No regard for patients!

Risperidone for monthly injection (Okedi®) was granted marketing authorisation on the basis of a randomised placebo-controlled trial in patients experiencing an acute exacerbation of schizophrenia (see "Risperidone as monthly injections" p. 242 of this issue).

This placebo-controlled trial was doubly disgraceful. First, there are many neuroleptics on the market, including some in injectable prolonged-release form. Denying appropriate treatment to patients in the placebo group was therefore unacceptable. The Declaration of Helsinki, which forms the basis of legislation intended to protect human participants in biomedical research, states that the comparator must be one of the "*best proven intervention(s)*" except in certain specified circumstances (1). A placebo for patients with acutely decompensated schizophrenia does not fit the bill (2).

Second, this trial did not comply with the recommendations of the European Committee for Medicinal Products for Human Use (CHMP) on the evaluation of efficacy of an injectable prolonged-release neuroleptic treatment, namely that the comparator should be an oral formulation or another prolonged-release neuroleptic (3). Pharmaceutical companies can request "scientific advice" from the European Medicines Agency (EMA), for a fee, when preparing a marketing authorisation application. In the case of Okedi®, the company did request the EMA's "advice", but chose not to follow it. It had been advised to "*follow the CHMP guideline for medicinal products including depot preparations in the treatment of schizophrenia* (...) *including* [the different proposals on the] *comparator arm*" (4,5).

Despite all this, the CHMP eventually issued a positive opinion on this marketing authorisation, which the European Commission granted. The company considers Okedi® a "hybrid" medicine, on the basis that it is similar to oral *risperidone*, but in a different pharmaceutical form. The CHMP consequently concluded that "*enough bridge has been established to efficacy and safety characteristics of the reference product*" (5,6).

The Agency can be pleased with itself for having been paid by the company for its (ultimately ignored) "advice". The company can be pleased with itself for having obtained marketing authorisation, from which it can generate revenue. The European Commission can be pleased with itself for having acted in accordance with regulations... But who stood up for patients' interests in all this?

Prescrire

References **1-** "WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects" accessed 27 July 2023: 4 pages. **2-** Prescrire Rédaction "Déclaration d'Helsinki de l'Association médicale mondiale" *Rev Prescrire* 2008; 28 (298): 570-573. **3-** EMA - CHMP "Guideline on clinical investigation of medicinal products, including depot preparations in the treatment of schizophrenia" 27 July 2023: 24 pages. **4-** Prescrire Rédaction ""Conseils scientifiques" de l'EMA aux firmes: menace pour l'indépendance" *Rev Prescrire* 2015; 35 (384): 780-781. **5-** EMA - CHMP "Public assessment report for Okedi. EMEA/H/C/005406/0000" 16 December 2021: 100 pages. **6-** Prescrire Rédaction "Médicaments hybrides et substitution: décryptage" *Rev Prescrire* 2020; 40 (444): 740-741.