, 1.31)	0.01
Payment type				
Government	Ref	Ref	Ref	Ref
Commercial	1.51 (1.47, 1.54)	<0.001	1.62 (1.56, 1.68)	<0.001
Provider specialty				
Primary care	Ref	Ref	Ref	Ref
Advance Practice Providers	1.05 (0.99, 1.10)	0.06	1.04 (0.98, 1.10)	0.21
Cardiology	1.44 (1.40, 1.48)	<0.001	1.39 (1.34, 1.44)	<0.001
Endocrinology	1.2 (1.13, 1.28)	<0.001	1.08 (1.01, 1.16)	0.03
Other specialty	1.01 (0.96, 1.07)	0.64	1.05 (0.97, 1.12)	0.23
Provider volume of prescriptions				
(1st quartile)	Ref	Ref	Ref	Ref
(2nd quartile)	1.17 (1.13, 1.22)	<0.001	1.16 (1.11, 1.21)	<0.001
(3rd quartile)	1.3 (1.25, 1.35)	<0.001	1.25 (1.20, 1.31)	<0.001
(4th quartile)	1.55 (1.49, 1.61)	<0.001	1.44 (1.38, 1.51)	<0.001
Current LLT				
Statins				
No statin	Ref	Ref	Ref	Ref
High intensity	1.03 (0.99, 1.06)	0.17	1.004 (0.95, 1.04)	0.88
Medium intensity	0.97 (0.93, 1.01)	0.09	0.97 (0.93, 1.02)	0.29
Low intensity	0.87 (0.81, 0.95)	<0.001	0.92 (0.83, 1.01)	0.09
Ezetimibe	0.81 (0.79, 0.83)	<0.001	0.86 (0.83, 0.89)	<0.001
PCSK9i	1.46 (1.38, 1.54)	<0.001	1.40 (1.31, 1.50)	<0.001

to difficulties initiating novel lipid-lowering therapies [13]. Further, in 2020, BA was initially approved for the indication of LDL-C lowering in HeFH or established ASCVD [14]. However, more recent outcomes data has led the FDA to expand its indication to include primary ASCVD risk reduction in December 2023 [1].

Though low, the approval and fill rate of BA is slightly higher than what had been previously shown in the first year of availability for PCSK9i, in which only 30.9 % ever received therapy due to a combination of high rejection rates (52.8 %) and high abandonment rates (34.7 %) [10]. In the case of PCSK9i, extensive prior authorization requirements and variability between individual insurance plans created numerous barriers for prescribers [15]. Additional patient-level barriers

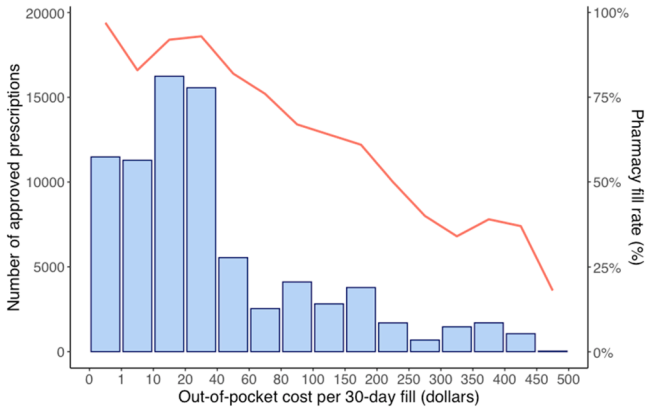


Fig. 2. Prescription fill rates of bempedoic acid by out-of-pocket cost.

Table 3
Changes in lipid-lowering therapy after 1 year of bempedoic acid rejection or abandonment.

	Rejected N = 32,518[1]	Abandoned, N = 12,467[1]
Started/increased evidence-based LLT*	11,780 (36.2 %)	4150 (33.3 %)
Statin initiation	4685 (14.4 %)	1801 (14.4 %)
Statin intensification	478 (1.5 %)	166 (1.3 %)
Ezetimibe initiation	5788 (17.8 %)	1857 (14.9 %)
PCSK9i initiation	2099 (6.5 %)	768 (6.2 %)

[1] n (%)
LLT: lipid-lowering therapy.
* Any of the following: statin initiation, statin intensification, ezetimibe initiation, or PCSK9i initiation (not mutually exclusive).

for PCSK9i included the burden of self-administered injections and high annual average wholesale price especially in the initial years after approval [10,16]. For BA, in addition to ease of administration, clinicians and health systems may have developed better practices and support systems to navigate the prior authorization process after the experience with PCSK9i. Still, national uptake of novel lipid-lowering therapies remains low [17].

