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D.6 Fluoxetine – Deletion from the WHO Model List of Essential Medicines for Children

MSF notices the proposal of the WHO Collaborating Centre for Research and Training in Mental Health and Service Evaluation to delete the serotonin reuptake inhibitor (SSRI) fluoxetine from the Complementary List of Section 24.2.1 “Medicines used in depressive disorders” of the WHO Model List of Essential Medicines for Children (EMLc).

In 2007, MSF supported the inclusion of fluoxetine in the WHO Model List of Essential Medicines (EML). The Committee recommended that fluoxetine be added to the Core List for short-term treatment of depressive disorders. Fluoxetine has also been included since 2007 in the first published EMLc, intended for use for children up to 12 years of age, for the treatment of depressive disorders in children aged >8 years. The Expert Committee had noted the discrepancies in the minimum age for fluoxetine approved by several regulatory authorities and endorsed the inclusion of fluoxetine in EMLc with an age restriction of 8 years. In 2013, a request for updating fluoxetine age restriction for the treatment of depression from > 8 years to >12 years (i.e. effective deletion from the EMLc) was submitted by the WHO Department of Mental Health and Substance Abuse. The Expert Committee decided to retain the minimum age for fluoxetine at 8 years as the evidence submitted to raise the age to 12 years was not considered sufficient. However, the need for a thorough review of the section was noted as a priority.

MSF would like to draw the attention of the Expert Committee to the following facts:

- Currently, fluoxetine is the only antidepressant included in the EMLc. Its deletion would imply the absence in EMLc of pharmacological treatment for children with depression.
- Fluoxetine is the recommended first-line medication for depression and anxiety disorders in children and adolescents¹. The American Academy of Child and Adolescent Psychiatry (AACAP) recommends that antidepressant medication alone could be considered, particularly if the presentation is severe and the patient is unable to engage in talking therapy, if psychological interventions are not available, or if this is the patient’s and family’s preference².

¹ Taylor, D. M., Barnes, T. R. E., & Young, A. H. (2021). *The Maudsley prescribing guidelines in psychiatry* (14th ed.). John Wiley & Sons.

² Birmaher B, et al. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. *J Am Acad Child Adolesc Psychiatry* 2007; 46:1503–1526.

- The UK National Institute for Health and Care Excellence (NICE) recommends that when an antidepressant is prescribed to a child or young person with moderate to severe depression, it should be fluoxetine as this is the only antidepressant for which clinical trial evidence shows that the benefits outweigh the risks³.
- The European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) have approved fluoxetine for children and adolescents aged 8 years and above. The EMA states that the indication is moderate to severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions, antidepressant medication should be offered to a child or young person with moderate to severe depression only in combination with a concurrent psychological therapy⁴.
- A recent met-analysis (including 71 trials, 9510 participants) shows that despite the scarcity of high-quality evidence, fluoxetine (alone or in combination with cognitive behavioural therapy) seems to be the best choice for the acute treatment of moderate-to-severe depressive disorder in children and adolescents. However, the effects of these interventions might vary between individuals, so patients, carers, and clinicians should carefully balance the risk-benefit profile of efficacy, acceptability, and suicide risk of all active interventions in young patients with depression on a case-by-case basis⁵.

In light of these elements, MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to retain fluoxetine in the Complementary List of Section 24.2.1 “Medicines used in depressive disorders” of the WHO Model List of Essential Medicines for Children, for the treatment of moderate-to-severe depressive disorder in children.



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³ Depression in children and young people: identification and management, June 2019.
<https://www.nice.org.uk/guidance/ng134/chapter/Recommendations>

⁴ https://www.ema.europa.eu/en/documents/referral/questions-answers-review-prozac-use-children-adolescents_en.pdf

⁵ Zhou X et al. Comparative efficacy and acceptability of antidepressants, psychotherapies, and their combination for acute treatment of children and adolescents with depressive disorder: a systematic review and network meta-analysis. *Lancet Psychiatry*. 2020 Jul;7(7):581-601.