This guide was prepared in coordination with the MHRA. As an additional risk minimising measure it is intended to ensure that health professionals who prescribe and bring Fintepla®▼(fenfluramine) into use are aware of and take into account the special safety requirements

Fintepla®▼(fenfluramine)

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

Please also note the Summary of Product Characteristics (SmPC) on Fintepla®.

▼ This medicine is subject to additional monitoring.
This allows for the quick 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.

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 In the late 1990s, it was **withdrawn worldwide** because of the **risks of valvular heart disease and pulmonary arterial hypertension,** which in some cases were severe or **fatal**[2-9] at doses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 risk of valvular heart disease and pulmonary arterial hypertension, a **controlled access programme** has been implemented for fenfluramine in the indication for Dravet syndrome or 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.

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®

The mandatory certification must be completed **before** you can prescribe fenfluramine for the first time. To obtain a prescriber identification number (prescriber **ID**), please see finteplacontrolledaccessprogramme.co.uk.

The prescriber ID must be noted on or provided with each prescription. Without this information, the pharmacist cannot give fenfluramine to the patient.

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

* Controlled access is a regulatory tool for minimising important risks with significant public health or individual patient impact for a product with clearly demonstrated benefits but which would not otherwise be available without a programme where patient access is contingent on fulfilling the Guideline on Good Pharmacovigilance Practices.

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.

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 risk 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 reason 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 for VHD, it is recommended to evaluate the benefit 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 echocardiogram 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 local guidelines for the treatment of aortic or mitral valvular heart disease, and latest guidelines 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 valvular heart disease 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 recommended to further the understanding of long-term safety of Fintepla® but is voluntary for patients. For further information, including details of how to enrol your patients, please contact UCBCares® at UCBCares.uk@ucb.com.

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 (Appendix 2)
  - The latest version of the Package Leaflet (Appendix 3)

REPORTING ADVERSE EVENTS

Post-authorisation reporting of suspected adverse events is of great importance. It allows continuous monitoring of the benefit-risk balance of the medicine. Adverse events should be reported. Reporting forms and information can be found at http://www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to UCB Pharma Ltd at UCBCares.uk@ucb.com or on +44 (0) 1753 777 100 or 0800 279 3177 (freephone).

LITERATURE

1. Fintepla® Summary of Product Characteristics https://www.medicines.org.uk/emc/product/11998/
2. Center for Disease Control and Prevention. Cardiac valvulopathy associated with exposure to fenfluramine or dexfenfluramine: U.S. Department of Health and Human Services Interim Public Health Recommendations, November 1997. Morbidity and Mortality Weekly Report 1997;46(45):1061-6.
3. Connolly HM, Crary JL, McGoon MD et al. Valvular heart disease associated with fenfluramine-phentermine. New Engl J Med 1997;337(9):581-8. Erratum in: New Eng J Med 1997;337(24):1783.
4. Wong J, Reddy SS, Klein AL. Anorectic drugs and valvular heart disease: a biological and clinical perspective. Cleve Clin J Med 1998;65(1):35-41.
5. Perez VA de Jesus. Drug-induced pulmonary hypertension: The First 50 years. Adv Pulm Hypertens 2017;15(3):133-7 et al.
6. Douglas JG, Munro JF, Kitchin AH, et al. Pulmonary hypertension and fenfluramine. Br Med J (Clin Res Ed) 1981;283(6296):881-3.
7. McMurray J, Bloomfield P, Miller HC. Irreversible pulmonary hypertension after treatment with fenfluramine. Br Med J (Clin Res Ed) 1986;293(6538):51-2.
8. Pouwels HM, Smeets JL, Cheriex EC, et al. Pulmonary hypertension and fenfluramine. Eur Respir J 1990;3(5):606-7.
9. Assessment report Fintepla®; 15 December 2022: https://www.ema.europa.eu/en/documents/variation-report/fintepla-h-c-3933-ii-0012-epar-assessment-report_en.pdf accessed on March 2025.

Appendix 1: Fintepla® Summary of Product Characteristics

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

Appendix 3: Fintepla® Package Leaflet