Our results are consistent with prior studies showing how payer rejections can blunt adoption of newer medications [10,18–20]. In 2023, almost 1 out of every 2 medications on the Medicare Part D formulary was subject to some form of utilization-management practice [21]. Private payers and government-administered insurance can have different review policies, resulting in inequity in access [8,21,22]. Prescriptions written by cardiologists and higher-volume prescribers had the highest approval rates, while those written by primary care providers and advanced practice practitioners had lower chances of success. This may be due to a different patient case mix or variable experience with prescribing. It may also indicate more support navigating the prior authorization process among higher-volume practices and cardiology practices. Presently, increasing attention is being placed on pharmacy benefit managers (PBMs), who implement the prior authorization requirements, as well as their influence on drug costs [23]. In 2024, the Centers for Medicare and Medicaid Services (CMS) finalized the "Interoperability and Prior Authorization Final Rule" which set new regulation for Medicare Advantage and Medicare programs regarding the prior authorization (PA) process. This new rule includes requirements for implementation of a system for electronic PA to decrease the provider burden and increase the efficiency of the PA process, time limits for PA reviews, a requirement for payers to report the reason for rejection, and public reporting of PA metrics [24,25]. Whether and how these changes impact the overall PA landscape remains unclear, as this regulation does not apply to commercial payers.

At an individual level, prescribers should be encouraged to appeal

initial rejections, as over half of those that were appealed were subsequently approved. Unfortunately, over half of prescriptions rejected initially (corresponding to 23.1 % of patients who were prescribed BA) were never appealed.

Even after approval, high patient costs result in limited patient access [10]. Even after receiving approval for BA, nearly 1 in 5 abandoned the prescription at the pharmacy. Most notably, fill rates dropped rapidly with increasing OOP costs, suggesting this is the main driver of abandonment. As those with government insurance are ineligible to use copay assistance programs, this likely accounts for the difference in abandonment rates by insurance status. Most patients with copay below $40 dispensed BA; however, less than half of patients with monthly cost above $200 filled the medication. Patients with government insurance were disproportionately affected by this higher monthly cost. This may be because patients with commercial insurance had additional access to manufacturer-sponsored patient-assistance programs to offset the cost. Unfortunately, those with government insurance are ineligible to use these programs due to the Social Security Act 1128B(b) [26]. Caps in OOP costs for Medicare beneficiaries under the 2022 Inflation Reduction Act may help reduce access challenges faced by those with Medicare due to high OOP costs [27]. Another factor driving patient OOP cost is PBMs. PBM-negotiated rebates from drug manufacturers can drive up list prices. Because patient OOP costs are often set as a percent of the drug's list price, this leads to higher patient OOP costs [23,28,29]. PBMs are currently under increased scrutiny by the Federal Trade Commission [30]. Whether this ultimately leads to policy reform remains to be seen.

Our analysis also raises concerns for potential inequity in early access to BA. Female sex, Black race, and Hispanic ethnicity were all associated with lower likelihood of therapy approval. Unfortunately, these minority groups have been under-recognized and under-treated for LDL-C lowering [31,32]. This may be from lack of perceived risk of cardiovascular disease, or existing biases against affordability and adherence. As administrative burden can be a mechanism of inequality in an organizational level creating unequal access to services [33,34], streamlining utilization management practices is important to ensure wider uptake of cholesterol-lowering therapies.

Among patients who failed to initiate BA, only one-third underwent an escalation in lipid-lowering therapy with a therapy shown to prevent cardiovascular events in clinical trials, such as a statin, ezetimibe, or PCSK9i, over the following year. Those patients who did undergo intensification of lipid-lowering therapy with a low-cost alternative to BA may represent "success stories" for the prior authorization process. On the other hand, the majority of patients who were unable to initiate BA had no evidence of escalation of lipid-lowering therapy. This raises concern that utilization-management practices may be leading to missed opportunities for cardiovascular risk reduction.

Our study had certain limitations. First, we were unable to link these pharmacy-exchange data to patient clinical information and thus were unable to determine the indication for the prescription, including the patient's lipid levels and clinical diagnoses. Second, full historical prescription data for all patients was not available, so we were unable to determine whether patients prescribed with BA who were not on a statin were truly statin-intolerant or had tried alternate therapies. Third, we only evaluated first fills of approved prescriptions and did not examine barriers to medication refills and long-term medication adherence. Lastly, we only included data from 2020 to 2022, which predated the results of CLEAR-OUTCOMES.

