Epidiolex® (cannabidiol)

A Comparison of Healthcare Resource Utilization (HCRU) in EPIDIOLEX® (cannabidiol) Patients Before and After Treatment Initiation

AMCP Science & Innovation Theater Webinar

October 5, 2021

This presentation is intended for US formulary decision makers.

AMCP = Academy of Managed Care Pharmacy

GREENWICH BIOSCIENCES™

Presenters

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Agenda

- Review data from a retrospective claims analysis that measured healthcare resource utilization and costs for patients on EPIDIOLEX using the IQVIA PharMetrics® Plus database
- Discuss the impact of EPIDIOLEX on hospital admissions, ER visits and length of stay, and concomitant AED
- Explore potential cost outcomes

AED = antiepileptic drug; ER = emergency room.

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Study Design

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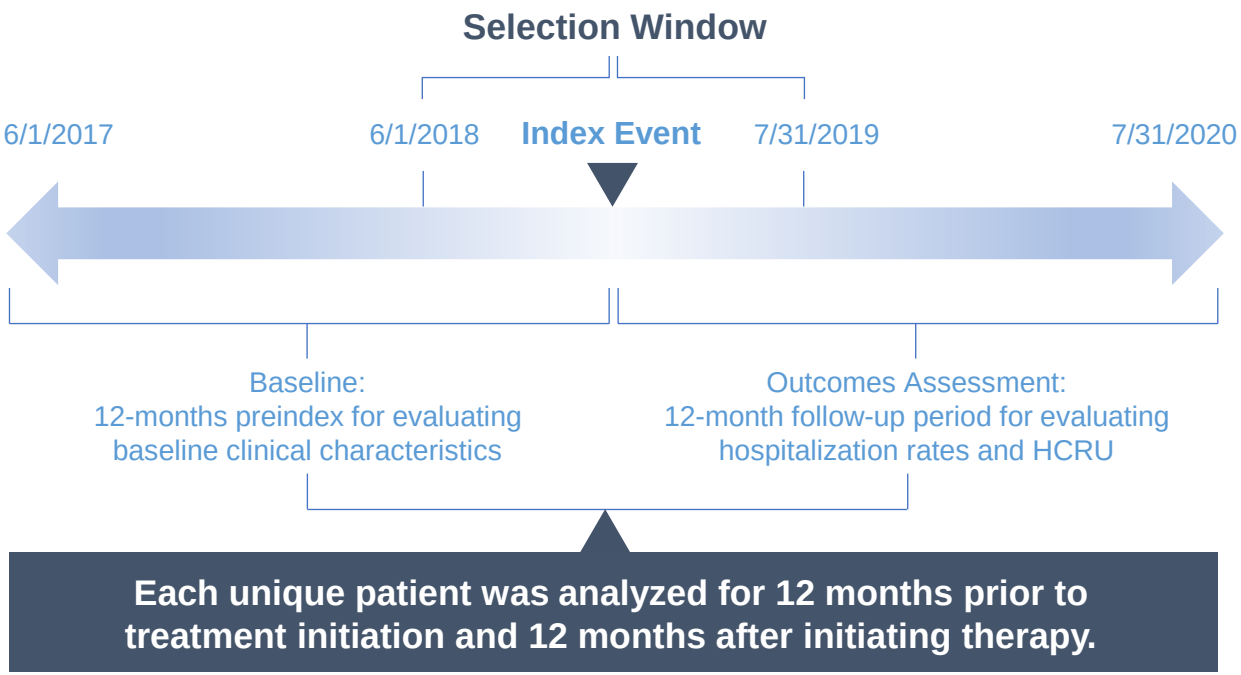
A Retrospective Claims Analysis Measured Healthcare Resource Utilization and Costs for Patients Using EPIDIOLEX[1]

This analysis included EPIDIOLEX users from the IQVIA PharMetrics® Plus database who began therapy between 2017 and 2020.



The aggregated IQVIA PharMetrics Plus database is comprised of adjudicated claims for:

- >140 million unique enrollees across the United States
- >60 health plans
- Diverse representation of geography, employers, payers, providers, and therapy areas
- Coverage of data from over 90% of US hospitals and over 90% of all US doctors

Please see Important Safety Information on slides 23-24 and EPIDIOLEX® (cannabidiol) full Prescribing Information.

Reference: 1. Data on file. Measuring the Impact of Epidiolex on Healthcare Utilization in the Real-World. Greenwich Biosciences, 2021.

