Healthcare Resource Utilization and Antiseizure Medication Claims in Patients With Lennox-Gastaut Syndrome Receiving Fenfluramine in the United States

Adam Strzelczyk, MD, MHBA, FEAN[1]; Jaya Khushalani, MD, PhD[2]; Heidi L. Henninger, MD[2]; Patrik Ohagen[3]; Renjie Li[4]; Nakul Yadav, PhD[4]; Wesley T. Kerr, MD, PhD[5]

[1]Goethe University Frankfurt, Frankfurt am Main, Germany; [2]UCB, Smyrna, GA, USA; [3]UCB, Uppsala, Sweden; [4]Ambit Inc., Morristown, NJ, USA; [5]University of Pittsburgh, Pittsburgh, PA, USA

Introduction

- Lennox-Gastaut syndrome (LGS) is a rare, severe, developmental and epileptic encephalopathy characterized by treatment-resistant seizures that begin in childhood and persist into adulthood
- Fenfluramine was approved for the management of seizures associated with LGS in patients ≥2 years old in the US in 2022[1]
- The mechanism of action of fenfluramine is unique among antiseizure medications (ASMs), acting as a dual modulator of the serotonergic and sigma-1 receptor pathways[2]
- There is limited real-world evidence on the impact of fenfluramine in patients with LGS

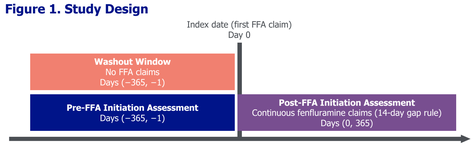
Objective

- Here, we examined healthcare resource utilization (HCRU) and ASM claims for patients with LGS before and after fenfluramine initiation using a large US healthcare database

Methods

- This was a retrospective study of patients with LGS (ICD-10, G40.81) from January 1, 2021–December 31, 2024, using the Komodo US healthcare claims database
- Eligible patients were required to have ≥1 fenfluramine prescription claim, ≥2 LGS claims (≥1 month apart), 12 months of claims data before and after fenfluramine initiation (first fenfluramine prescription claim), and received fenfluramine for 12 months with no gaps >14 days (**Figure 1**)
- The patient selection period was January 1, 2022–December 31, 2023

Figure 1. Study Design



FFA, fenfluramine.

- The primary endpoints were to evaluate differences in HCRU (including all-cause and seizure-related inpatient hospitalizations, all-cause and seizure-related emergency room [ER] visits, office visits, and ambulance use) and number of unique ASMs and average ASM claims (excluding fenfluramine) between the pre- and post-fenfluramine initiation periods
- Change in the average number of HCRU and ASM claims in the pre- and post-index periods were evaluated using paired *t*-tests
- In addition, interrupted time series (ITS) analyses using a generalized estimating equation were conducted to control for time trends in the data
- Lastly, propensity score-matched cohort difference-in-difference (DiD) regression analyses were used to determine robustness of the results when compared with a matched control group (patients with ≥1 LGS claim and no fenfluramine prescription claims)

Results

- Overall, 148 patients with LGS met the eligibility criteria
- Of comorbidities, developmental complications (80%) and respiratory complications (70%) were most common
- Most patients (74%) visited centers of excellence prior to their LGS diagnosis (**Table 1**)

Overview

QUESTION

What are the real-world effects on HCRU and ASM claims for patients with LGS before and after starting treatment with fenfluramine?

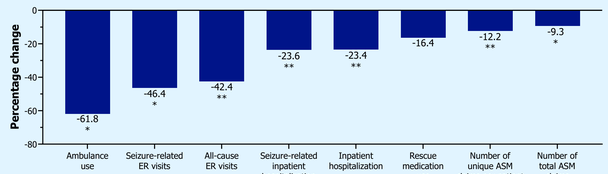
INVESTIGATION

- A retrospective study of patients with LGS (ICD-10, G40.81) from January 1, 2021, to December 31, 2024, using the Komodo US healthcare claims database
- Eligible patients were required to have ≥1 fenfluramine prescription claim, ≥2 LGS claims (≥1 month apart), 12 months of continuous claims data before and after fenfluramine initiation (first fenfluramine prescription claim), and ≥12 months persistent fenfluramine use after the first fenfluramine prescription with no gaps >14 days between 2 fenfluramine claims
- The primary endpoints evaluated the changes in clinical outcomes, ASMs and rescue medication use, and HCRU after 12 months of persistent fenfluramine use
- Change in the average number of HCRU and ASM claims in the pre- and post-index periods were evaluated using paired *t*-tests

RESULTS

- Of 148 patients who met the eligibility criteria, significant reductions in ambulance use, seizure-related and all-cause ER visits, inpatient hospitalization (including seizure-related), unique ASM claims, and total ASM claims were observed in the post-fenfluramine initiation period compared with pre-fenfluramine initiation (**Figure**)

Figure. Percentage Change in HCRU Measures in Pre- vs. Post-Fenfluramine Initiation Periods (N=148)



*P<0.05. **P<0.01.

