Real-World Use and Associated Healthcare Resource Utilization Among Patients With Epilepsy Receiving Rescue Midazolam Nasal Spray

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Background

- Some patients with epilepsy may experience acute repetitive seizures or seizure clusters (SCs) that differ from their usual seizure pattern.[1] SCs are associated with progression to status epilepticus,[2] hospital admissions,[2] reduced quality of life,[3] and increased risk of mortality.[4]
- SCs are associated with high healthcare resource utilization (HCRU) and costs; however, published data are limited.
- Rescue medications, such as benzodiazepines, can be used in the outpatient treatment of SCs. However, they may be underutilized.[3]
- Midazolam nasal spray (MDZ-NS) is a fast-acting benzodiazepine administered intranasally for the acute treatment of SCs in patients with epilepsy aged ≥12 years.[5]

Objective

- To assess the characteristics, HCRU, and costs in patients with epilepsy who were newly prescribed MDZ-NS.

Methods

STUDY DESIGN

- This was a retrospective cohort analysis of de-identified data from Merative MarketScan database of commercial, Medicare Supplemental, and Medicaid enrollees.
- The index date was defined as the date of first MDZ-NS prescription in the identification period: December 1, 2019, through January 31, 2023.
- The cohort comprised patients with epilepsy aged ≥12 years who were newly prescribed MDZ-NS for SCs (based on secondary use) during the identification period.
  - Diagnosis of epilepsy was based on ≥1 inpatient or outpatient claim related to an *International Classification of Diseases, Ninth Revision* [*ICD-9*] code (345.X, 780.39), or an *ICD-10* code (G40.X, R56.9) in any position.
  - Note that *ICD-9 and ICD-10* did not include codes for SCs.
- Rescue medication included a prescription claim for clonazepam, diazepam, lorazepam, or midazolam (excluding MDZ-NS).
- Epilepsy-related HCRU and costs (total of payer- and patient-paid costs; reported in 2023 US dollars) were captured 12 months before (baseline) and 6 months after (follow-up) MDZ-NS initiation and were stratified according to 1 or ≥2 MDZ-NS prescription fills during follow-up.

[b]By default, enrollment is required on the index date; [d]Prior pharmacy claim of MDZ-NS, absence of prior epilepsy diagnosis 365 days before and including the index date; †Time since first epilepsy diagnosis is assessed from start of data to index date; [d]Disease characteristics, comorbidities, prior ASMs; [e]Earliest of: death, 180 days of follow-up, end of data, or disenrollment. ASM, antiseizure medication; HCRU, healthcare resource utilization.

Overview

QUESTION

What are the characteristics, healthcare resource use (HCRU), and associated costs before and after initiation of midazolam nasal spray (MDZ-NS) in patients with epilepsy, according to the number of prescriptions filled (1 vs ≥2)?

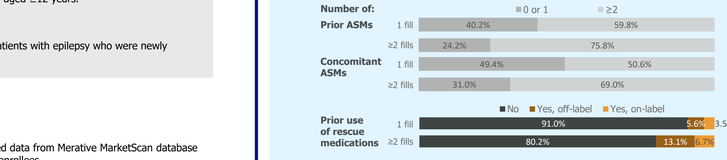
INVESTIGATION

A retrospective cohort study assessed HCRU and costs associated with the number of MDZ-NS prescription fills (date of first fill = index date), using a US claims database of insured patients (aged ≥12 years) with epilepsy. Epilepsy-related HCRU and costs (2023 US dollars) were captured 12 months before (baseline) and 6 months after (follow-up) MDZ-NS initiation and stratified according to 1 or ≥2 MDZ-NS prescription fills during follow-up.

RESULTS

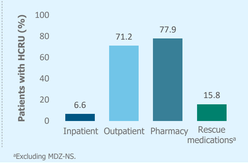
Patient characteristics

Antiseizure medication (ASM) and rescue medication use at baseline, by number of MDZ-NS fills post-index



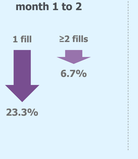
HCRU

Epilepsy-related HCRU the month before index (MDZ-NS initiation)



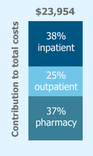
[a]Excluding MDZ-NS.