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Study Participation Inclusion Criteria[1]

- One or more pharmacy claims for EPIDIOLEX with a service date during the period 6/1/2018 and 7/31/2019
- The date of the first claim is the index event
- Continuous enrollment in the PharMetrics® Plus database for at least 12 months prior to the index event and 12 months after the index event
- Patient is diagnosed with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), tuberous sclerosis complex (TSC), or some type of refractory epilepsy, based on claims data up to 1 year prior to the index event

Almost 90% of patients had probable LGS, DS, or TSC.[1]

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Patient Selection[1]

Due to limitations in ICD-10 coding, an algorithm was used to identify appropriate patients

Probable DS:

- ≥1 medical claim with a diagnosis code representing intractable/refractory epilepsy AND
- ≥1 medical claim with a diagnosis code for intellectual disability or developmental delay AND
- ≥1 pharmacy claim for at least 2 different AEDs or ≥1 medical claim with a diagnosis code for febrile seizures AND
- <91 cumulative days of supply for specific AEDs that rule out DS AND
- No medical claims with a diagnosis code for LGS or TSC AND
- No medical claims with a diagnosis code indicative of abnormal brain imaging

Probable LGS:

- Based on diagnosis code: ≥1 medical claim with a diagnosis code for LGS OR
- Based on epilepsy and intellectual disability:
  - ≥1 medical claim with a diagnosis code representing intractable/refractory epilepsy AND
  - ≥1 medical claim with a diagnosis code for intellectual disability or developmental delay AND
  - No medical claims with a diagnosis code for a condition that would normally preclude LGS AND
  - Not identified for probable DS or probable LGS based on diagnosis code

Probable TSC:

- ≥1 medical claim with a diagnosis code for TSC AND not identified for probable DS or LGS

Other Refractory Epilepsy:

- Based on diagnosis code: Did not meet criteria for DS, LGS, or TSC AND had ≥1 medical claim with diagnosis for intractable/ refractory epilepsy OR
- Based on AED use:
  - ≥1 Rx fill for ≥3 distinct AED AND
  - Not identified for probable DS, LGS, TSC or other refractory epilepsy

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Study Population (N=434)[1]

Indication[1]	
Probable LGS	81.6%
Probable DS	3.7%
Probable TSC	3.0%
Other refractory epilepsies	11.8%

Age Group[1]	
0-2	<11%
3-8	23.0%
9-14	24.9%
15-18	16.4%
19-34	28.3%

Payer Type[1]	
Commercial	98.6%
Medicaid	<11%
Medicare Advantage	<11%

Values indicating <11% are not a precise percentage. Due to data privacy issues, outcomes in <11% of people were marked as such to mask values.

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Statistical Analyses[1]

All statistical analyses were conducted using SAS® version 9.4 and Stata® 16, with tests conducted assuming a two-tailed test of significance and alpha level set a priori at 0.05.

Patient Demographics

- Reported as summary statistics
- Categorical variables assessed using Chi-square tests
- Continuous variables computed using t-tests or Mann-Whitney U tests (Wilcoxon rank-sum test) of medians

HCRU and Cost Analyses

- Cost and count variables assessed using paired t-tests
- Rates assessed using tests of proportions
- Sensitivity analyses for costs used 90% and 98% winsorization[a]
- Outcomes stratified by age, sex, and EPIDIOLEX PDC[b]
- Analyses conducted at person level

COVID-10 Impact Analysis

- March 1, 2020, was used as the cutoff date as that was the month in which COVID-19 was characterized as a pandemic and governments and nationwide shutdowns began
- Analysis compared HCRU and associated costs in patients whose follow-up ended pre-March vs March 1 and after

[a]Winsorization is a way to minimize the influence of outliers in data by modifying outlier data points to increase robustness of statistical inferences.[2]
[b]PDC was calculated by summing the day supply of EPIDIOLEX over the course of the post-index period/360.
PDC = proportion of days covered.

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Reference: 1. Data on file. Measuring the Impact of Epidiolex on Healthcare Utilization in the Real-World. Greenwich Biosciences, 2021. **2.** Statistics How To. Accessed September 14, 2021. https://www.statisticshowto.com/winsorize/

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Study Limitations[1]

- This study may not be generalizable beyond the study database
- Medical coding errors and missing information may impact the study findings
- This analysis only captures drugs with specific billing codes and not alternative forms of treatment
- Due to the FDA approval of EPIDIOLEX for the treatment of seizures associated with TSC in August 2020, this analysis will not capture patients who began EPIDIOLEX treatment for TSC after its approval
- It is unclear whether the estimated impact of EPIDIOLEX will be causal
- Patients in this analysis may have participated in expanded access programs, and therefore, exposed to cannabidiol doses before the baseline period in this study, which cannot be ascertained from claims data

