This guide was approved by the Health Products Regulatory Authority (HPRA). It is intended to ensure that health professionals who prescribe fenfluramine are aware of the risks associated with this medicine and take into account the special monitoring requirements.

Fintepla® ▼ (fenfluramine)

PRESCRIBER GUIDE ON REDUCING THE RISKS RELATED TO FINTEPLA®

Please read the Summary of Product Characteristics (SmPC) on Fintepla® before prescribing this medicine.

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

See the last page for information on reporting suspected adverse reactions.

IE-N-FA-OT-2300001, Mar 2023

VALVULAR HEART DISEASE AND PULMONARY ARTERIAL HYPERTENSION

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

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 extensively used in an off-label 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 In the late 1990s, it was **withdrawn worldwide** because of the **risks of valvular heart disease and pulmonary arterial hypertension**, which in some cases were severe or **fatal**[1-8], at doses 2-4 times higher than the maximum daily dose approved for seizures associated with Dravet syndrome or Lennox-Gastaut syndrome (26 mg/day fenfluramine without concomitant stiripentol). The exact mechanism of drug-induced valvular heart disease remains unclear.

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

OFF-LABEL USE FOR WEIGHT MANAGEMENT

Fenfluramine can cause decreased appetite and weight loss (see sections 4.4 and 4.8 of the SmPC). An additive effect on decreased appetite can occur when fenfluramine is combined with other anti-epileptic medicines, for example stiripentol. The decrease in weight appears to be dose related. A benefit risk evaluation should be undertaken prior to commencing treatment with fenfluramine in patients with a history of anorexia nervosa or bulimia nervosa.

Fenfluramine should **not be** prescribed or used **for weight management**, as the **benefit-risk of such use** is **negative** in that indication. The currently approved indication must be strictly adhered to, therefore access is controlled to ensure physicians are informed of the risks before prescribing (please refer to section `Controlled Access Programme' below).

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

CONTROLLED ACCESS PROGRAMME

In Ireland, Fintepla® will only be made available to patients through a global access portal.

This access portal is being implemented to:

- prevent off-label use in weight management since the benefit-risk ratio in this population is known to be negative and
- confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla® due to the potential risk of valvular heart disease and pulmonary arterial hypertension.

Mandatory declarations and bona fide checks must be completed before prescribing fenfluramine for the first time. To obtain an individualised link to the dedicated portal, the prescriber must send an email to zogenix@durbinglobal.com. The prescriber must register and confirm his/her understanding of the prescribing requirements before this treatment can be prescribed.

CARDIAC MONITORING

Because of reported cases of valvular heart disease and pulmonary arterial hypertension (PAH) that may have been caused by fenfluramine at higher doses used to treat adult obesity, cardiac monitoring must be performed using echocardiography when treating patients with Dravet syndrome or Lennox-Gastaut syndrome. 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. There were no cases of valvular heart disease or PAH reported during these studies. However due to the low incidence of PAH, the clinical trial experience with fenfluramine is inadequate to determine if fenfluramine increases the risk of PAH in patients with Dravet syndrome or Lennox-Gastaut syndrome.

If an echocardiogram indicates pathological valvular changes or PAH or if treatment with fenfluramine is stopped because of pathological changes in the heart valves or PAH, appropriate monitoring and follow-up should be provided (Appendix 1 (SmPC)) in accordance with local guidelines (guidelines of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) from 2015).

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

Fenfluramine is contraindicated in patients with PAH or aortic or mitral valvular heart disease.

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

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RECOMMENDATIONS FOR AORTIC OR MITRAL VALVULAR HEART DISEASE

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 treatment is stopped because of aortic or mitral valvular heart disease, appropriate monitoring and follow-up should be provided in accordance with local guidelines for the treatment of aortic or mitral valvular heart disease.

RECOMMENDATIONS FOR PULMONARY ARTERIAL HYPERTENSION

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 the echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as "intermediate probability" by the 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines, it should lead to a benefit-risk evaluation of continuation of Fintepla® by the prescriber, carer, and cardiologist.

If the echocardiogram finding, after confirmation, suggests a high probability of pulmonary arterial hypertension, as defined by the 2015 ESC and ERS Guidelines, it is recommended fenfluramine treatment should be stopped.

EDUCATIONAL MATERIAL FOR YOUR PATIENTS

- Please discuss the enclosed guide on the `Important information about Fintepla® for Patients and Caregivers' so your patient/caregiver understands the risks associated with fenfluramine, including the need for echocardiography assessments before and during treatment.

  Please provide them with the following:

  - Important information about Fintepla® for Patients and Caregivers (Appendix 1)
  - The latest version of the Package Leaflet (**https://www.ema.europa.eu/en/medicines/human/EPAR/fintepla#product-information-section**)

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REPORTING ADVERSE EVENTS

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via HPRA Pharmacovigilance. Website **www.hpra.ie**

For further information, including reporting of suspected adverse drug reactions to the marketing authorisation holder, please contact UCB (Pharma) Ireland Ltd at **UCBCares.IE@ucb.com** or on +353 1 463 2371.

LITERATURE

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RELATED DOCUMENTS

Fintepla® Summary of Product Characteristics and Fintepla® Package Leaflet can be found at **https://www.ema.europa.eu/en/medicines/human/EPAR/fintepla#product-information-section**

Appendix 1: Important Information about Fintepla® for Patients and Caregivers

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