



Fenfluramine Treatment in Adults With Developmental and Epileptic Encephalopathies: a Systematic Narrative Review

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Introduction and Objective

- Fenfluramine, approved as add-on therapy in the EU and UK for management of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients ≥ 2 years old,¹ targets serotonin release and signalling at multiple serotonin receptors and modulates sigma-1 receptor signalling²
- Efficacy of fenfluramine, both in seizures and global functioning, as well as its safety and tolerability have been demonstrated in phase 3 studies of paediatric and adult patients with DS,³⁻⁶ LGS,^{7,8} and cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder⁹
 - Real-world evidence is needed to confirm results from clinical studies
- Much of the published literature describing management of developmental and epileptic encephalopathies (DEEs) is focused on the paediatric population, with data in adult patients remaining limited
 - Treatment consensus for DEE management in adult patients is needed

Here we review and summarize currently published data describing fenfluramine use in adult patients with DEEs

Study Design and Endpoints

Databases

- BIOSIS Previews®, Embase®, MEDLINE®, Northern Light Life Sciences Conference Abstracts
- Manual search of AES congress abstracts

Search terms

- Fenfluramine/FFA/Fintepla + adult + DEEs/Developmental and epileptic encephalopathy *OR* Dravet or Lennox-Gastaut *OR* CDKL5 deficiency/CDKL5 disorder

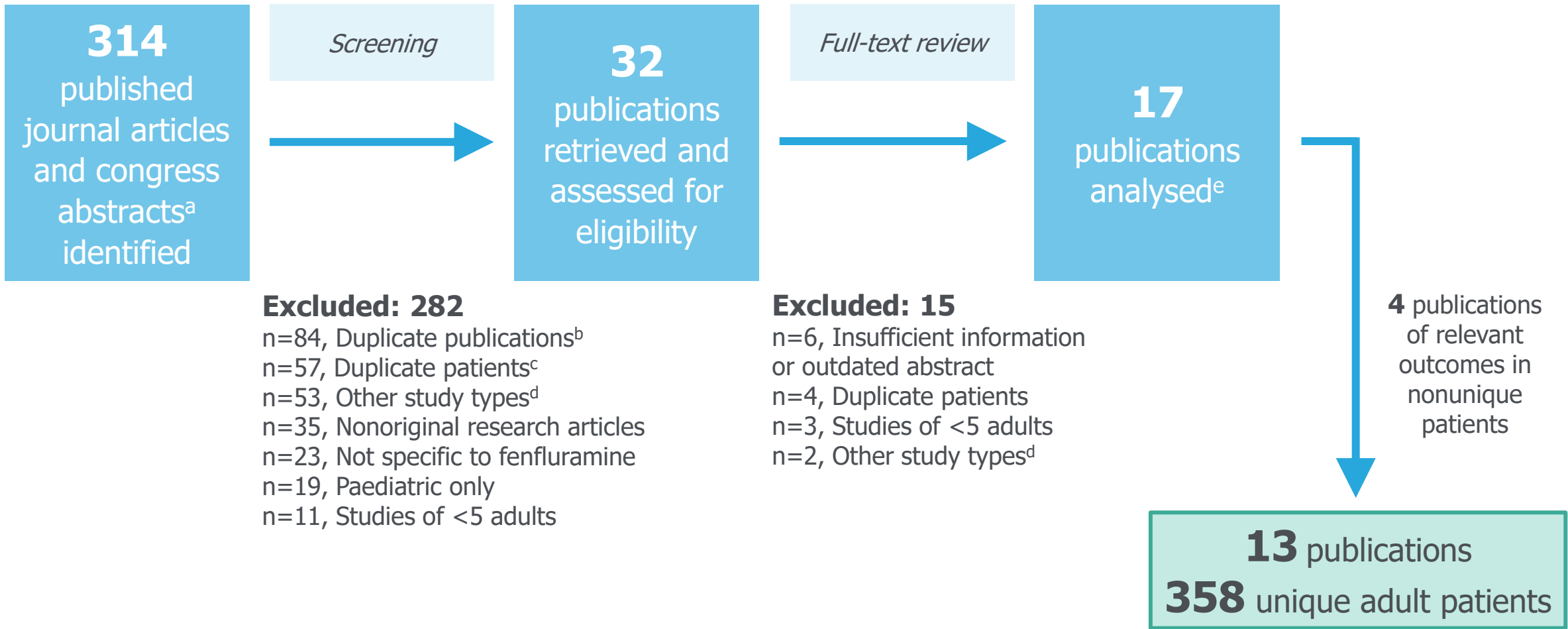
Selection criteria

- English-language publications
- Original research journal articles and congress abstracts
- Published before 10 July 2026
- Outcomes described in ≥ 5 adult patients
- Adult-only data available
- Unique patients, not described in prior publications^a

