This guide was approved by the Health Products Regulatory Authority (HPRA). It is intended to ensure that health professionals who prescribe Fintepla®▼ (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.

Inspired by patients. Driven by science.

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.[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 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 In the late 1990s, it was **withdrawn worldwide** because of the **risks of valvular heart disease and pulmonary arterial hypertension,** which in some cases were severe or **fatal**[1-9] at doses 2-4 times higher than the maximum recommended 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 and pulmonary arterial hypertension remains unclear.

The risk of developing valvular heart problems seemed to be related to the dose and the length of time patients took the medicine.[10]

Because of the important risks of valvular heart disease and pulmonary arterial hypertension, a **controlled access programme** has been implemented for fenfluramine in the indication for Dravet syndrome and Lennox-Gastaut syndrome. This programme is designed to ensure that the currently approved indication is strictly adhered to and that physicians are adequately informed before prescribing.

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

IMPROPER 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.

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

CONTROLLED ACCESS PROGRAMME (CAP)

A controlled access programme 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.

This mandatory certification must be completed **before** you can prescribe fenfluramine for the first time.

Once you have completed this certification you will be provided a prescriber ID confirming that you can prescribe and your name will be added to the High Tech Hub through which you will be able to prescribe Fintepla.

To obtain a prescriber identification number (prescriber ID) there are a number of steps in this process.

- Please log onto the finteplacontrolledaccessprogramme.ie.
- As the prescriber you must register through this portal before you can prescribe Fintepla. By doing this you will confirm your understanding of the prescribing requirements before this treatment can be prescribed.
- Registration through the portal will take you no longer than 10 minutes.
- Once you have successfully registered you will then be validated by a member of the UCB medical team. This process will be completed within a 24-hour timeframe.
- Once completed you will receive your CAP ID from the medical team.
- At the same time the medical team will alert the PCRS to open your access to the High-Tech Hub.
- This further process should take no longer than a further 24 hours.
- Once completed the PCRS will make you aware via an e mail communication that your access has been opened to prescribe Fintepla via the High-Tech Hub.
- You can then prescribe Fintepla via the High-Tech Hub in the same way as per all prescriptions for High-Tech medicines.

EXCEPTIONAL CIRCUMSTANCES

For prescription and supply of Fintepla outside of the High-Tech Arrangement, please contact UCB at UCBCares.IE@ucb.com, or +353 1 463 2371.

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

CARDIAC MONITORING

Given the important risks of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH), periodic cardiac monitoring must be performed using echocardiography 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 establish a baseline prior to initiating treatment and 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 reason 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 the echocardiogram are observed or the echocardiogram findings suggest 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 local guidelines for the treatment of aortic or mitral valvular heart disease, and latest guidelines of of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) (Appendix 1 (SmPC)).

FENFLURAMINE REGISTRY

A registry has been set up to collect data on the long-term safety of fenfluramine in routine practice and on the important risks of VHD and PAH, thereby improving the safety of the medicine. Healthcare professionals are asked to encourage patients to participate in this registry. Participation in the registry is highly desirable, but is voluntary for patients. For further information, including details of how to enrol your patients, please contact Medical Information at UCBcares.IE@ucb.com.

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, during, and after treatment.

Please provide them with the following:

- Important information about Fintepla® for Patients and Caregivers (Appendix 2)
- The latest version of the Package Leaflet (Appendix 3)

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**

Adverse events should be reported. Reporting forms and information can be found at www.hpra.ie/homepage/about-us/report-an-issue. Adverse events should also be reported to UCB (Pharma) Ireland Ltd at ucbcares.ie@ucb.com or 1800 930075.

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#productinformation-section

Appendix 1: Important Information about Fintepla for Patients and Caregivers