CONCLUSIONS

- For patients who persisted with treatment for ≥12 months, fenfluramine use in LGS was associated with reductions in ambulance use, ER visits (all-cause and seizure-related), and inpatient hospitalizations (all-cause and seizure-related)
- Meaningful reductions in rescue medication claims, unique ASMs per patient, and ASM claims observed in pediatric and adult patients reflects the effectiveness of fenfluramine
- These results indicate that fenfluramine treatment for 12 months led to significant reductions in HCRU and ASM drug load, which may be associated with better quality of life and lower economic burden

For a copy of the poster, scan:

Abbreviations: ASM, antiseizure medication; ER, emergency room; HCRU, healthcare resource utilization; LGS, Lennox-Gastaut syndrome.

Table 1. Patient Demographics and Characteristics

Variable, n (%)	Patients With LGS N=148
Male	76 (51)
Age at index date	
≥1 to <3	2 (1)
≥3 to <6	19 (13)
≥6 to <11	27 (18)
≥11 to <21	61 (41)
≥21	39 (26)
Comorbidities pre-fenfluramine initiation[a]	
Developmental complications	118 (80)
Respiratory & CV complications	104 (70)
Gastrointestinal issues	81 (55)
Behavioral/psychiatric disorders	53 (36)
Mobility issues/wheelchair use	52 (35)
Sleep disturbances	45 (30)
Payer type	
Commercial	84 (57)
Medicaid	41 (28)
Medicare	10 (7)
Unknown	13 (9)
Prescribing physician	
Epileptologist	35 (24)
Pediatric neurologist	35 (24)
Pediatric neurologist/epileptologist	29 (20)
Neurologist	12 (8)
Adult neurologist/epileptologist	11 (7)
Pediatric	10 (7)
Nurse practitioner or physician's assistant	1 (1)
Unknown	15 (10)
Specialty physician type, pre-fenfluramine initiation	
Center of excellence	109 (74)
Epileptologist[b]	22 (15)
Pediatric neurologist	14 (9)
Neurologist	3 (2)
Other, non-prescription treatments[c]	
Yes	81 (55)
No	67 (45)

[a]Patients may have more than 1 comorbidity.
[b]Outside of centers of excellence.
[c]Includes vagal nerve stimulation, deep brain stimulation, neurostimulation, and epilepsy surgery.
CV, cardiovascular; LGS, Lennox-Gastaut syndrome.

- There were significant reductions in all-cause inpatient hospitalizations, seizure-related inpatient hospitalizations, all-cause ER visits, seizure-related ER visits, ambulance use, all ASM claims, and average number of unique ASMs from pre- to post-fenfluramine initiation periods (**Table 2**)
- Changes in status epilepticus claims, office visits, and seizure-related office visits were not significant from pre- to post-fenfluramine initiation periods

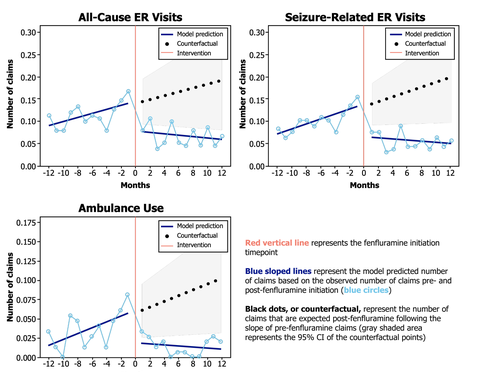
Table 2. Number of HCRU and ASM Claims Pre- and Post-Fenfluramine Initiation (N=148)

	Pre-FFA Initiation, mean	Post-FFA Initiation, mean	Percentage Change	*P* Value
Inpatient hospitalization[a]	4.0	3.1	−23.4	0.04
Seizure-related inpatient hospitalization[a]	4.0	3.0	−23.6	0.04
All-cause ER visits[a]	1.4	0.8	−42.4	<0.01
Seizure-related ER visits[a]	1.3	0.7	−46.4	<0.01
Ambulance use[a]	0.5	0.2	−61.8	<0.01
Number of total ASM claims[b,c]	31.9	28.9	−9.3	<0.01
Number of unique ASM claims per patient[b,c]	3.4	3.0	−12.2	<0.01
Rescue medication use[b]	3.3	2.8	−16.4	0.08

[a]P<0.05 is considered significant.
The index date is the date of the first fenfluramine prescription claim.
[b]Paired *t*-tests performed to assess the difference in the average number of claims pre- and post-index.
[c]Paired *t*-tests performed to assess the difference in the average number of claims per patient pre- and post-index.
[d]ASMs excluding fenfluramine.
ASM, antiseizure medication; ER, emergency room; FFA, fenfluramine; HCRU, healthcare resource utilization.