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HCRU Outcomes at 12 Months

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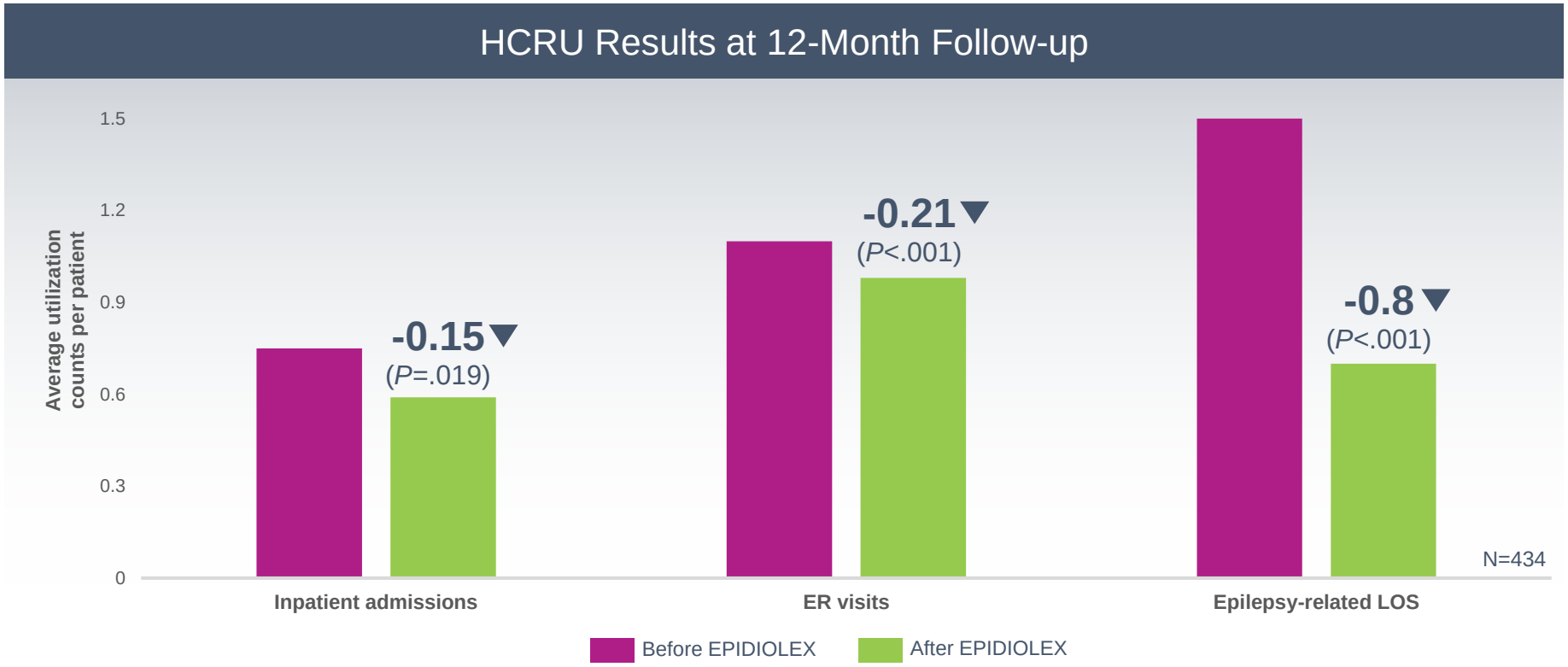
After Starting EPIDIOLEX, Patients Had Significantly Fewer Hospital Admissions, ER Visits, and Shorter Length of Stays[1]



Healthcare utilization was significantly reduced after 12 months on EPIDIOLEX.

LOS = length of stay.

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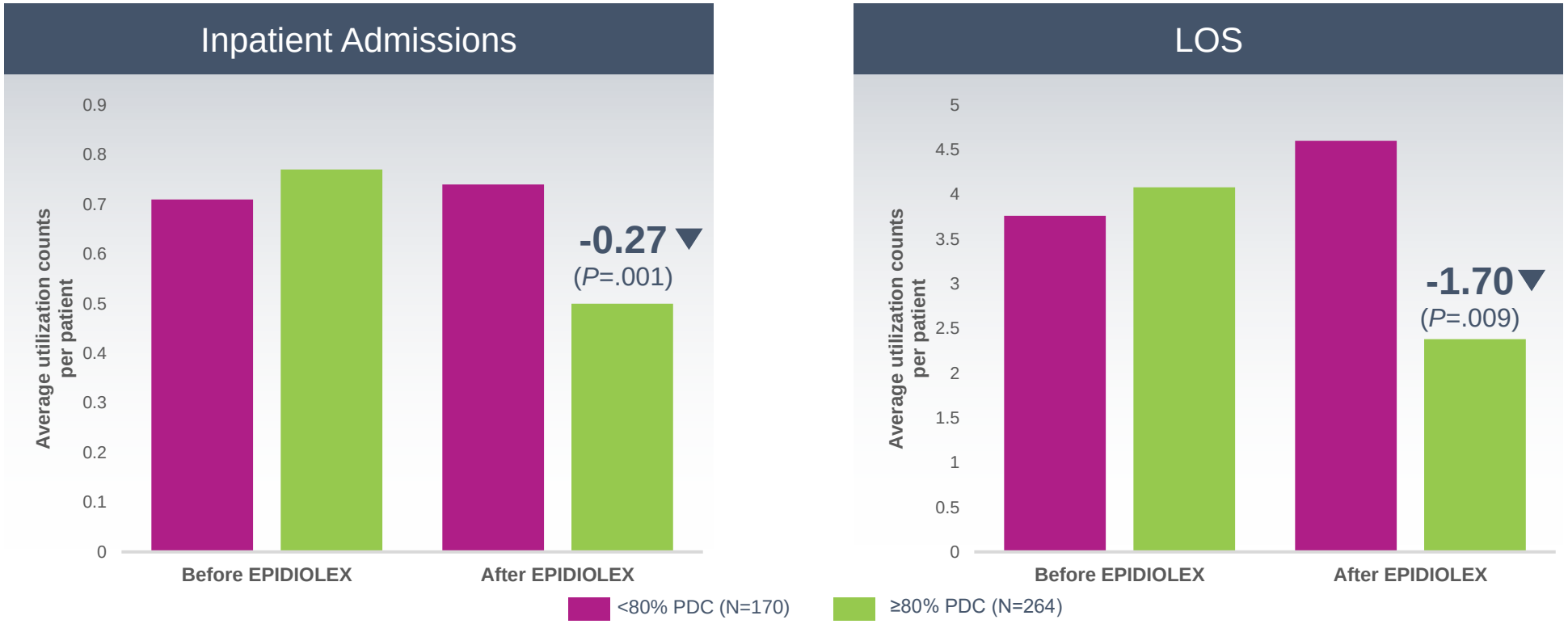
Patients With Higher Adherence (Proportion of Days Covered) Had Significantly Fewer Inpatient Admissions and Shorter Length of Stays vs Those With Lower Adherence[1]



