Pharmacological management of narcolepsy in children and adolescents

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LETTER TO THE EDITOR

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Dear Editor,

Narcolepsy is often a paediatric disorder with symptoms that can commence in early childhood, and new diagnoses that peak at 15 years of age (Postiglione et al., 2018). For this reason we need controlled safe and effective pharmacological treatments to manage narcolepsy symptoms in young people. This has been a continued struggle for paediatric patients with narcolepsy, who have been at risk of becoming therapeutic orphans, without considerable advocacy (Lecendreux et al., 2012).

In 2021 Claudio Bassetti with other narcolepsy experts including most of the authors of this letter, on behalf of European Academy of Neurology, European Sleep Research Society, and European Narcolepsy Network, published, in this Journal, the European guidelines on the management of narcolepsy in adults and children (Bassetti et al., 2021). This document, based on the evidence available, reported that among drugs registered in many European countries for adults' narcolepsy symptoms, only one, sodium oxybate, had data supporting its use in paediatric patients and related European Medicine Agency (EMA) approval, while other drugs are used off-label on the basis of experts' opinion and clinical practice or under single Country approval (see Figure 1). Since the publication of these guidelines, other clinical controlled pharmacological trials in children with narcolepsy have also been conducted or are ongoing with results still unpublished.

Pitolisant, a selective antagonist/inverse agonist of the central nervous system H3 histamine receptor, already licensed to treat narcolepsy symptoms in adults, underwent efficacy and safety trials in paediatric patients (Dauvilliers et al., 2023).

