This guide is intended to ensure that healthcare professionals who prescribe and bring fenfluramine into use are aware of and take into account the special safety requirements (as an additional risk minimizing measure

Fintepla®▼(fenfluramine) 2.2 mg/ml oral solution

GUIDE ON REDUCING THE RISKS RELATED TO MEDICINES AND THEIR ADMINISTRATION – PRESCRIBERS

▼ This medicine is subject to additional monitoring. This allows for the rapid identification of new safety findings. Healthcare professionals are asked to report any suspected adverse reactions. See the last page for information on reporting adverse events.

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA

VALVULAR HEART DISEASE AND PULMONARY ARTERIAL HYPERTENSION

Fenfluramine is indicated for the treatment of seizures associated with Dravet syndrome or Lennox-Gastaut syndrome as an add-on therapy to other antiepileptic medicines for patients 2 years of age and older.[1]

Fenfluramine hydrochloride was first approved in Europe in the **1960s** at a dose of 60-120mg per day as an appetite suppressant for the treatment of obesity in adults. Fenfluramine hydrochloride was also often used in combination with phentermine in this indication. In the late 1990s, it was **withdrawn worldwide** because of the **risks of valvular heart disease and pulmonary arterial hypertension**, which in some cases were severe or **fatal**[2-9] at doses 2-4 times higher than the maximum recommended dose approved for seizures associated with Dravet syndrome or Lennox-Gastaut syndrome (26mg fenfluramine without concomitant stiripentol).
The exact mechanism of drug-induced valvular heart disease and pulmonary arterial hypertension remains unclear.
Because of the important risks of valvular heart disease and pulmonary arterial hypertension, a **controlled access program** has been implemented for fenfluramine in the indication for Dravet syndrome and Lennox-Gastaut syndrome. This program is designed to ensure that the currently approved indication is strictly adhered to and that physicians are adequately informed before prescribing.

CONTROLLED ACCESS PROGRAMME (CAP)

A controlled access program has been created to

- prevent off-label use in weight management and
- Confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla®

Fintepla® should be initiated and supervised by physicians with experience in the treatment of epilepsy.

OFF-LABEL USE FOR WEIGHT CONTROL

Fenfluramine can cause decreased appetite and weight loss (see sections 4.4 and 4.8 of the SmPC).
Fenfluramine should **not be** prescribed or **used for weight management** as the **benefit-risk of such use** is **negative** in that indication. The indication stated in the SmPC must be strictly adhered to.
If you suspect that fenfluramine might be used to control the weight of other people, remind the patient or their parents/caregivers that fenfluramine should only be taken by the person for whom it was prescribed and not by anyone else.

Please also inform parents/caregivers about the negative benefit-risk use of fenfluramine in weight management.

CARDIAC MONITORING

Given the important risks of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH), periodic echocardiography must be performed when treating patients with Dravet syndrome or Lennox-Gastaut syndrome. There were no cases of VHD or PAH reported in patients in the clinical trials for the treatment of Dravet syndrome or Lennox-Gastaut syndrome, but post-marketing data show that VHD and PAH can also occur with doses used to treat Dravet syndrome or Lennox-Gastaut syndrome (see section 4.8 of the SmPC).

Prior to starting treatment, all patients must undergo an echocardiogram to exclude any pre-existing valvular heart disease or pulmonary arterial hypertension.

Echocardiogram monitoring must be conducted every 6 months for the first 2 years and annually thereafter during fenfluramine treatment.

Once treatment is discontinued for any reasons, a final echocardiogram should be conducted 3-6 months after the last dose of treatment with fenfluramine.

- If an echocardiogram indicates pathological valvular changes, a follow-up echocardiogram should be considered at an earlier timeframe to evaluate whether the abnormality is persistent. If pathological abnormalities on the echocardiogram are observed, it is recommended to evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver, and cardiologist.
- If echocardiogram findings are suggestive of pulmonary arterial hypertension, a repeat echocardiogram should be performed as soon as possible and within 3 months to confirm these findings. If pathological abnormalities on theechocardiogram are observed or the echocardiogram finding suggests an increased probability of pulmonary arterial hypertension, it is recommended to evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver, and cardiologist.
- Treatment should be stopped and/or appropriate monitoring and follow-up should be provided in accordance with in accordance with Appendix 1 (SmPC) or local guidelines for the treatment of valvular heart disease and latest guidelines of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

EDUCATIONAL MATERIAL FOR YOUR PATIENTS

- Please discuss the enclosed guide on the important information about Fintepla® for patients and caregivers so they understand the risks associated with fenfluramine, including the need for echocardiography assessments before, during, and after treatment. Please provide them with the following:
  - Important information about Fintepla® for Patients and Caregivers
  - The latest version of the Package Leaflet

REPORTING ADVERSE EVENTS

Post-authorization reporting of suspected adverse events is of great importance. It allows continuous monitoring of the benefit-risk balance of the medicine.
Healthcare professionals are requested to report any suspected case of adverse events to your national regulatory agency and safety@nbpharma.com.

The National Pharmacovigilance Centre (NPC- Saudi Food and Drug Authority (SFDA)):
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

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Appendix 1: Fintepla® Summary of Product Characteristics

Appendix 2: Important Information about Fintepla® for Patients and Caregivers

Appendix 3: Fintepla® Package Leaflet