Adherent patients experienced greater reductions in inpatient admissions and length of stays compared to nonadherent patients.

*PDC was calculated by summing the day supply of EPIDIOLEX over the course of the post-index period/360.
PDC = proportion of days covered.

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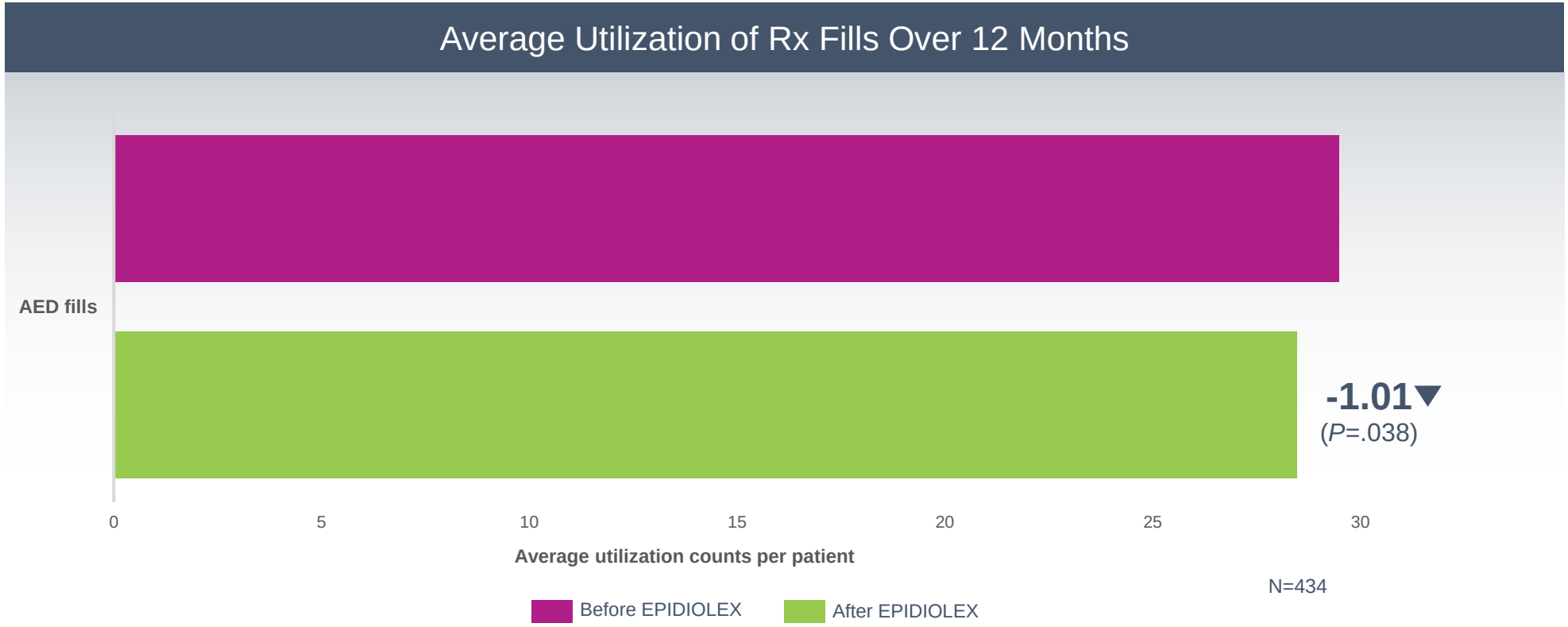
After Starting EPIDIOLEX, Patients Experienced a Statistically Significant Decrease in Fills for Concomitant AEDs[1]



Rx = prescription.

