

Antipsychotic Long-Acting Injection Prescribing Algorithm

Introduction

Antipsychotic long-acting injections (LAIs) in the form of depot injections, containing an active ingredient dissolved in a naturally occurring oil base (e.g. coconut oil or sesame oil) have been available for use since 1967. The first-generation antipsychotic (FGA) medicines in this class include haloperidol decanoate, flupentixol decanoate and zuclopenthixol decanoate (pipotiazine palmitate was withdrawn from the UK market in 2014 and production of fluphenazine decanoate will cease in mid 2018).

Since 2002, second-generation antipsychotic (SGA) medicines have become available including Risperdal Consta (risperidone encapsulated in polymeric microspheres), olanzapine pamoate (suspended in aqueous solution), paliperidone palmitate (nanocrystals suspended in aqueous solution) and aripiprazole (suspended in aqueous solution).

Despite a lack of head-to-head comparisons of FGA and SGA LAIs in use, there has been a growing trend towards the use of SGA antipsychotics. Given the cost differential between the current range of FGA and SGA LAI medications (appendix I), the relative cost-effectiveness of these agents should be taken into account when prescribing. A review of the available evidence comparing these medicines together with a large difference in their acquisition costs suggests that a step-wise approach to LAI prescribing is rational.

A recent audit was conducted within 3 CMHTs on behalf of PMG-MH to look at whether the advice within this algorithm provides clinically effective treatment for patients. Overall, the results support the algorithm, with patients on FGA LAIs shown to, on average, have:

- Longer duration of treatment
- Reduced hospital admissions
- Reduced length of stay in hospital
- Increased medication use to manage side effects (though this does not appear to impact discontinuation rates)

For SGA LAI initiation, it appears that the algorithm is not being followed as many patients (66.3%) did not receiving a trial of a FGA LAI first.

First-Line Choice of an Antipsychotic LAI

A first-generation depot antipsychotic should be chosen from the NHSGG&C Formulary*

Current evidence indicates that zuclopenthixol decanoate is more effective in preventing relapse than other FGA depots.¹

Shajahan et al² compared the use of risperidone, flupentixol and zuclopenthixol LAIs with respect to loss of efficacy and adverse effects leading to treatment discontinuation. They concluded that overall zuclopenthixol was less likely to be discontinued than risperidone or flupentixol. Where efficacy was concerned, findings favoured zuclopenthixol over the other LAIs and adverse effects did not differ between the three LAIs.

Cordiner et al³ studied prescribing patterns and outcomes for zuclopenthixol, paliperidone and risperidone LAIs and found poorer outcomes for paliperidone over zuclopenthixol or risperidone.

A recent local study⁴ assessed LAI use in one GG&C CMHT that had similar number of patients prescribed FGA and SGA LAIs. Patients receiving FGA LAIs complained of significantly fewer adverse effects than those receiving SGA LAIs. Average doses of FGA LAI were less than 15% BNF maximum where as average SGA LAI doses were approximately 80% of the BNF maximum. This study indicated that FGA LAIs were better tolerated and at least as efficacious as SGA LAIs.

The Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS I)⁵ compared FGAs including FGA LAIs and oral SGAs, although it did not include any SGA LAIs. It concluded there was no disadvantage in terms of quality of life or symptom control over a one year period in commencing treatment with FGAs rather than non-clozapine SGAs in people with schizophrenia whose medication was being changed because of intolerance or inadequate response.

**The differential in acquisition costs of FGA LAIs vs SGA LAIs.
Therefore clearly favours the prescription of FGA LAI medicines.**

*Exception to first line choice of FGA LAI: Where there is good evidence of effect and tolerability with a specific SGA oral medication favouring its use as an LAI and where adherence with the oral medication is problematic.

Paliperidone LAI is the SGA LAI of choice within GGC due to acquisition cost. Risperidone LAI should not be started in new patients and paliperidone should be initiated for patients who have responded well to oral risperidone and fit the exception criteria. Patients maintained on risperidone LAI should be considered for switching to paliperidone if clinically appropriate and based on individual patient's needs.

