This guide was prepared in coordination with the Israeli Ministry of Health. As an additional risk minimising measure it is intended to ensure that health professionals who prescribe and bring 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

Please consult the Physician Prescribing Information (PPI) for full prescribing information.

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.

MEDISON ZOGENIX

VALVULAR HEART DISEASE AND PULMONARY ARTERIAL HYPERTENSION

Fenfluramine is indicated for the treatment of seizures associated with Dravet 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. In the late 1990s, it was **withdrawn worldwide** because of the **risks of valvular heart disease and pulmonary arterial hypertension**, which in some cases were severe or **fatal**[1-7] at doses 2-4 times higher than the maximum dose approved for seizures associated with Dravet syndrome (26mg fenfluramine). Fenfluramine hydrochloride was also often used in combination with phentermine for the treatment of obesity. 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.

IMPROPER USE FOR WEIGHT CONTROL

Fenfluramine can cause decreased appetite and weight loss (see sections 4.4 and 4.8 of the PPI).

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 PPI 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

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, periodic echocardiography must be performed when treating patients with Dravet syndrome. There were no cases of valvular heart disease or PAH reported in patients in the clinical trials for the treatment of Dravet syndrome. Due to the small number of patients in clinical trials and the low incidence of this condition, it is not known at this time whether fenfluramine increases the risk of PAH in patients with Dravet syndrome.

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

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

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 in accordance with clinical guidelines (guidelines of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) from 2015).

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 and during treatment.
  Please ensure that every patient prescribed Fintepla receives the Patient and Caregiver Leaflet.
  Patient and Caregiver Leaflets are available on www.health.gov.il or by calling 03-9250250.

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 can be reported to the Ministry of Health using the online form for adverse event reporting which can be found on the Ministry of Health website: www.health.gov.il or by using the following link: https://sideeffects.health.gov.il

Adverse events can be also reported to Medison Pharma Ltd. by email: pv@medison.co.il or fax: 03-9234218

This guide was revised and approved by the Ministry of Health in December 2021

LITERATURE

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