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Cost Outcomes

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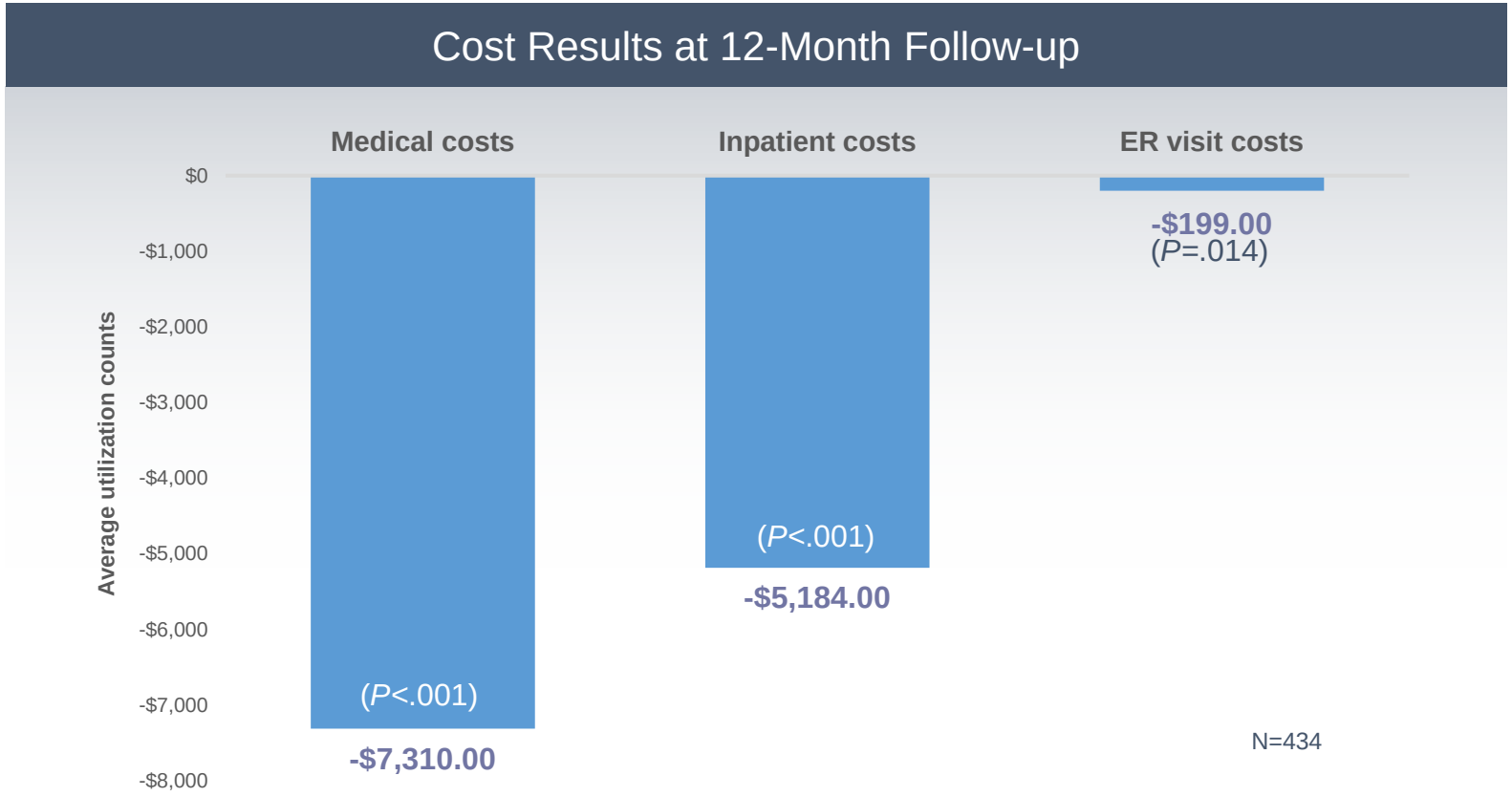
Healthcare Spend for EPIDIOLEX Patients Is Offset by Decreased HCRU[1]