- No formal statistical evaluation was performed

^aStudies of nonunique (or duplicate) patients were included if unique outcomes were described; in that case, the publication with the most comprehensive baseline information was used for reporting demographics. AES, American Epilepsy Society; CDKL5, cyclin-dependent kinase-like 5; DEE, developmental and epileptic encephalopathies; FFA, fenfluramine.

Search Results and Overview of Study Selection



^aOf these, 30 were abstracts from a manual search of the American Epilepsy Society database. ^bAs in the case of encore presentations. ^cIncludes data from patients in post hoc analyses and/or interim open-label extension studies. ^dIncludes preclinical, pharmacokinetic, health economic outcome reporting, or pharmacovigilance studies, etc. ^eFull list of publications analysed is in [Appendix](#).

Unique Adult Patients: Publication Characteristics

Characteristic	13 publications ^a
Publication type, n (%)	
Congress abstract ^b	6 (46)
Journal articles	7 (54)
Type of study, n (%)	
Real-world	10 (77)
Early-access programme	2 (15)
Open-label extension	1 (8)
Study region, n (%)	
Europe/United Kingdom ^c	9 (69)
United States	2 (15)
Japan	1 (8)
International	1 (8)
“Adult” definition, n (%)	
≥18 years	8 (62)
≥16 years	2 (15)
Not defined	3 (23)

^aPublications containing unique patients are available in [Appendix](#). ^bWith or without accompanying presentation. ^cStudies could have been single centre or multicentre.

Unique Adult Patients: Baseline Characteristics

174/358 (49%)
patients with **DS**

166/358 (46%)
patients with **LGS**

10/358 (3%)
patients with **DS or LGS**
(not specified)

8/358 (2%)
patients with **"other DEE"**
(not specified)

- Study disposition was reported for 292 patients; 255 (87%) patients completed the studies
- Baseline demographic characteristics were reported for 278 patients

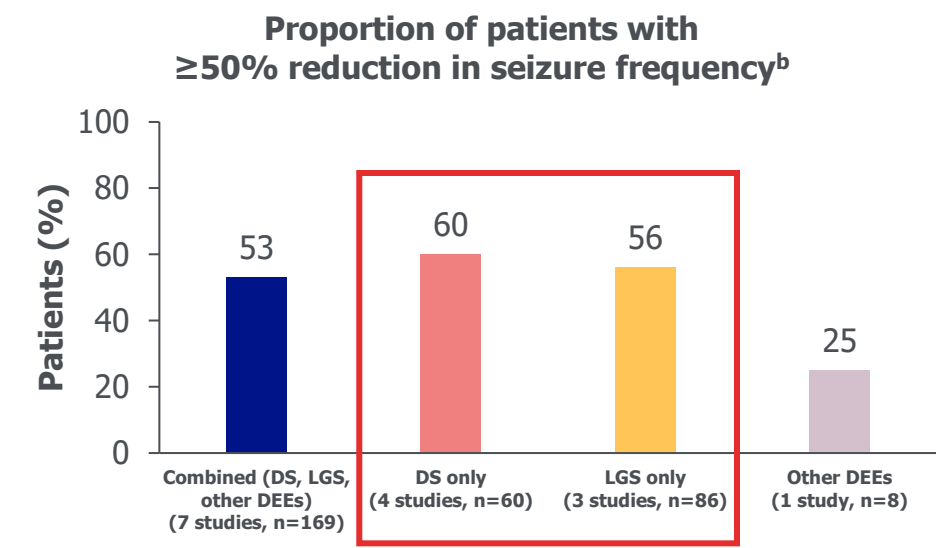
Characteristic	n=278
Sex, n (%)	
Male	142 (51.1)
Female	136 (48.9)
Age, years	
Range of medians reported (n=246)	21-31
Min-max reported (n=206) ^a	17-49
Mean reported (n=26) ^b	22.5, 33

