MEDISON

We are **Always Ahead** | We **Grow as One** | We **Care**

יוני 2025

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

הריני להודיעכם על עדכון העלון – החמרה -של התכשיר:

FINTEPLA **פינטפלה**

ORAL SOLUTION

מרכיב פעיל : **Fenfluramine 2.2 mg /ml**

להלן העדכונים בעלון לרופא :

המינונים המומלצים אוחדו בטבלה אחת עבור 2 ההתוויות הרשומות

4.2 Posology and method of administration

Table 1: Dosage recommendations for Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS)

	Without concomitant stiripentol*		**With concomitant** stiripentol (DS patients only)	
	Weight based dosage⁺⁺	**Maximal recommended daily dose**	**Weight based dosage⁺⁺**	**Maximal recommended daily dose**
Day 0 (Starting dose)⁺	0.1 mg/kg taken twice daily	26 mg (13 mg twice daily i.e. 6.0 ml twice daily)	0.1 mg/kg taken twice daily	17 mg (8.6 mg twice daily i.e. 4.0 ml twice daily)
Day 7	0.2 mg/kg twice daily		Maintenance dose 0.2 mg/kg twice daily	
Day 14**	0.35 mg/kg twice daily		Not applicable	

*For patients not on concomitant stiripentol requiring more rapid titration, the dose may be increased every 4 days.
⁺For patients with Dravet syndrome, dosage may be increased based on clinical response to the maximum recommended dose, as needed.
**For patients with Lennox-Gastaut syndrome, dosage should be increased as tolerated to the recommended maintenance dose (i.e., Day 14)

⁺⁺To calculate the dose volume up to the maximal recommended dose, you must use the formula:

Weight (kg) x Weight-based dosage (mg/kg) ÷ 2.2 mg/ml = ml dose to be taken **twice daily**

The calculated dose should be rounded to the nearest graduated increment.

If the calculated dose is 3.0 ml or less, the green printed 3 ml syringe should be used.
If the calculated dose is more than 3.0 ml, the purple printed 6 ml syringe should be used.

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עדכונים המהווים החמרות - (מסומנים בצהוב):

אוחדו תופעות הלוואי ללא הפרדה בין ההתוויות , עודכנו שכיחויות של תופעות לוואי שכבר דווחו ונוספו תופעות לוואי

4.4 Special warnings and precautions for use

Aortic or mitral valvular heart disease and pulmonary arterial hypertension

Because of reported cases of valvular heart disease and pulmonary arterial hypertension that may have been caused by fenfluramine at higher doses used to treat adult obesity, cardiac monitoring must be performed using echocardiography. Patients with valvular heart disease or pulmonary arterial hypertension were excluded from the controlled clinical studies of fenfluramine for the treatment of Dravet syndrome and Lennox-Gastaut syndrome.

Neither pulmonary arterial hypertension nor valvular heart disease were observed during these studies. However, post-marketing data show that they can also occur with doses used to treat Dravet syndrome and Lennox-Gastaut syndrome (see section 4.8).

Serotonin syndrome

…If serotonin syndrome is suspected, a dose reduction or discontinuation of the therapy with Fintepla and/or other serotonergic agents should be considered.

4.8 Undesirable effects

Summary of the safety profile

A total of 414 patients have been treated with fenfluramine in double blind randomized-placebo controlled studies for Dravet syndrome and Lennox-Gastaut syndrome, the most commonly reported adverse reactions are decreased appetite (31.9%), fatigue (17.6%), diarrhoea (16.7%), and somnolence (15%).

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Table 3: Adverse reactions ~~for Dravet Syndrome~~

MedDRA System Organ Class	Very common	Common	Not known
Infections and infestations	~~Upper respiratory infection~~	Bronchitis	
Metabolism and nutrition disorders	Decreased appetite		
Psychiatric disorders		Abnormal behaviour Aggression Agitation Insomnia Mood swings	Irritability

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Nervous system disorders	Somnolence	Ataxia Hypotonia Lethargy Seizure Status epilepticus Tremor	Serotonin syndrome
Cardiac disorders			Valvular heart disease
Respiratory, thoracic and mediastinal disorders			Pulmonary arterial hypertension
Gastrointestinal disorders	Diarrhoea	Constipation Salivary Hypersecretion Vomiting	
Skin and subcutaneous tissue disorders		Rash	
General disorders and administration site conditions	~~Pyrexia~~ Fatigue		
Investigations	~~Blood glucose decreased~~ ~~Echocardiogram abnormal*(trace regurgitation)~~	Weight decreased Blood glucose decreased Blood prolactin increased	