Change in epilepsy-related HCRU from post-index month 1 to 2

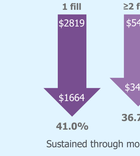


Costs

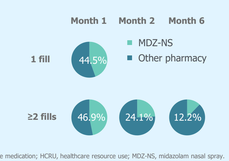
Total epilepsy-related costs over baseline



Change in epilepsy-related costs from post-index month 1 to 2



Proportion of epilepsy-related pharmacy costs due to MDZ-NS



ASM, antiseizure medication; HCRU, healthcare resource use; MDZ-NS, midazolam nasal spray.

CONCLUSIONS

Epilepsy-related HCRU and costs were highest in the month before and the first month following MDZ-NS initiation; HCRU and costs decreased after the first post-index month. MDZ-NS users with ≥2 fills during follow-up had greater resource use and costs overall (all-cause or epilepsy-related).

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Results

PATIENTS

Baseline demographics and patient characteristics

	OVERALL MDZ-NS (N=8364)	1 FILL MDZ-NS (n=4157)	≥2 FILLS MDZ-NS (n=2107)
Age, mean (SD), years	21.9 (11.8)	21.7 (11.8)	21.3 (10.7)
Male, n (%)	4517 (54.0)	2204 (53.0)	1157 (54.9)
Payer plan type, n (%)			
Commercial	3984 (47.6)	2229 (53.6)	1020 (48.4)
Medicaid	4315 (51.6)	1893 (45.5)	1077 (51.1)
Medicare	65 (0.8)	35 (0.8)	10 (0.5)
Type of seizure/epilepsy, n (%)			
POS/focal	2197 (26.3)	1131 (27.2)	520 (24.7)
Generalized	1241 (14.8)	646 (15.5)	295 (14.0)
Unspecified	1411 (16.9)	671 (16.1)	368 (17.5)
Seizure/convulsion	1323 (15.8)	677 (16.3)	289 (13.7)
Other	702 (8.4)	340 (8.2)	209 (9.9)
Mixed	1490 (17.8)	692 (16.6)	426 (20.2)
ESCI score, mean (SD)	0.94 (2.53)	0.84 (2.44)	0.94 (2.25)
Comorbidities occurring in ≥10% of all patients, n (%)			
Cardiac arrhythmias	1400 (16.7)	620 (14.9)	387 (18.4)
Anxiety	1952 (23.3)	934 (22.5)	502 (23.8)
Depression	1197 (14.3)	566 (13.6)	306 (14.5)
Prior ASMs, n (%)			
0 or 1	2955 (35.3)	1672 (40.2)	509 (24.2)
≥2	5409 (64.7)	2485 (59.8)	1598 (75.8)
Concomitant ASMs, n (%)			
0 or 1	3627 (43.4)	2053 (49.4)	653 (31.0)
≥2	4737 (56.6)	2104 (50.6)	1454 (69.0)
Prior rescue medication,[a] n (%)			
No	7330 (87.6)	3781 (91.0)	1689 (80.2)
Yes, off-label	642 (7.7)	231 (5.6)	276 (13.1)
Yes, on-label	392 (4.7)	145 (3.5)	142 (6.7)

[a]Prior rescue medication included a prescription claim for clonazepam, diazepam, lorazepam, midazolam, or branded diazepam, diazepam nasal spray, or midazolam nasal spray during the baseline period. ASM, antiseizure medication; ESCI, epilepsy-specific comorbidity index; POS, partial-onset seizure.

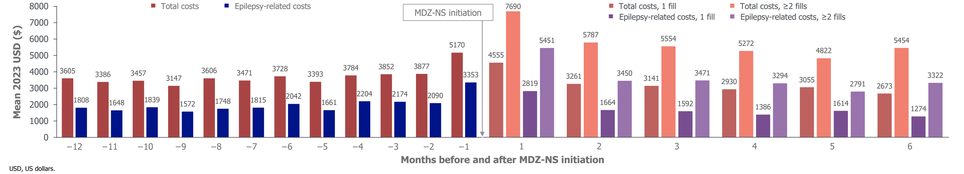
HCRU AND COSTS

All-cause and epilepsy-related HCRU in the 12 months before and 6 months after MDZ-NS initiation