- Mean, median, or range of 0-17 prior ASMs^c in 198 patients
- Mean, median, or range of 4-9 concomitant ASMs^c in 233 patients
- Mean, median or range fenfluramine doses: 0.06-0.64 mg/kg/day^d in 280 patients

^aOne study reported only min and max, no mean or median provided. ^bThree additional studies reported both mean and median; the 2 included here *only* reported mean. ^cPrior ASMs generally considered to be ASMs patients received and discontinued prior to initiating fenfluramine and concomitant ASMs were those patients received while also receiving fenfluramine, but not all publications provided the definitions used in the study. ^dMaximum dose of 0.7 mg/kg/day (26 mg/day) without stiripentol or 0.4 mg/kg/day (17 mg/day) with concomitant stiripentol.
ASM, antiseizure medication; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Effectiveness: Seizure Reduction

- Quantifiable changes in seizure frequency were reported in 11 studies for 272 patients^a: 102 (38%) with DS, 162 (60%) with LGS, and 8 (3%) with other DEE
 - Follow-up periods ranged from 3 to 60 months or duration of the study
 - GTCS reduction among 6 patients with DS or LGS ranged from 50% to 100% (2 studies)
- One additional study described “stable seizure frequency” and “decreased duration of seizures” among 6/10 patients with DS or LGS

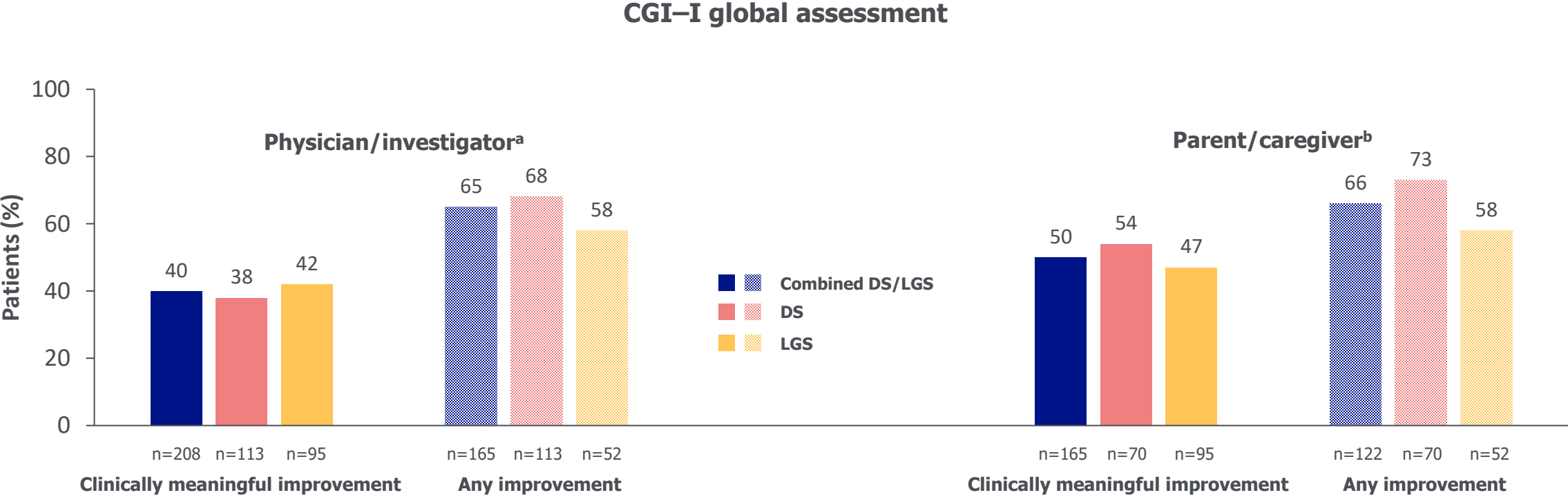


Seizure reduction reported	Study details	Response
≥75% reduction	1 study (DS) n=22	50%
100% reduction (seizure freedom)	7 studies ^c n=139	15%

