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I.4 Fluoxetine - anxiety disorders

MSF strongly supports the proposal from the WHO Collaborating Centre for Research and Training in Mental Health and Service Evaluation to include fluoxetine, as a representative of selective serotonin reuptake inhibitor antidepressants (SSRIs), with a squared box symbol restricted to citalopram, escitalopram, fluvoxamine, paroxetine, and sertraline, for the treatment of adults with anxiety disorders, in the Core List of the Section 24.3 “Medicines for anxiety disorders” in the WHO Model List of Essential Medicines (EML). The application proposes also to add an asterisk to fluoxetine with the following statement: “For generalized anxiety disorder, panic disorder, and social anxiety disorder.”

Since 2007, fluoxetine is included in the Core List of the Section 24.2.1 “Medicines used in depressive disorders” of the EML.

In 2019, MSF strongly supported the WHO Collaborating Centre for Research & Training in Mental Health & Service Evaluation proposal to add a square box symbol to fluoxetine, the first representative of the therapeutic class of SSRIs for the treatment of depressive disorders in the EML. The square box symbol indicates therapeutic equivalence between SSRIs with comparable efficacy, acceptability and safety profiles and MSF recommended that the square box symbol be restricted to citalopram, escitalopram, fluoxetine, sertraline and paroxetine, SSRIs for which there is the strongest evidence for both efficacy and acceptability. The 2019 Expert Committee recommended the addition of a square box symbol to the current listing of fluoxetine on the Core List of the EML for treatment of depressive disorders with the following list of therapeutic alternatives: citalopram, escitalopram, fluvoxamine, paroxetine, and sertraline.

Currently, the Section 24.3 “Medicines for anxiety disorders” includes only diazepam and no antidepressants are listed in this section.

Anxiety disorders can be treated by SSRIs, tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and benzodiazepines (BZDs). SSRIs are recommended as the first-line pharmacological treatment, as they are more effective in reducing anxiety symptoms than placebo and have a safer profile than the above-mentioned therapeutic classes, including in case of acute intoxication. After a comprehensive review of the highest-quality scientific evidence, the authors concluded that fluoxetine and other SSRIs have similar efficacy and tolerability profiles and that

fluoxetine, the first SSRI being approved in 1987, should be included in the EML in Section 24.3 “Medicines for anxiety disorders” with a square box symbol. This square box symbol is restricted to citalopram, escitalopram, fluvoxamine, paroxetine, and sertraline which could be substituted to fluoxetine if needed as they are considered to be valid therapeutic alternatives. These medicines are worldwide available as generics and included in most national pharmacopoeias.

The authors considered that there is no sufficient evidence to endorse the other SSRIs (i.e., zimeldine, alaproclate and etoperidone). The authors highlighted that the application reviewed the evidence for generalized anxiety disorder, panic disorder (with or without agoraphobia), and social anxiety disorder and accordingly propose to add an asterisk to fluoxetine with the following statement: “For generalized anxiety disorder, panic disorder, and social anxiety disorder”.

In 2023, the Guidelines Development Group of WHO Mental Health Gap Action Programme (mhGAP) revision is considering recommending that “SSRIs should be considered for adults with panic disorder and that SSRIs should be considered for adults with generalized anxiety disorder”.

SSRIs are essential medicines in low- and middle-income countries (LMICs), due to their efficacy, safety profile, worldwide availability and affordability, and ease of administration (one daily oral intake). MSF guidelines recommends prescribing SSRIs for the treatment of generalised anxiety disorder that lasts more than 2 months and does not improve with psychosocial interventions.

MSF would like to draw the attention of the Expert Committee to the fact that in post-traumatic stress disorder (PTSD), psychological intervention should be completed by pharmacological treatment in case of severe symptoms. According to recent guidelines and Cochrane review, SSRIs are first-line medicines for the pharmacotherapy of PTSD¹². Fluoxetine, paroxetine and sertraline are the preferred SSRIs according to systematic reviews and meta-analysis³⁴. In light of these elements, MSF recommends to include this indication in the statement attached to the asterisk add to fluoxetine: “For generalized anxiety disorder, panic disorder, social anxiety disorder and post-traumatic stress disorder.”

MSF has been using fluoxetine, paroxetine and sertraline in its programs, since 2002, 2011 and 2017 respectively.

In light of these elements, MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to include fluoxetine, as a representative of the selective serotonin reuptake inhibitors antidepressant, with an asterisk with the following statement “For generalized anxiety disorder, panic

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

² Williams T, Phillips NJ, Stein DJ, Ipser JC. Pharmacotherapy for post-traumatic stress disorder (PTSD). Cochrane Database of Systematic Reviews 2022, Issue 3. Art. No.: CD002795.

³ Hoskins M, et al. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. *Br J Psychiatry* 2015;206:93–100

⁴ Lee DJ, et al. Psychotherapy versus pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analyses to determine first-line treatments. *Depress Anxiety* 2016; 33:792–806.

disorder, social anxiety disorder and post-traumatic stress disorder” and with a squared box, restricted to citalopram, escitalopram, fluvoxamine, paroxetine, and sertraline, in the Core List of the Section 24.3 “Medicines for anxiety disorders” in the WHO Model List of Essential Medicines.

A handwritten signature in black ink, consisting of a large, stylized 'D' followed by a horizontal line and a small flourish.

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