5. Conclusions

Close to one-half of patients prescribed BA failed to initiate therapy, either through prescription rejections or abandonment. Cardiology providers and high-volume providers had increased approval rates, suggesting that provider proficiency may influence success. Prescription abandonment, driven by high OOP cost, was a substantial barrier to obtain BA, particularly in those with government insurance. This calls for attention to the need streamline utilization management practices and implement measures to improve equitable access.

CRediT authorship contribution statement

Jimin Hwang: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Eric Peterson:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Anand Gupta:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Evelyn Sarnes:** Writing – review & editing, Resources, Methodology. **Kristin Gillard:** Writing – review & editing, Resources, Methodology. **Ann Marie Navar:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Ann Marie Navar reports financial support was provided by Esperion Therapeutics Inc. Eric Peterson reports a relationship with Amgen that includes: consulting or advisory and funding grants. Eric Peterson reports a relationship with Novo Nordisk that includes: consulting or advisory. Eric Peterson reports a relationship with Janssen that includes: consulting or advisory. Eric Peterson reports a relationship with Esperion that includes: funding grants. Ann Marie Navar reports a relationship with Esperion Therapeutics Inc that includes: consulting or advisory and funding grants. Ann Marie Navar reports a relationship with Amgen that includes: funding grants. Ann Marie Navar reports a relationship with Bristol-Myers Squibb that includes: funding grants. Ann Marie Navar reports a relationship with AstraZeneca that includes: consulting or advisory. Ann Marie Navar reports a relationship with Bayer that includes: consulting or advisory. Ann Marie Navar reports a relationship with Boehringer Ingelheim that includes: consulting or advisory. Ann Marie Navar reports a relationship with Janssen that includes: consulting or advisory and funding grants. Ann Marie Navar reports a relationship with Eli Lilly and Company that includes: consulting or advisory. Ann Marie Navar reports a relationship with NewAmsterdam Pharma that includes: consulting or advisory. Ann Marie Navar reports a relationship with Novartis that includes: consulting or advisory. Ann Marie Navar reports a relationship with Novo Nordisk that includes: consulting or advisory. Ann Marie Navar reports a relationship with Pfizer that includes: consulting or advisory. Ann Marie Navar reports a relationship with Silence Therapeutics that includes: consulting or advisory. Evelyn Sarnes reports a relationship with Esperion Therapeutics Inc that includes: employment and equity or stocks. Kristin Gillard reports a relationship with Esperion Therapeutics Inc that includes: employment and equity or stocks. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2025.100940.

References

[1] Nissen SE, Lincoff AM, Brennan D, Ray KK, Mason D, Kastelein JJP, Thompson PD, Libby P, Cho L, Plutzky J, Bays HE, Moriarty PM, Menon V, Grobbee DE, Louie MJ, Chen CF, Li N, Bloedon L, Robinson P, Horner M, Sasiela WJ, McCluskey J, Davey D, Fajardo-Campos P, Petrovic P, Fedacko J, Zmuda W, Lukyanov Y, Nicholls SJ. Bempedoic acid and cardiovascular outcomes in statin-intolerant patients. N Engl J Med 2023;388:1353–64. https://doi.org/10.1056/NEJMoa2215024.

[2] Nissen SE, Menon V, Nicholls SJ, Brennan D, Laffin L, Ridker P, Ray KK, Mason D, Kastelein JJP, Cho L, Libby P, Li N, Foody J, Louie MJ, Lincoff AM. Bempedoic acid