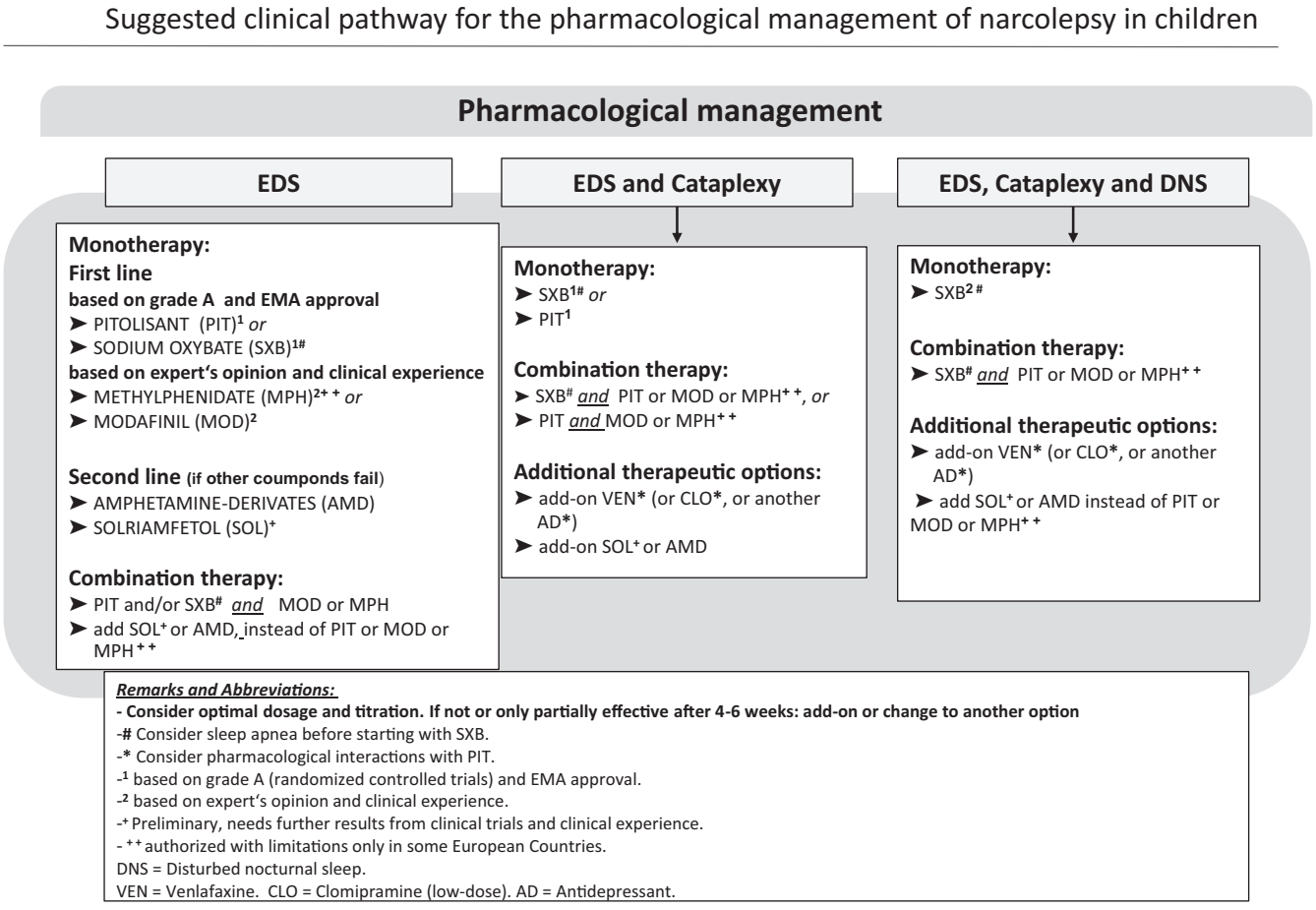

FIGURE 1 Suggested clinical pathway for the pharmacological management of narcolepsy in children.

The seminal double-blind, randomised, placebo-controlled study (Dauvilliers et al., 2023) involved 11 sleep centres in five European countries and enrolled 110 paediatric patients (mean age 12.9 ± 3.0 years), most of them (82%) with type 1 narcolepsy. Significant improvements, compared with placebo, of the Ullanlinna Narcolepsy Scale (UNS) total score, UNS–cataplexy sub-score, and Paediatric Daytime Sleepiness Scale (PDSS) showed that pitolisant was safe and effective in treating the main symptoms of narcolepsy. This trial found a similar favourable safety profile to the adult trials, with a similar prevalence of treatment-emergent adverse events in the pitolisant (31%) and in the placebo (34%) groups. The most frequently reported adverse events in children and adolescents were headache and insomnia, as in adults.

Based on these data, in February 2023 the EMA approved pitolisant for the treatment of narcolepsy with or without cataplexy of children and adolescents from the age of 6 years. The drug's efficacy, safety, and potential was also confirmed by a real world study (Triller et al., 2023). Further studies are planned to confirm its long-term efficacy and safety in children and adolescents.

While awaiting results from new clinical trials, the above recent studies now place pitolisant within the "first-line" registered drugs for the treatment of both daytime sleepiness and cataplexy in paediatric patients with narcolepsy (see Figure 1). The dearth of significant side effects is reassuring for physicians who know that early appropriate patient-centred multimodal treatment of narcolepsy will reduce later physical, learning, and social consequences (Plazzi et al., 2018).

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Giuseppe Plazzi: Conceptualisation; writing – original draft; supervision; validation. **Fabio Pizza:** Validation; Conceptualisation; writing – original draft; supervision. **Michel Lecendreux:** Supervision; validation; Conceptualisation; writing – original draft. **Paul Gringras:** Conceptualisation; supervision; validation; writing – original draft. **Lucie Barateau:** Conceptualisation; validation; supervision; writing – original draft. **Oliviero Bruni:** Conceptualisation; writing – original draft; validation; supervision. **Patricia Franco:** Supervision; validation; Conceptualisation; writing – original draft. **Alex Iranzo:** Supervision; Conceptualisation; writing – original draft; validation. **Poul Jennum:** Supervision; validation; Conceptualisation; writing – original draft. **Ramin Khatami:** Supervision; Conceptualisation; writing – original draft; validation. **Stine Knudsen-Heier:** Validation; supervision; Conceptualisation; writing – original draft. **Silvia Miano:** Validation; supervision; Conceptualisation; writing – original draft. **Lino Nobili:** Conceptualisation; writing – original draft; validation; supervision. **Markku Partinen:** Supervision; validation; Conceptualisation; writing – original draft. **Paul Reading:** Conceptualisation; writing – original draft; validation; supervision. **Karel Sonka:** Conceptualisation; writing – original draft; validation; supervision. **Attila Szakacs:** Conceptualisation; writing – original draft; validation; supervision. **Massimo Zenti:** Supervision; validation; Conceptualisation; writing – original draft. **Ulf Kallweit:** Conceptualisation; writing – original draft; validation; supervision. **Gert J. Lammers:** Writing – original draft; Conceptualisation; validation; supervision. **Yves Dauvilliers:** Conceptualisation; validation; writing – original draft; supervision. **Claudio L. A. Bassetti:** Conceptualisation; writing – original draft; validation; supervision.

DATA AVAILABILITY STATEMENT

No data reported.

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