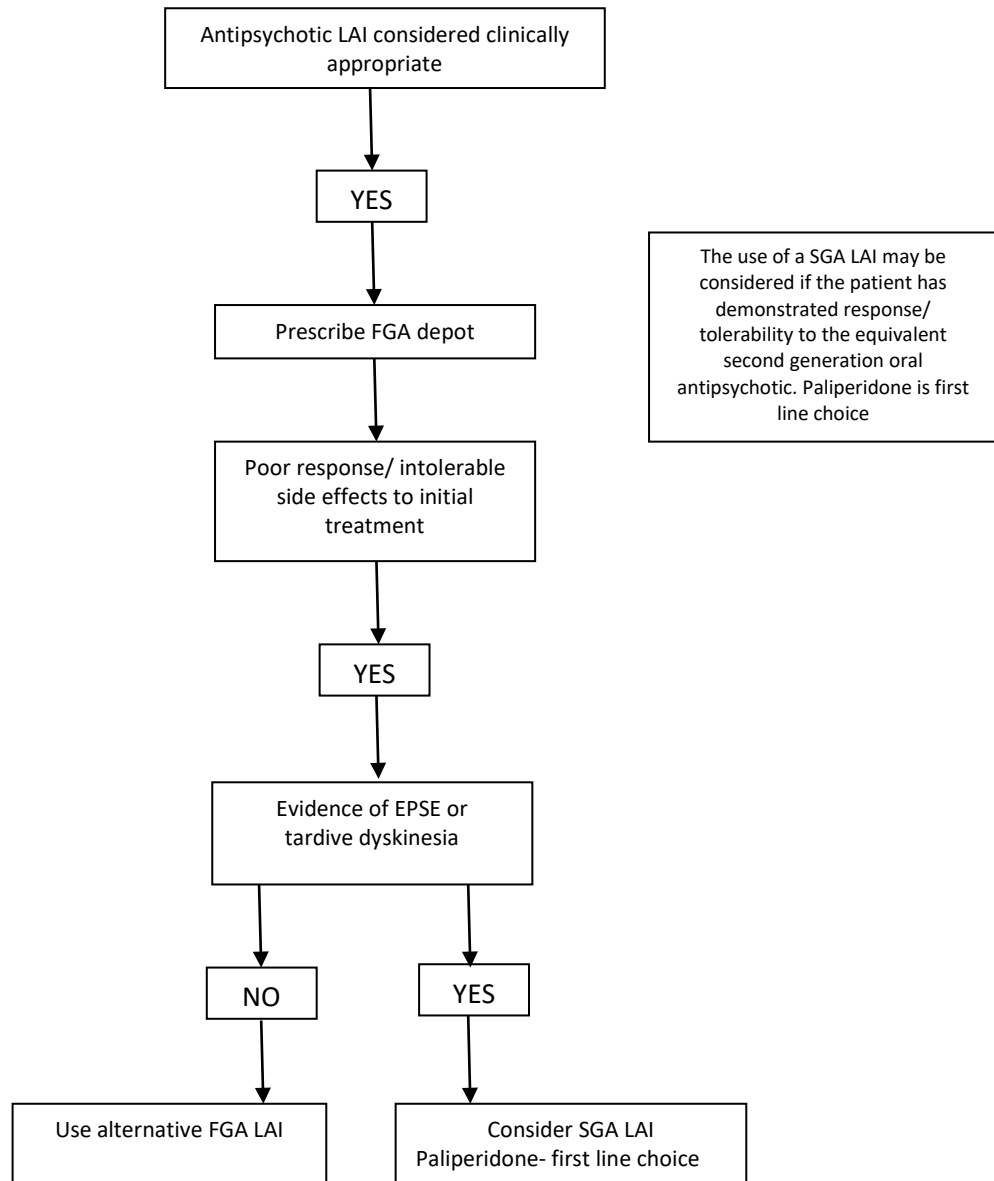
Second-Line Choice of an Antipsychotic LAI

(In the event of treatment failure or emergent, intolerable side-effects with the first-line choice)

An alternative first-generation depot medicine should be chosen from NHSGG&C Formulary*