for primary prevention of cardiovascular events in statin-intolerant patients. JAMA 2023;330:131–40. https://doi.org/10.1001/jama.2023.9696.
[3] Ray KK, Bays HE, Catapano AL, Lalwani ND, Bloedon LT, Sterling LR, Robinson PL, Ballantyne CM. Safety and efficacy of bempedoic acid to reduce LDL cholesterol. N Engl J Med 2019;380:1022–32. https://doi.org/10.1056/NEJMoa1803917.
[4] Goldberg AC, Leiter LA, Stroes ESG, Baum SJ, Hanselman JC, Bloedon LT, Lalwani ND, Patel PM, Zhao X, Duell PB. Effect of Bempedoic acid vs placebo added to maximally tolerated statins on low-density lipoprotein cholesterol in patients at high risk for cardiovascular disease: the CLEAR Wisdom randomized clinical Trial. JAMA 2019;322:1780–8. https://doi.org/10.1001/jama.2019.16585.
[5] Ballantyne CM, Banach M, Mancini GBJ, Lepor NE, Hanselman JC, Zhao X, Leiter LA. Efficacy and safety of bempedoic acid added to ezetimibe in statin-intolerant patients with hypercholesterolemia: a randomized, placebo-controlled study. Atherosclerosis 2018;277:195–203. https://doi.org/10.1016/j.atherosclerosis.2018.06.002.
[6] Warden BA, Cardiology BA, Purnell JQ, Duell PB, Fazio S. Real-world utilization of bempedoic acid in an academic preventive cardiology practice. J Clin Lipidol 2022;16:94–103. https://doi.org/10.1016/j.jacl.2021.11.013.
[7] GoodRx, Nexletol coupons, (2024). https://www.goodrx.com/nexletol/ (accessed May 18, 2024).
[8] Schwartz AL, Brennan TA, Verbrugge DJ, Newhouse JP. Measuring the scope of prior authorization policies: applying private insurer rules to Medicare part B. JAMA Health Forum 2021;2:e210859. https://doi.org/10.1001/jamahealthforum.2021.0859.
[9] Trapani D, Kraemer L, Rugo HS, Lin NU. Impact of prior authorization on patient access to cancer care. Am Soc Clin Oncol Educ Book 2023;43:e100036. https://doi.org/10.1200/EDBK_100036.
[10] Navar AM, Taylor B, Mulder H, Fievitz E, Monda KL, Fievitz A, Maya JF, López JAG, Peterson ED. Association of prior authorization and out-of-pocket costs with patient access to PCSK9 inhibitor therapy. JAMA Cardiol 2017;2:1217–25. https://doi.org/10.1001/jamacardio.2017.3451.
[11] Trudo F, Kallenbach L, Vasey J, Chung Y, Wilk A, Slipski L, O'Brien D, Strange C. Clinical and economic burden of eosinophilic COPD In A large retrospective US cohort. Int J Chron Obstruct Pulmon Dis 2019;14:2625–37. https://doi.org/10.2147/COPD.S220009.
[12] ICON PLC, Symphony Health: turning data, analytics, and technology into actionable strategy, (2024). https://www.iconplc.com/solutions/technologies/symphony-health (accessed February 9, 2024).
[13] Cortez C, Mansour O, Qato DM, Stafford RS, Alexander GC. Changes in short-term, long-term, and preventive care delivery in US office-based and telemedicine visits during the COVID-19 pandemic. JAMA Health Forum 2021;2:e211529. https://doi.org/10.1001/jamahealthforum.2021.1529.
[14] R. Tummala, M. Gupta, A.R. Devanabanda, D. Bandyopadhyay, W.S. Aronow, K.K. Ray, M. Mamas, R.K. Ghosh, Bempedoic acid and its role in contemporary management of hyperlipidemia in atherosclerosis, Ann Med 54 (n.d.) 1287–96. 10.1080/07853890.2022.2059559.
[15] Nasir K, Angraal S, Virani SS. PCSK9 Inhibitors prior authorization. Circ Cardiovasc Qual Outcomes 2019;12:e005910. https://doi.org/10.1161/CIRCOUTCOMES.119.005910.
[16] Manniello M, Pisano M. Alirocumab (Praluent): first in the new class of PCSK9 inhibitors. P T 2016;41:28–53.
[17] Bradley CK, Kolkailah AA, Shah NP, Page CB, Peterson ED, Navar AM. Uptake of non-statin lipid-lowering therapies for secondary prevention in community practice. J Clin Lipidol 2023;17:412–4. https://doi.org/10.1016/j.jacl.2023.03.006.
[18] Navar AM, Mulder HM, Wojdyla DM, Peterson ED. Have the major cardiovascular outcomes trials impacted payer approval rates for PCSK9 inhibitors? Circ Cardiovasc Qual Outcomes 2020;13:e006019. https://doi.org/10.1161/CIRCOUTCOMES.119.006019.