	MONTHS PRE-INITIATION													MONTHS POST-INITIATION											
	−12	−11	−10	−9	−8	−7	−6	−5	−4	−3	−2	−1		1		2		3		4		5		6	
HCRU, n (%)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)	(N=8364)		1 FILL (n=7271)	≥2 FILLS (n=849)	1 FILL (n=6437)	≥2 FILLS (n=1409)	1 FILL (n=5840)	≥2 FILLS (n=1703)	1 FILL (n=5205)	≥2 FILLS (n=1913)	1 FILL (n=4680)	≥2 FILLS (n=1992)	1 FILL (n=4157)	≥2 FILLS (n=2107)
All-cause	7247 (86.6)	7123 (85.2)	7168 (85.7)	7190 (86.0)	7172 (85.7)	7250 (86.7)	7255 (86.7)	7221 (86.3)	7296 (87.2)	7357 (88.0)	7531 (90.0)	8119 (97.1)		7271 (100.0)	849 (100.0)	5825 (90.5)	1387 (98.4)	5275 (90.3)	1657 (97.3)	4650 (89.3)	1845 (96.4)	4126 (88.2)	1913 (96.0)	3716 (89.4)	2007 (95.3)
Inpatient	164 (2.0)	172 (2.1)	167 (2.0)	167 (2.0)	188 (2.2)	166 (2.0)	183 (2.2)	162 (1.9)	194 (2.3)	214 (2.6)	266 (3.2)	567 (6.8)		189 (2.6)	47 (5.5)	152 (2.4)	54 (3.8)	108 (1.8)	68 (4.0)	83 (1.6)	73 (3.8)	72 (1.5)	54 (2.7)	52 (1.3)	66 (3.1)
Outpatient	5711 (68.3)	5461 (65.3)	5459 (65.3)	5493 (65.7)	5530 (66.1)	5669 (67.8)	5537 (66.2)	5521 (66.0)	5550 (66.4)	5602 (67.0)	5842 (69.8)	7359 (88.0)		5664 (77.9)	733 (86.3)	4381 (68.1)	1135 (80.6)	3862 (66.1)	1326 (77.9)	3413 (65.6)	1491 (77.9)	3014 (64.4)	1511 (75.9)	2744 (66.0)	1630 (77.4)
Pharmacy	6457 (77.2)	6266 (74.9)	6314 (75.5)	6388 (76.4)	6325 (75.6)	6448 (77.1)	6443 (77.0)	6457 (77.2)	6547 (78.3)	6583 (78.7)	6723 (80.4)	7331 (87.6)		7271 (100.0)	849 (100.0)	5267 (81.8)	1347 (95.6)	4781 (81.9)	1601 (94.0)	4228 (81.2)	1759 (91.9)	3732 (79.7)	1813 (91.0)	3343 (80.4)	1914 (90.8)
Epilepsy-related	5658 (67.6)	5463 (65.3)	5523 (66.0)	5590 (66.8)	5574 (66.6)	5697 (68.1)	5682 (67.9)	5704 (68.2)	5855 (70.0)	5885 (70.4)	6200 (74.1)	7703 (92.1)		7271 (100.0)	849 (100.0)	4935 (76.7)	1315 (93.3)	4423 (75.7)	1545 (90.7)	3902 (75.0)	1709 (89.3)	3426 (73.2)	1748 (87.8)	3040 (73.1)	1856 (88.1)
Inpatient	133 (1.6)	143 (1.7)	141 (1.7)	143 (1.7)	148 (1.8)	143 (1.7)	164 (2.0)	131 (1.6)	173 (2.1)	183 (2.2)	237 (2.8)	551 (6.6)		171 (2.4)	46 (5.4)	142 (2.2)	51 (3.6)	100 (1.7)	66 (3.9)	75 (1.4)	70 (3.7)	64 (1.4)	52 (2.6)	45 (1.1)	61 (2.9)
Outpatient	2537 (30.3)	2263 (27.1)	2232 (26.7)	2248 (26.9)	2336 (27.9)	2647 (31.6)	2342 (28.0)	2316 (27.7)	2436 (29.1)	2361 (28.2)	2706 (32.4)	5954 (71.2)		3614 (49.7)	510 (60.1)	1952 (30.3)	660 (46.8)	1708 (29.2)	772 (45.3)	1506 (28.9)	846 (44.2)	1259 (26.9)	829 (41.6)	1193 (28.7)	902 (42.8)
Pharmacy	5279 (63.1)	5065 (60.6)	5119 (61.2)	5161 (61.7)	5152 (61.6)	5228 (62.5)	5230 (62.5)	5269 (63.0)	5407 (64.6)	5400 (64.6)	5599 (66.9)	6514 (77.9)		7271 (100.0)	849 (100.0)	4513 (70.1)	1276 (90.6)	4096 (70.1)	1486 (87.3)	3584 (68.9)	1645 (86.0)	3157 (67.5)	1669 (83.8)	2791 (67.1)	1785 (84.7)
Rescue medications[a]	959 (11.5)	888 (10.6)	868 (10.4)	879 (10.5)	892 (10.7)	902 (10.8)	891 (10.7)	914 (10.9)	898 (10.7)	882 (10.5)	913 (10.9)	1325 (15.8)		822 (11.3)	186 (21.9)	501 (7.8)	257 (18.2)	440 (7.5)	306 (18.0)	356 (6.8)	337 (17.6)	325 (6.9)	322 (16.2)	301 (7.2)	334 (15.9)
MDZ-NS	0	0	0	0	0	0	0	0	0	0	0	0		7271 (100.0)	849 (100.0)	0	803 (57.0)	0	682 (40.0)	0	685 (35.8)	0	532 (26.7)	0	554 (26.3)