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COVID-19 Impact Analysis

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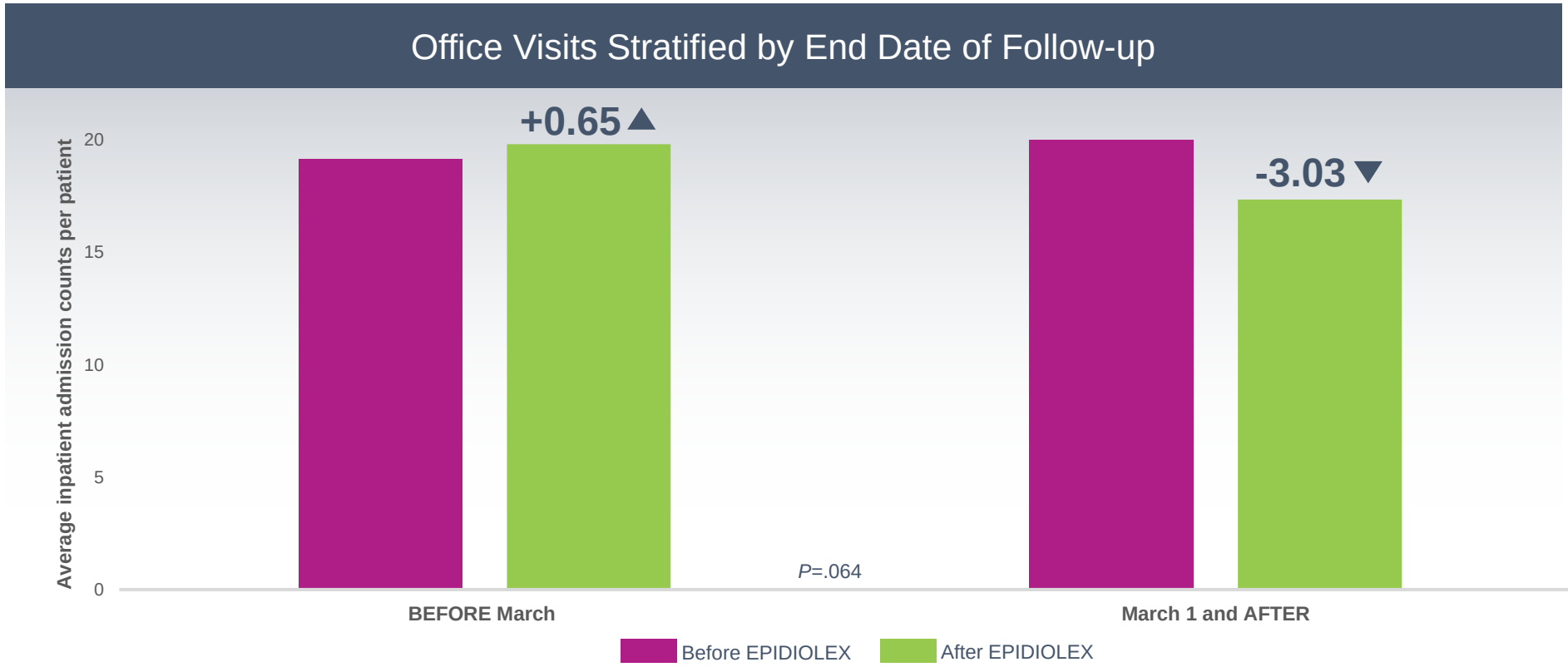
Patients Whose Follow-up Ended Post Pandemic Had Fewer Office Visits Compared to Those With Earlier Follow-up Dates[1]



Patients whose follow-up ended AFTER March 2020 had 3.68 fewer offices visits.

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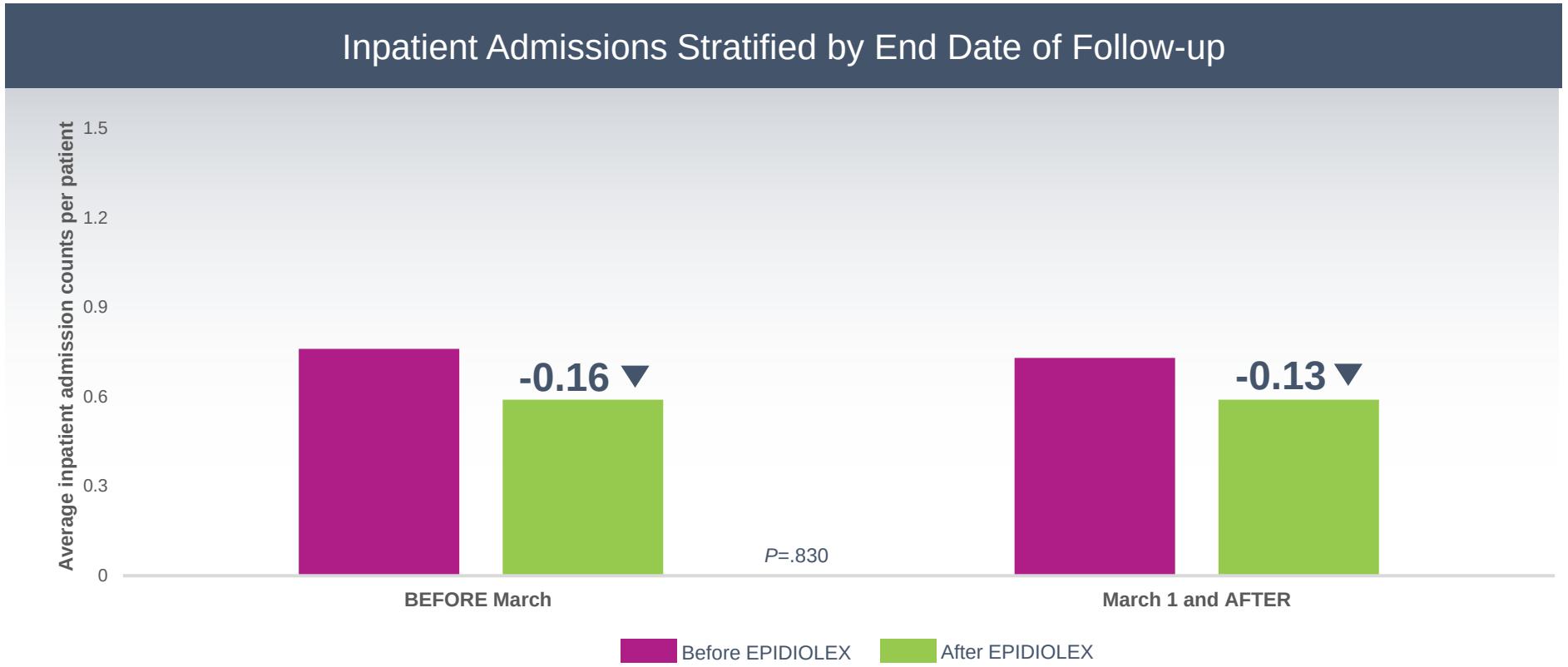
HCRU Trends Were Similar in Both Patient Cohorts[1]