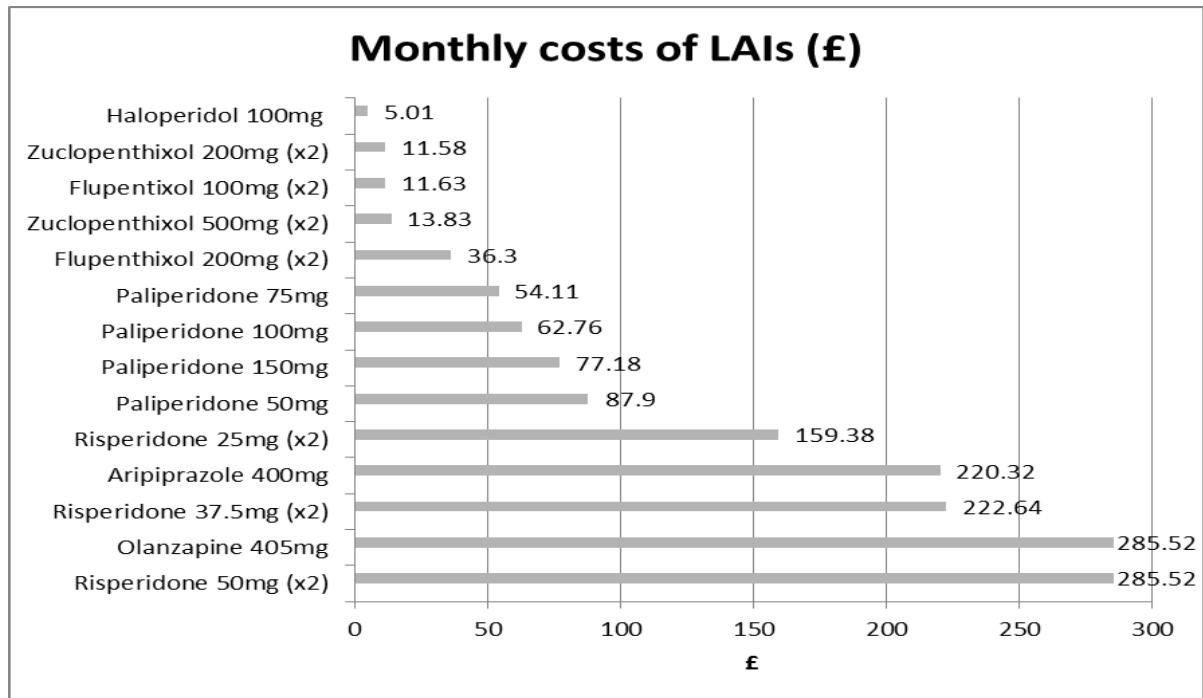
*Exception: If emergent side-effects include extrapyramidal side effects or tardive dyskinesia then consider a formulary SGA LAI, paliperidone is SGA LAI of choice.

Antipsychotic Long-Acting Injection Prescribing Algorithm: Flowchart



CD: clinical director, EPSE: extrapyramidal side effects, FGA: first generation antipsychotic, LAI: long-acting injection, SGA: second generation antipsychotic

Appendix 1: Comparative costs of various First and Second-Generation LAIs



Note: All costs from obtained from Ascribe and correct as of January 2024.

Olanzapine LAI injection is non-formulary and requires a full PACS2 request submitted to PMG-MH for consideration and approval.

Both paliperidone and aripiprazole LAIs are monthly injections, not 4 weekly. They should be prescribed and administered on, for example, the first Monday of each month. Prescribing as 4 weekly instead of monthly would result in administration of one additional injection per year with associated costs.

References:

1. da Silva Freire Coutinho E, Fenton M, Quaraishi SN. Zucloperthixol decanoate for schizophrenia and other serious mental illnesses. *Cochrane Database of Systematic Reviews* 1999, Issue 3. Art. No.: CD001164. DOI: 10.1002/14651858.CD001164.
2. Shajahan P, Spence E, Taylor, M Darlington D, Pelosi A. Comparison of the effectiveness of depot antipsychotics in routine clinical practice. *Psych Bull* 2010, 34: 273-279
3. Cordiner M, Shajahan P, McAvoy S, Bashir M, Taylor M. Effectiveness of long-acting antipsychotics in clinical practice: 1. A retrospective, 18-month follow up and comparison between paliperidone palmitate, risperidone long-acting injection and Zucloperthixol decanoate. *Ther Adv Psychopharmacol* 2016; 6(2): 66
4. Watson, D. Evaluation of the prescribing practice of long acting injectable antipsychotics: A pilot study. MSc thesis 2016
5. Jones PB et al. Randomized Controlled Trial of the Effect on Quality of Life of Second- vs First-Generation Antipsychotic Drugs in Schizophrenia: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). *Arch Gen Psychiatry*. 2006;63:1079-1087