^aThis also included median percent reduction in seizures associated with a fall in 1 LGS study (n=70). ^bAmong the 7 studies, 3 were DS only; 2 were LGS only; and 2 reported data in patients with DS, LGS, and/or other DEEs. In 1 of those (n=15 patients), 50% response was provided but not discernible by specific DEE (DS or LGS). Those results are included in the “combined” data, but not individual DEE results. ^cAmong the 7 studies reporting seizure freedom, 4 were DS only; 1 was LGS only; and 2 reported data in patients with DS, LGS, and/or other DEEs.
DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; GTCS, generalised tonic-clonic seizure; LGS, Lennox-Gastaut syndrome.

Effectiveness: Global Functioning

- Physician-reported Clinical Global Impression–Improvement (CGI–I) assessments to describe clinically meaningful improvement were available in 208 adult patients; of these, ratings by caregiver were reported in 165 patients



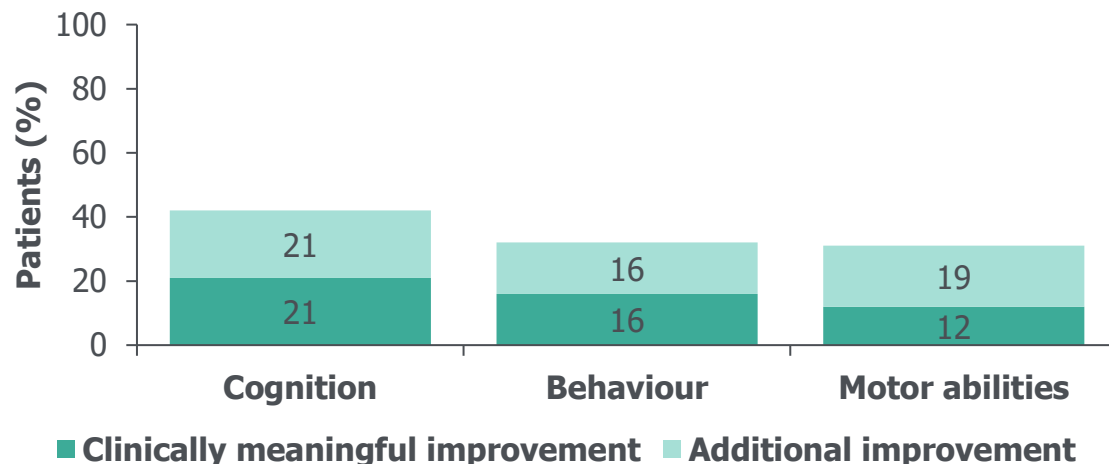
^aClinically meaningful improvement scores by physician/investigator were provided in 4 studies (n=208; 2 DS, 1 LGS, 1 DS/LGS), but scores of any improvement were provided in 3 studies (n=165; 2 DS, 1 DS/LGS).
^bClinically meaningful improvement scores by parent/caregiver were provided in 2 studies (n=165; 1 LGS, 1 DS/LGS), but scores of any improvement was provided in 1 study (n=122; 1 DS/LGS).
CGI–I, Clinical Global Impression–Improvement; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Effectiveness: Other Outcomes

Assessments in subdomains of cognition, behaviour, and motor abilities in DS or LGS

- Reported by physician/investigator in 141 adult patients with DS or LGS
 - Other clinical benefits: improved communication, interaction, verbal expression, alertness, attention, and concentration

Improvement in subdomains by physician/investigator^a



Assessment of executive function (BRIEF®)

- In a post hoc analysis describing adults with LGS:
 - Caregivers reported clinically meaningful improvements in everyday executive function (on BRIEF®-A indexes and composite) at Month 12 of an OLE in 26%-47% of adult patients with LGS (n=41)

Assessment of changes in treatment regimen in adults with DS

- In an update of the European Early Access Programme, adjustments to concomitant ASMs were reported in 47 of 77 adults with DS
 - In 29 adults (62%), doses of concomitant ASMs were reduced
 - In 18 adults (38%), a concomitant ASM was withdrawn; stiripentol, topiramate, and potassium bromide were the most common

^aTwo studies (1 DS, 1 DS/LGS, n=141).

ASM, antiseizure medication; BRIEF®-A, Behavior Rating Inventory of Executive Function®-Adult; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; OLE, open-label extension.