** Consisted of trace and mild mitral regurgitation, and trace aortic regurgitation, which are considered*

Table 4- Adverse reactions for Lennox-Gastaut syndrome -**erased**

Description of selected adverse reactions

Decreased appetite and weight loss

Fenfluramine can cause decreased appetite and weight loss. In the controlled trials of children and young adults with Dravet syndrome 34.7% of fenfluramine-treated patients had an adverse

reaction of decreased appetite, compared to 7.6% of patients on placebo, and approximately 7.4% of fenfluramine-treated patients had a decrease in weight, compared to 0.8% of patients on placebo. In the controlled clinical trials of children and adults with Lennox-Gastaut syndrome, 28.8% of fenfluramine-treated patients had an adverse reaction of decreased appetite, compared to 15.3% of patients on placebo, and approximately 8.1% of fenfluramine-treated patients had a decrease in weight, compared to 3.1% of patients on placebo. The decreases in appetite and weight appeared to be dose related. Most subjects resumed weight gain over time while continuing fenfluramine treatment

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Status epilepticus and seizures (Epilepsy, Seizure cluster, Change in seizure)

…. In the controlled trials in patients with Dravet syndrome, adverse reactions of seizures were reported less frequently in fenfluramine-treated patients (6.9%)

than in patients on placebo (10.6%). However, seizures assessed as related to the study drug were more commonly reported in fenfluramine treated patients than placebo, 3.7% of fenfluramine-treated patients compared to 1.5% of patients on placebo. In the LGS trial, seizures were reported with a similar frequency in the fenfluramine treated patients (9.1%) and patients on placebo (9.2%). However, seizures assessed as related to the study drug were more commonly reported in fenfluramine treated patients than placebo, 6.1% of fenfluramine-treated patients compared to 1.0% of patients on placebo.

Echocardiographic safety assessments

Valvular heart disease and pulmonary arterial hypertension were evaluated via echocardiography in the clinical studies for Dravet syndrome and Lennox-Gastaut syndrome. No patient developed valvular heart disease or pulmonary arterial hypertension in the completed clinical studies for both indications. The percentage of trace and mild mitral regurgitation and trace aortic regurgitation from pooled double blinded DS and LGS clinical studies are shown below. These are defined as non-pathologic findings by the ESC/EACTS guidelines. Where trace mitral or aortic regurgitation were observed, the results were often transient.

- Trace of mitral regurgitation:
  - Combined fenfluramine group: 18.6% (77/414)
  - Placebo: 13.9% (32/230)
- Mild mitral regurgitation:
  - Combined fenfluramine group: 0.7% (3/414)
  - Placebo: 0% (0/230)
- Trace aortic regurgitation:
  - Combined fenfluramine group: 2.4% (10/414)
  - Placebo: 0.9% (2/230)

Pulmonary arterial hypertension in a child associated with fenfluramine for Dravet syndrome has been reported post-marketing. The patient discontinued fenfluramine and the reaction resolved post-discontinuation. Valvular heart disease in a child associated with fenfluramine for Dravet syndrome has also been reported post-marketing (see section 4.4).

Lethargy, somnolence, and fatigue (grouping of fatigue/asthenia/malaise/decreased activity)

In the controlled trials in subjects with Dravet syndrome, lethargy was commonly reported in 9.7%, and somnolence and fatigue were very commonly reported in 13.9% and 19%, respectively in the fenfluramine treatment groups combined. In the controlled study with Lennox-Gastaut syndrome, lethargy was commonly reported in 4.5% of subjects in the fenfluramine treatment group. Fatigue and somnolence were very commonly reported in 16.2% and 16.2% of subjects, respectively. The majority of the adverse reactions of lethargy, somnolence, and fatigue/asthenia were reported in the first 2 weeks of treatment with fenfluramine and were mild or moderate in severity. Discontinuation due to lethargy, somnolence, and fatigue/asthenia was rare and, in most cases, these adverse events resolved or

improved with ongoing treatment. In the controlled trials with Dravet syndrome, 0.5% and 1.4% of subjects in the fenfluramine treatment groups combined discontinued due to lethargy and somnolence, respectively. In the LGS study 4, 1.5% of subjects in the fenfluramine treatment group discontinued due to somnolence.

Infections and infestations disorders -removed

להלן העדכונים בעלון לצרכן המהווים החמרות (מסומנים בצהוב):

תופעות לוואי נוספות:

~~**תסמונת דרווה**~~

תופעות לוואי שכיחות מאוד (תופעות המופיעות ביותר ממטופל אחד ב-10)

- ~~זיהום בדרכי הנשימה~~
- ירידה תיאבון
- ~~ישנוניות~~ נמנום ...
- שלשולים
- ~~חום~~
- תחושת עייפות, ישנוניות או חולשה
-
- ~~ירידה ברמות סוכר בדם~~
- ~~אקו לב חריג~~

תופעות לוואי שכיחות (תופעות המופיעות במטופל אחד ב-10)

- ...
- הפרשת רוק מוגברת
- הקאות
- פריחה
- ירידה ברמות הסוכר
- רמת פרולקטין מוגברת

תופעות לוואי בשכיחות לא ידועה (שכיחות לא ניתנת להערכה מהנתונים הזמינים)

- **נרגנות**
- **תסמונת סרוטונין**
- **יתר לחץ דם עורקי ריאתי (PAH)**
- **מחלת מסתמי לב**

תסמונת לנוקס-גסטו- בוטל הסעיף

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העלון לרופא והעלון לצרכן נמצאים בקישור, וכן מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בברכה,

מדיסון פארמה בע"מ

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