Inpatient utilization did not significantly vary between patients whose follow-up ended BEFORE March 2020 versus patients whose follow-up ended AFTER March 2020.

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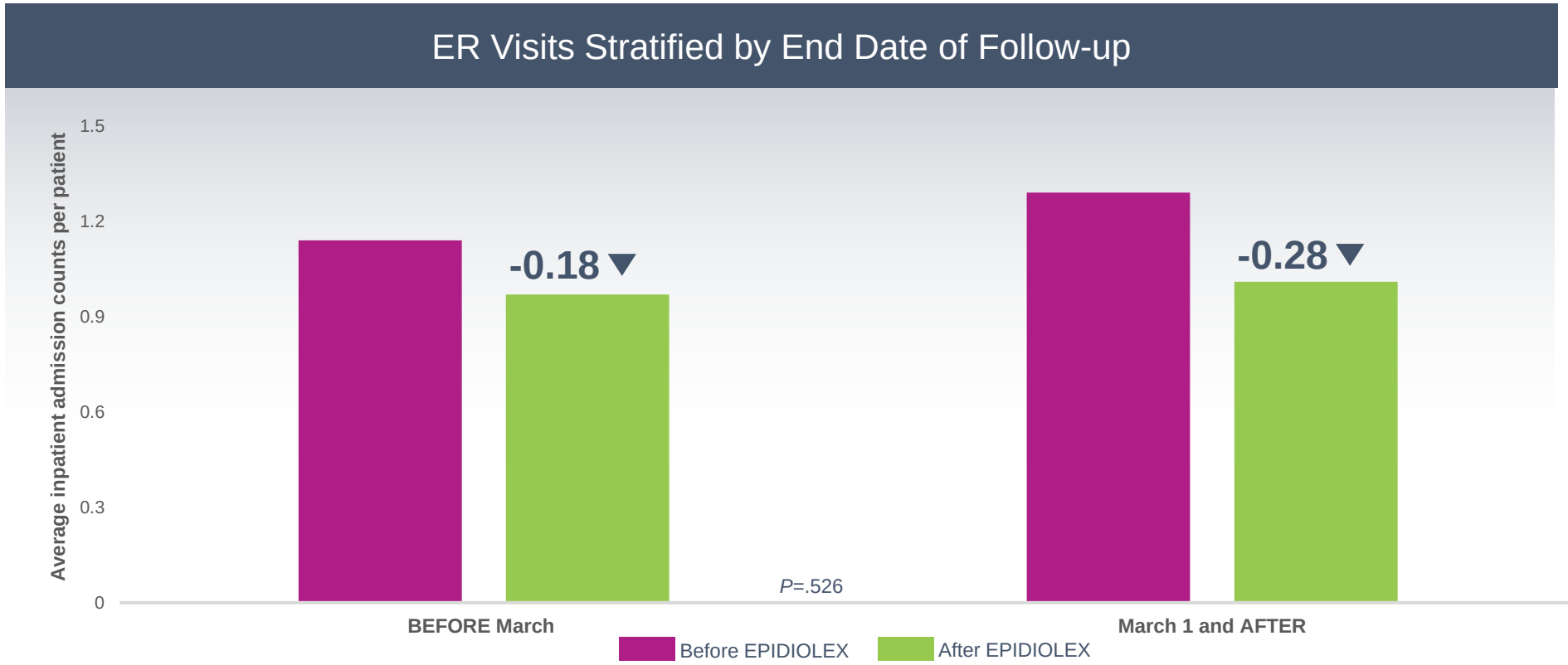
ER Visits Did Not Significantly Vary Between Cohorts[1]



The decrease in number of office visits did not impact patients' health adversely enough to result in higher inpatient utilization.