Safety Summary

- Safety data were reported in 337 patients from 11 studies
 - Specific TEAEs were reported in 312 patients from 8 studies
 - The proportion of patients with reports of any TEAE was described in 7 studies (n=290); 182 (63%) reported ≥1 TEAE

TEAEs Reported in ≥3% of Patients, n (%)	n=312
Coronavirus	35 (11)
Somnolence	28 (9)
Decreased appetite	24 (8)
Seizure	19 (6)
Pyrexia	15 (5)
Weight loss	13 (4)
Nasopharyngitis	12 (4)
Agitation	9 (3)

- Overall, no VHD or PAH were reported among the 337 patients in 11 studies

Conclusions

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- In this systematic narrative literature search, 358 unique adult patients with DEEs who had received ≥ 1 dose of fenfluramine were identified from 13 studies
- Among 169 adult patients with DEEs, 53% achieved $\geq 50\%$ reduction in seizures, with similar proportion across DS and LGS
- Benefits in other relevant DEE symptoms were reported, although some were difficult to quantify, including improved communication, alertness, and mobility
- No new safety signals were described in the analysed adult population
- Published evidence supports that fenfluramine may provide clinically relevant seizure, behaviour, and cognition benefits in adults with DEEs, with a well-established safety and tolerability profile
- Additional adult-specific evidence and a more unified approach to outcome reporting are needed to support treatment consensus and clarify the full impact of therapy in this subpopulation of adults with DEE

Appendix

Appendix: Overview of Data Availability (N=17)

Short Citation	Disposition	Basic demographics	Fenfluramine dosing	Effectiveness (seizure reduction)	Effectiveness (global functioning)	Safety
Breuillard – AES 2025	NA	NA	NA	NA	NA	NA
Ceulemans 2016 Epilepsia	✓	✓	✓	✓		✓
Clayton 2024 Epilepsia (EEC)	✓	✓		✓		✓
Dolezalova 2026 Eur J Neurol (EAN)	✓			✓		✓
Gil-Nagel 2026 Epilepsia	✓	✓	✓		✓	✓
Guerrini 2022 Epilepsia	✓	✓	✓	✓	✓	✓
Jakobsen 2025 Eur J Paediatr Neurol (EPNS)		✓	✓	✓		✓
Knupp 2025 Epilepsy Behav	NA	NA	NA	✓	NA	NA
Kumar – AES 2023	✓					
Lattanzi 2026 CNS Drugs	✓	✓	✓	✓	✓	✓
Massaroni 2026 Epilepsy Behav	✓	✓		✓		
Perry – AES 2020	✓	✓			✓	✓
Pringsheim – AES 2024	NA	NA	NA	NA	NA	NA
Samarasekera – AES 2025		✓				✓
Sanchez-Carpintero – AES 2023	NA	NA	NA	✓	NA	NA
Takeda 2025 CUREUS	✓	✓	✓	✓		✓
Villanueva 2026 Epilepsia			✓	✓		✓
TOTAL	10 studies	10 studies	7 studies	11 studies	4 studies	11 studies

NA, not applicable; only relevant outcomes are described for the 4 studies with non-unique patients.

AES, American Epilepsy Society; EAN, European Academy of Neurology; EEC, European Epilepsy Congress; EPNS, European Paediatric Neurology Society.