[19] O'Neil A, Calderbank S, Brown J, Vandigo J, Yin P, Bratti K, Howell S. Quantification of utilization management barriers for patients initiating therapy to lower lipid levels. JAMA Netw Open 2022;5:e2240513. https://doi.org/10.1001/jamanetworkopen.2022.40513.
[20] Chamberlain AM, Gong Y, Shaw KM, Bian J, Song W, Linton MF, Fonseca V, Price-Haywood E, Guhl E, King JB, Shah RU, Puro J, Shenkman E, Pawloski PA, Margolis KL, Hernandez AF, Cooper-DeHoff RM. PCSK9 Inhibitor use in the real world: data from the National patient-centered research network. J Am Heart Assoc 2019;8:e011246. https://doi.org/10.1161/JAHA.118.011246.
[21] Medicare Payment Advisory Commission, Health Care Spending and the Medicare Program: a data book July 2023, (2023).
[22] G. Jacobson, T.N. Published, Prior authorization in Medicare Advantage plans: how often is it used?, 2018. https://www.kff.org/medicare/issue-brief/prior-authorization-in-medicare-advantage-plans-how-often-is-it-used/ (accessed November 21, 2023).
[23] Mattingly TJ, Hyman DA, Bai G. Pharmacy benefit managers: history, business practices, economics, and policy. JAMA Health Forum 2023;4:e233804. https://doi.org/10.1001/jamahealthforum.2023.3804.
[24] Kannarkat JT, Warring W, Brennan T. Advancing interoperability and Prior authorization reform. JAMA Health Forum 2024;5:e241193. https://doi.org/10.1001/jamahealthforum.2024.1193.
[25] Centers for Medicare and Medicaid Services, CMS finalizes rule to expand access to health information and improve the prior authorization process, (2024). https://www.cms.gov/newsroom/press-releases/cms-finalizes-rule-expand-access-health-information-and-improve-prior-authorization-process (accessed August 2, 2024).
[26] National Council for Prescription Drug Programs, Inc., Recommendations for use of the NCPDP telecommunication standard to prevent use of copayment coupons by Medicare Part D beneficiaries and applicability to other federal programs, version 1.1, (2017).
[27] Centers for Medicare and Medicaid Services, Anniversary of the Inflation Reduction Act: update on CMS implementation, (2023). https://www.cms.gov/newsroom/fact-sheets/anniversary-inflation-reduction-act-update-cms-implementation (accessed August 2, 2024).
[28] Plummer E, Socal MP, Ballreich JM, Anderson GF, Bai G. Trends of prescription drug manufacturer rebates in commercial health insurance plans, 2015-2019. JAMA Health Forum 2022;3:e220888. https://doi.org/10.1001/jamahealthforum.2022.0888.
[29] Yeung K, Dusetzina SB, Basu A. Association of branded prescription drug rebate size and patient out-of-pocket costs in a nationally representative sample, 2007-2018. JAMA Netw Open 2021;4:e2113393. https://doi.org/10.1001/jamanetworkopen.2021.13393.
[30] Federal Trade Commission, Pharmacy benefit managers: the powerful middlemen inflating drug costs and squeezing Main Street pharmacies, 2024. https://www.ftc.gov/system/files/ftc_gov/pdf/pharmacy-benefit-managers-staff-report.pdf (accessed August 2, 2024).
[31] Jacobs JA, Addo DK, Zheutlin AR, Derington CG, Essien UR, Navar AM, Hernandez I, Lloyd-Jones DM, King JB, Rao S, Herrick JS, Bress AP, Pandey A. Prevalence of statin use for primary prevention of atherosclerotic cardiovascular disease by race, ethnicity, and 10-year disease risk in the US: national Health and Nutrition Examination Surveys, 2013 to March 2020. JAMA Cardiol 2023;8:443–52. https://doi.org/10.1001/jamacardio.2023.0228.
[32] Balla S, Ekpo EP, Wilemon K, Knowles JW, Rodriguez F. Women living with familial hypercholesterolemia: challenges and considerations surrounding their care. Curr Atheroscler Rep 2020;22:60. https://doi.org/10.1007/s11883-020-00881-5.
[33] Ray V, Herd P, Moynihan D. Racialized burdens: applying Racialized organization theory to the administrative State. J Public Adm Res Theory 2023;33:139–52. https://doi.org/10.1093/jopart/muac001.
[34] Herd P, Hoynes H, Michener J, Moynihan D. Introduction: administrative burden as a mechanism of inequality in policy implementation. RSF Russell Sage Found J Soc Sci 2023;9:1–30.