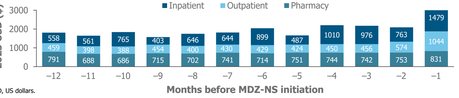
[a]Excluding MDZ-NS. HCRU, healthcare resource utilization.

Total and epilepsy-related costs before and after MDZ-NS initiation



USD, US dollars.

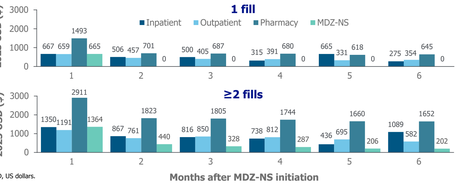
Mean epilepsy-related costs during the baseline period



USD, US dollars.

- During baseline, the highest mean epilepsy-related inpatient and outpatient HCRU and costs occurred in the month before index date.

Mean epilepsy-related costs in patients with 1 and ≥2 fills of MDZ-NS



USD, US dollars.

- During post-index month 1, MDZ-NS constituted 44.5% and 46.9% of epilepsy-related pharmacy costs in patients with 1 fill and ≥2 fills, respectively.
  - By 6 months, MDZ-NS was 12.2% of epilepsy-related pharmacy costs in patients with ≥2 fills.
- Mean MDZ-NS costs constituted 36.4% ($665/$1824) and 38.3% ($1364/$3558) of total pharmacy costs in the 1 and ≥2 fills groups, respectively, within 1 month post-index, and 18.7% ($440/$2348) and 9.7% ($202/$2092) in post-index months 2 and 6, respectively, for the ≥2 fills group.

Limitations

- The indication for SCs could not be confirmed; no code for SCs was available in *ICD-9/ICD-10*; drug use during hospital stay was largely underreported; and indirect costs were not considered.
- The study period coincided with the COVID-19 pandemic, which influenced patients' use of health services; also, delayed access to healthcare resulting from lockdown measures may have impacted post-COVID data (ie, led to underestimates).

Conclusions

- HCRU and costs were high in the month before MDZ-NS initiation and decreased after the first month, which may suggest a precipitating event preceding the need for MDZ-NS.
- Compared with patients with epilepsy who received 1 fill for MDZ-NS, those who received ≥2 MDZ-NS fills may have had more severe epilepsy, as shown by a greater likelihood of having ≥2 prior/concomitant antiseizure medications and higher epilepsy-related HCRU and costs.
- Over the follow-up period, MDZ-NS was a minor contributor to pharmacy costs.

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