Appendix: Full Citations for Publications Included in Analysis

1. Breuillard D, Knupp K, Strzelczyk A, et al. Association of fenfluramine treatment and everyday executive functioning in adult patients with Lennox-Gastaut syndrome [abstract]. Presented at American Epilepsy Society Annual Meeting, December 5-9, 2025, Atlanta, GA, USA.
2. Ceulemans B, Schoonjans AS, Marchau F, Paelinck BP, Lagae L. Five-year extended follow-up status of 10 patients with Dravet syndrome treated with fenfluramine. *Epilepsia*. 2016;57(7):e129-e134.
3. Clayton LM, Grundmann A, Nashef L, et al. Fenfluramine treatment in adults with Dravet syndrome: experience so far from four UK centres [abstract]. Presented at European Epilepsy Congress (EEC), September 7-11, 2024, Rome, Italy. *Epilepsia* 2025;65(suppl1):1-508.
4. Dolezalova I, Strycek O, Kocvarova J, Pail M, Brazdil M. Real-world effectiveness and safety of fenfluramine in adults with Dravet syndrome and Lennox-Gastaut syndrome: a retrospective single-centre study [abstract]. Presented at European Academy of Neurology (EAN), 27-30 June 2026, Geneva, Switzerland. *Eur J Neurol*. 2026;33(suppl 1):1-1039.
5. Gil-Nagel A, Knupp KG, Gunning B, et al. Prolonged fenfluramine use in open-label studies of Dravet or Lennox-Gastaut syndromes: long-term safety, tolerability, patient global functioning, and considerations for interpreting effectiveness. *Epilepsia*. 2026;doi:10.1002/epi.70371. [Epub ahead of print].
6. Guerrini R, Specchio N, Aledo-Serrano Á, et al. An examination of the efficacy and safety of fenfluramine in adults, children, and adolescents with Dravet syndrome in a real-world practice setting: a report from the fenfluramine European Early Access Program. *Epilepsia Open*. 2022;7(4):578-587.
7. Jakobsen A, Gjerulfsen CE, Nikanorova M, et al. Prospective evaluation of non-seizure benefits of treatment with fenfluramine in pediatric and adult patients with Dravet syndrome [abstract]. Presented at European Paediatric Neurology Society, July 8-12, 2025, Munich, Germany.
8. Knupp KG, Scheffer IE, Schoonjans AS, et al. Final analysis from an open-label extension study of fenfluramine for the treatment of seizures in Lennox-Gastaut syndrome: Long-term impact on patients and caregivers. *Epilepsy Behav*. 2025;173:110753.
9. Kumar V, Amin U, Rivera-Cruz A, et al. Single-center use of fenfluramine [abstract]. Presented at American Epilepsy Society Annual Meeting, December 1-5, 2023, Orlando, FL.
10. Lattanzi S, Di Gennaro G, Bisulli F, et al. Adjunctive fenfluramine in adults with Lennox-Gastaut syndrome: effectiveness and tolerability in real-world clinical practice. *CNS Drugs*. 2026;40:1307-1322. doi:10.1007/s40263-026-01307-7.
11. Massaroni V, Ascione F, Porto C, et al. Beyond seizure control: functional and caregiver-reported outcomes of long-term fenfluramine treatment in Dravet syndrome. *Epilepsy Behav*. 2026;180:111059.
12. Perry MS, Knupp KG, Wirrell E, et al. Fenfluramine (FINTEPLA) provides comparable clinical benefit in adults and children with Dravet syndrome: real-world experience from the US Early Access Program [abstract]. Presented at American Epilepsy Society Annual Meeting, December 4-8, 2020, Virtual.
13. Pringsheim M, Aledo-Serrano A, Darra F, et al. Antiseizure medication regimen adjustment after fenfluramine initiation: lessons learned from European early access program in pediatric and adult patients with Dravet syndrome [abstract]. Presented at American Epilepsy Society (AES) Annual Meeting, December 6-10, 2024, Los Angeles, CA, USA.
14. Samarasekera S. Fenfluramine for adults with Lennox-Gastaut syndrome – what is the impact? [abstract]. Presented at American Epilepsy Society Annual Meeting, December 5-9, 2025, Atlanta, GA, USA.
15. Sanchez -Carpintero R, Devinsky O, Gil-Nagel A, et al. Descriptive analysis of fenfluramine use in adult patients with Dravet syndrome enrolled in an open-label extension study [abstract]. Presented at American Epilepsy Society Annual Meeting, December 1-5, 2023, Orlando, FL, USA.
16. Takeda M, Kitazawa Y, Sonoda M, et al. Efficacy of Low-Dose Fenfluramine on Adult Patients With Lennox-Gastaut Syndrome. *Cureus*. 2025;17(7):e87250. doi:10.7759/cureus.87250.
17. Villanueva V, González-Alguacil E, Smeyers P, et al. Effectiveness and tolerability of fenfluramine in pediatric and adult patients with developmental and epileptic encephalopathies: a multicenter, retrospective, real-world clinical-practice study. *Epilepsia*. 2026; doi:10.1002/epi.70342. [Epub ahead of print].