Use of Fenfluramine for treating seizures associated with Lennox-Gastaut Syndrome – Clinical experience

Dear Committee

Following the recent publication of the draft guidance regarding the use of Fenfluramine for seizures associated with Lennox-Gastaut Syndrome (LGS) [ID 1651], I write to you on behalf of the undersigned group of paediatric and adult epilepsy specialists to request reconsideration of the NICE committee decision to not recommend fenfluramine.

We base our request on the high unmet need of patients with LGS and their families.

LGS encompasses a heterogenous group of developmental and epileptic encephalopathies (DEE) which requires individualisation of treatments to meet care needs. Patients can suffer hundreds of seizures per week; the impact on both the family and on health-care utilisation is considerable.

In spite of the range of anti-seizure therapies: medications (including standard of care anti-seizure medications and newer medications such as Cannabidiol with Clobazam), dietary (ketogenic diet) and surgical (corpus callosotomy and VNS), patients may continue to experience uncontrolled seizures.

There is therefore a clear potential role for additional therapies such as Fenfluramine.

On behalf of this group, I am writing to detail my clinic experience using Fenfluramine for adult patients with LGS. As far as I am aware, I am the only clinician with this degree of experience in the UK. I am clinical lead for epilepsy in the West Midlands – based at University Hospitals Birmingham and our team looks after over 100 adult patients prescribed Cannabidiol for LGS.

Each of the three patients for whom Fenfluramine has been prescribed has a developmental epileptic encephalopathy (DEE) within the LGS spectrum. In each case the primary indication for requesting Fenfluramine (via Individual Funding Request) was to reduce the frequency and severity of prolonged convulsive seizures in patients with a high risk of SUDEP (sudden death in epilepsy) and recurrent hospitalisations.

Two patients were prescribed Cannabidiol at the time of starting Fenfluramine. One was unable to tolerate Clobazam and so was ineligible for Cannabidiol.

All three have been prescribed Fenfluramine for between 5 and 10 months.

Patient A experienced a dramatic reduction in seizure-related hospitalisations -from an average of 1 per month pre Fenfluramine to none since Fenfluramine was commenced 10 months ago.

Patient B experienced a reduction in hospitalisations from 1 per 2 months to none since initiation of Fenfluramine 10 months ago.

Patient C experienced a 50% reduction in buccal midazolam use since Fenfluramine initiation 5 months ago and a corresponding reduction in paramedic call outs.

Initiation of Fenfluramine has enabled a reduction in the dose of Cannabidiol. With respect to other therapies tried, these patients tried a number of standard of care medications including Topiramate and Rufinamide. Two patients were refractory to VNS (inserted in childhood), one deferred VNS because of the concern about surgical risk. The ketogenic diet had been considered in all cases and corpus callosotomy offered in one case (again rejected because of concerns about surgical risk).

Fenfluramine appears to have a clear role in the reduction of convulsive seizures (and so reduction in SUDEP risk) in those with refractory convulsive seizures in the context of DEE. Families whose young people are experiencing regular breakthrough convulsive seizures on Cannabidiol are accepting of the limitations of Cannabidiol. Reducing the dose of Cannabidiol to enable adjunctive use of Fenfluramine has clear cost-neutral implications. The cost-effectiveness of minimising hospitalisations in this highly refractory cohort is self-evident.

As clinicians looking after patients with DEE, we are all too aware of the need for effective adjunctive treatments to reduce both the risk of life limiting injury and the burden on emergency care services. This is clearly demonstrated in these cases.

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