- ITS analyses illustrated immediate reductions in claims at fenfluramine initiation and continual improvement for 12 months post-index in all-cause and seizure-related ER visits and ambulance use claims (**Figure 2**)
- A separate DiD regression analyses confirmed that these reductions were significant when compared with those in the matched control group

Figure 2. Interrupted Time Series Analysis (N=148)



Red vertical line represents the fenfluramine initiation timepoint

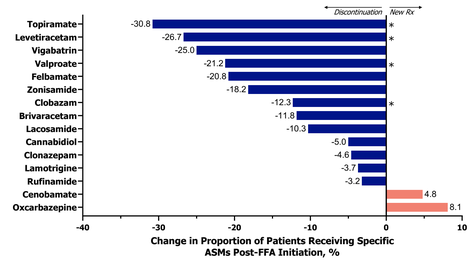
Blue sloped lines represent the model predicted number of claims based on the observed number of claims pre- and post-fenfluramine initiation (blue circles)

Black dots, or counterfactual, represent the number of claims that are expected post-fenfluramine following the slope of pre-fenfluramine claims (gray shaded area represents the 95% CI of the counterfactual points)

The red vertical line (intervention) represents the fenfluramine initiation timepoint. The blue lines (model prediction) represent the prediction of the number of claims based on the observed number of claims (represented by the blue circles) pre- and post-fenfluramine. The black dots (counterfactual) represent the number of claims that are expected post-fenfluramine if following the slope of pre-fenfluramine claims. The gray shaded area represents the 95% CI of the counterfactual points. A generalized estimating equation was used: $y(t) = \beta 1 * \text{time from start} + \beta 2 * \text{treatment variable } (0/1) + \beta 3 * \text{time since treatment} + \varepsilon$.
CI, confidence interval; ER, emergency room.

- A significant proportion of patients discontinued topiramate, levetiracetam, valproate, and clobazam post-fenfluramine initiation (**Figure 3**)

Figure 3. Proportion of Patients With a Change in Concomitant ASM Prescriptions From Pre- to Post-Fenfluramine Initiation



*P<0.05.
ASM, antiseizure medication; Rx, prescription.

Conclusions

- Fenfluramine use in patients with LGS was associated with reductions in ambulance use, ER visits (all-cause and seizure-related), and inpatient hospitalizations (all-cause and seizure-related)
- The results for ER visits and ambulance use remain robust, following more rigorous analytical approaches, including ITS and matched cohort DiD regression
- The average number of all ASM claims and unique ASMs per patient decreased following fenfluramine initiation, suggesting that treatment with fenfluramine reduces the concomitant ASM drug load in patients with LGS
- This study used a mixed open and closed claims database, Komodo US healthcare; a limitation of this study was that patients were required to receive fenfluramine for 12 months with no gap >14 days, which may introduce a selection bias against those who discontinued fenfluramine
- For patients who remained on treatment for 12 months, fenfluramine was associated with significant improvements in real-world outcomes such as HCRU burden and ASM drug load

References

1. FINTEPLA® (fenfluramine) oral solution [prescribing information]. Smyrna, GA: UCB, Inc.; December 2023.
2. Martin P, et al. *Epilepsy Behav.* 2020;105:106989.

Acknowledgements

UCB-sponsored. The authors acknowledge Bobby Jacob, PharmD (UCB), for managing the development of the poster, and Eric Scocchera, PhD, and Courtney Breuel, ELS, of the Sensified Division of Woven Health Collective, LLC, for writing and editorial assistance, which were funded by UCB.

Disclosures

AS: Received personal fees and grants from Angelini Pharma, Biocodex, Desitin Arzneimittel, Eisai, Jazz Pharmaceuticals, Takeda, UCB, and UNEEG Medical.
JK: Employee of UCB with stock ownership.
HLH, PO: External contractor of UCB.
RL, YN: Employee of Ambit Inc.
WTK: Associate Editor of *Epilepsia*; authored review articles for MedLink Neurology; consultant for Acuta, Azurity, Biohaven Pharmaceuticals, Capsida, Cerebral Therapeutics, the Epilepsy Study Consortium, EpiTel, Epygenix, Jazz Pharmaceuticals, Neurelis, Neurona, Neuropace, Noema, Quralis, Rapport, SK Life Science, UCB, Ventus; collaborative or data use agreements with Eisai, GSK, Janssen, Johnson & Johnson, Praxis, and Radius Health; site investigator for Équilibre Pharmaceuticals, UCB.

For a copy of this poster, use your smartphone to scan the QR code or contact UCBCares®
Phone: +1-844-599-CARE (2273)
Email: UCBCares@ucb.com

American Epilepsy Society 79th Annual Meeting
Atlanta, GA, USA | December 5–9, 2025