



International Office

140 Route de Ferney, Case Postale 1224

CH-1211 Geneva 1, SWITZERLAND

Phone: +41 (0)22 849 84 00

Fax: +41 (0)22 849 84 88

www.msf.org

C.3 Chlorpromazine - Fluphenazine (decanoate or enantate) - Haloperidol (FGAs)

MSF strongly supports all the proposals from the WHO Department of Mental Health and Substance Abuse (MSD) regarding the first generation antipsychotics (FGAs), chlorpromazine, fluphenazine decanoate or enantate and haloperidol listed in Section 24.1 “Medicines used in psychotic disorders” of the WHO Model List of Essential Medicines (EML).

Currently, haloperidol (injection), chlorpromazine (injection and oral formulations), fluphenazine decanoate or enantate (injection) are the FGAs included in the Section 24.1 “Medicines used in psychotic disorders”, all with an unrestricted square box symbol indicating that any FGA can be considered as a valid therapeutic alternative. The second generation antipsychotics listed are injectable prolonged-release paliperidone with a restricted square box (therapeutic alternative: injectable risperidone) and solid dosage oral forms of risperidone.

As pointed out by the authors, the most recent and high-quality meta-analytical evidence on both the acute and maintenance treatment of schizophrenia-spectrum disorders¹² showed differences between FGAs, for both oral and injectable formulations, regarding efficacy and tolerability. The review of the evidence led the WHO MSD to the selection of oral chlorpromazine, haloperidol, and long-acting haloperidol decanoate, fluphenazine decanoate or enantate, and zuclopenthixol decanoate as the relevant FGAs to retain in the EML.

Moreover, as both haloperidol and chlorpromazine are listed with a square box indicating any FGA can be considered as a valid therapeutic alternative, the proposal from the WHO MSD is to retain only haloperidol among oral FGAs, with a restricted square box indicating only chlorpromazine as a valid therapeutic alternative.

Among long-acting FGAs, WHO MSD proposal is to retain fluphenazine decanoate/enantate, with a restricted square box indicating haloperidol decanoate and zuclopenthixol decanoate as the two valid therapeutic alternatives.

¹ Huhn M, Nikolakopoulou A, Schneider-Thoma J, Krause M, Samara M, Peter N, Arndt T, Bäckers L, Rothe P, Cipriani A, Davis J, Salanti G, Leucht S. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. *Lancet*. 2019 Sep 14;394(10202):939-951.

² Leucht S, Chaimani A, Krause M, Schneider-Thoma J, Wang D, Dong S, Samara M, Peter N, Huhn M, Priller J, Davis JM. The response of subgroups of patients with schizophrenia to different antipsychotic drugs: a systematic review and meta-analysis. *Lancet Psychiatry*. 2022 Nov;9(11):884-893.

Moreover, WHO MSD suggests to include some new formulations in the Section 24.1 “Medicines used in psychotic disorders”: haloperidol decanoate, solution for injection (ampoules 50 mg/mL and 100 mg/mL), and zuclopenthixol decanoate solution for injection (ampoules 200 mg/mL and 500 mg/mL).

All the above-mentioned FGAs are included in many National Lists and broadly available as generics.

According to the WHO MSD, the Guidelines Development Group of WHO Mental Health Gap Action Programme (mhGAP) revision is considering recommending these medications as representative of FGAs for the treatment of schizophrenia and related psychoses.

MSF would like to draw the attention of the Expert Committee to the fact that the proposal doesn't mention the status of the rapid-acting injectable FGAs (haloperidol and chlorpromazine) and would like to highlight that if haloperidol is the oral drug retained for treatment of schizophrenia-spectrum disorders (with a restricted square box for chlorpromazine as therapeutic alternative), an injectable dosage form for the treatment of acute psychotic episodes should be also retained in the EML.

MSF is using all the antipsychotics listed above, except zuclopenthixol decanoate, in its programs.

MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to accept all the proposals from the WHO Department of Mental Health and Substance Abuse regarding the first generation antipsychotics listed in the Section 24.1 “Medicines used in psychotic disorders” of the WHO Model List of Essential Medicines.



Dr. Daniela Belen Garone

Infectious Diseases specialist and DTM&H
International Medical Coordinator

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