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Important Safety Information & Indications

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Important Safety Information

CONTRAINDICATION: HYPERSENSITIVITY

EPIDIOLEX (cannabidiol) oral solution is contraindicated in patients with a history of hypersensitivity to cannabidiol or any ingredients in the product.

WARNINGS & PRECAUTIONS

Hepatocellular Injury:
EPIDIOLEX can cause dose-related transaminase elevations. Concomitant use of valproate and elevated transaminase levels at baseline increase this risk. Transaminase and bilirubin levels should be obtained prior to starting treatment, at one, three, and six months after initiation of treatment, and periodically thereafter, or as clinically indicated. Resolution of transaminase elevations occurred with discontinuation of EPIDIOLEX, reduction of EPIDIOLEX and/or concomitant valproate, or without dose reduction. For patients with elevated transaminase levels, consider dose reduction or discontinuation of EPIDIOLEX or concomitant medications known to affect the liver (e.g., valproate or clobazam). Dose adjustment and slower dose titration is recommended in patients with moderate or severe hepatic impairment. Consider not initiating EPIDIOLEX in patients with evidence of significant liver injury.

Somnolence and Sedation:
EPIDIOLEX can cause somnolence and sedation that generally occurs early in treatment and may diminish over time; these effects occur more commonly in patients using clobazam and may be potentiated by other CNS depressants.

Suicidal Behavior and Ideation:
Antiepileptic drugs (AEDs), including EPIDIOLEX, increase the risk of suicidal thoughts or behavior. Inform patients, caregivers, and families of the risk and advise to monitor and report any signs of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior. If these symptoms occur, consider if they are related to the AED or the underlying illness.

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Important Safety Information and Indications

WARNINGS & PRECAUTIONS (cont'd)

Withdrawal of Antiepileptic Drugs:

As with most AEDs, EPIDIOLEX should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus.

ADVERSE REACTIONS:

The most common adverse reactions in patients receiving EPIDIOLEX (≥10% and greater than placebo) include transaminase elevations; somnolence; decreased appetite; diarrhea; pyrexia; vomiting; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; and infections. Hematologic abnormalities were also observed.

PREGNANCY:

EPIDIOLEX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Encourage women who are taking EPIDIOLEX during pregnancy to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry.

DRUG INTERACTIONS:

Strong inducers of CYP3A4 and CYP2C19 may affect EPIDIOLEX exposure. EPIDIOLEX may affect exposure to CYP2C19 substrates (e.g., clobazam, diazepam, stiripentol) or others. Concomitant use of EPIDIOLEX and valproate increases the incidence of liver enzyme elevations. No drug interaction studies have been completed, but case reports suggest a potential for elevations of mammalian target of rapamycin (mTOR) or calcineurin inhibitors when used with EPIDIOLEX. Dosage adjustment of EPIDIOLEX or other concomitant medications may be necessary.

INDICATIONS:

EPIDIOLEX® (cannabidiol) oral solution is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

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Summary

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Summary[1]

- A retrospective claims analysis measured healthcare resource utilization and costs for patients on EPIDIOLEX using the IQVIA PharMetrics® Plus database
- After starting EPIDIOLEX, patients had statistically significant fewer hospital admissions, ER visits, and shorter length of stays at 12 months
- Patients with higher EPIDIOLEX adherence had statistically significant fewer inpatient admissions and LOS vs those with lower adherence at 12 months
- After starting EPIDIOLEX, patients experienced a statistically significant decrease in fills for concomitant AEDs at 12 months
- Similar trends were also seen in the preliminary 6-month follow-up analysis, which found nonsignificant numerical decreases in inpatient and ER admissions as well as shorter LOS, with an 11.4%, 10.7%, and 15% decline in utilization and LOS, respectively
- Healthcare spend for EPIDIOLEX patients is offset by decreased HCRU
- A subgroup analysis was performed to ensure that results were not confounded by HCRU reductions due to the COVID-19 pandemic
- Because HCRU trends were also seen in the preliminary 6-month follow-up analysis, further research on EPIDIOLEX with longer follow-up periods may be beneficial in painting a true picture of its impact on HCRU and costs

Real-world data show the positive impact of EPIDIOLEX on HCRU and costs.

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Polling Questions

How often do you use these types of data when making formulary and UM criteria decisions?

- Always
- Often
- Seldom
- Never

What other types of HEOR data regarding EPIDIOLEX would be meaningful to have for your decision making? (Please select all that apply.)

- Quality of life
- Patient-reported outcomes
- Adherence
- Hospital readmissions
- Caregiver burden
- Other (please specify)

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Questions and Discussion

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