

**South African National Essential Medicine List
Adult Hospital Level Medication Review Process
Component: Mental Health**

EVIDENCE SUMMARY

Date: 27 October 2022

Reviewers: Prof L Robertson

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QUESTION: Use of olanzapine, oral, as a doctor initiated prescription rather than specialist initiated prescription, and eventual removal of chlorpromazine in the treatment algorithm.

Background

Olanzapine, oral is currently in the treatment algorithm for schizophrenia for poor response or tolerability to haloperidol, risperidone, and/or chlorpromazine. Its use requires specialist initiation, whereas haloperidol, risperidone, and chlorpromazine may be initiated by medical officers.

However, at tender prices, olanzapine costs less than chlorpromazine. In addition, chlorpromazine may not offer any advantage in terms of efficacy or tolerability.

Introduction

As detailed in the current treatment algorithm for schizophrenia below, olanzapine, oral requires specialist initiation. The rationale for this requirement is unclear. Olanzapine may have greater efficacy than chlorpromazine, is no less tolerable, and is cheaper at October 2022 tender prices. However, many practitioners in South Africa are more familiar with chlorpromazine than olanzapine, and supply of chlorpromazine may be more reliable in South Africa and neighbouring countries.

15.5.2 SCHIZOPHRENIA SPECTRUM DISORDERS

F20-F20.9; F22.0-22.9; F25.0-25.9 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

Initiate treatment:

- Haloperidol, oral.
 - Initial dose: 0.75–1.5 mg daily, increasing to 5 mg daily.

If good response/ tolerability to haloperidol, or patients' preference:

- Depot antipsychotic, e.g:
- Flupenthixol decanoate, IM, 10–40 mg every 4 weeks.

OR

Zuclopenthixol decanoate, IM, 200–400 mg every 4 weeks.

If poor response/ poorly tolerated/ high risk of tardive dyskinesia/ extra-pyramidal side effects:

- Risperidone, oral
 - Initial dose: 2–4 mg at night.
 - Maximum dose: 6 mg daily.
 - Assess efficacy after 4–6 weeks:
 - If a partial response is noted, optimise the dosage.
 - If no response is noted, switch treatment.

OR

- Chlorpromazine, oral, 75–300 mg daily in divided doses.

If poor response/tolerability to haloperidol, risperidone or chlorpromazine:

- Olanzapine, oral (specialist initiated).
 - Initial dose: 5 mg at night, increase to 10 mg at night.
 - Maximum dose: 20 mg at night.

If poor response/ tolerability to olanzapine:

- Clozapine, oral (specialist initiated, preferably as inpatient):
 - Initial dose: 12.5–25 mg at night.
 - Usual dose: 200–450 mg per day in divided doses.
 - Maximum dose: 900 mg/day in divided doses.

Summary of the evidence

The medicine review: 'Olanzapine, oral for schizophrenia-Adult review_13June2019' refers.ⁱ

While no direct comparisons between olanzapine and chlorpromazine were found, a good quality network meta-analysis by Leucht et al., 2013,ⁱⁱ found that, vs placebo:

- olanzapine ranked higher in efficacy than chlorpromazine, measured as a reduction of the PANSS score (SMD -0.59, 95% CI -0.65 to -0.53 for olanzapine vs SMD -0.38, 95% CI -0.54 to -0.23 for chlorpromazine)
- olanzapine appears to have better or similar acceptability and tolerability than chlorpromazineⁱⁱⁱ
 - discontinuation of medicine occurred less with olanzapine than with chlorpromazine
 - weight gain was similar for both medications, as was increased prolactin
 - extra-pyramidal side effects occurred with chlorpromazine but not with olanzapine
 - sedation may be more with chlorpromazine than with olanzapine

At October 2022 tender prices,ⁱⁱⁱ olanzapine is considerably cheaper than chlorpromazine at equivalent doses:

Medicine Pack	Price	Standard dose	Cost per month
Chlorpromazine; 100mg; Tablet; 56 Tablets	R78.90	300mg per day	R118.35
Olanzapine; 10mg; Tablet; 28 Tablets	R22.43	10mg at night	R22.43

Conclusion

There is no cost, efficacy, or tolerability advantage of chlorpromazine in the treatment of schizophrenia if olanzapine is widely available.

Proposal

To alter prescribing level of olanzapine in schizophrenia to doctor initiated and to remove chlorpromazine from the treatment algorithm. However, chlorpromazine to remain on national tender to allow for supply adjustment of olanzapine.

References

ⁱ Olanzapine, oral for schizophrenia-Adult review_13June2019, available from <https://www.knowledgehub.org.za/elibrary/hospital-level-adults-medicine-reviews-2017-2020> (accessed 23 October 2022).

ⁱⁱ Leucht S, Cipriani A, Spineli L, Mavridis D, Örey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: A multiple-treatments meta-analysis. *Lancet*. 2013;382(9896):951–62. DOI: 10.1016/S0140-6736(13)60733-3

ⁱⁱⁱ NDOH Tenders, available from <https://www.health.gov.za/tenders/> (accessed 23 October 2022)

NEMLC MEETING OF 8 DECEMBER 2022:

NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee (see above)