NHS GG&C Mental Health Services

MHS MRG 05 - 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this class include haloperidol decanoate, flupentixol decanoate and zuclopenthixol decanoate (pipotiazine palmitate was withdrawn from the UK market in 2014 and production of fluphenazine decanoate will cease in mid 2018).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.

This algorithm was initially developed in March 2015 and has been updated to accommodate new evidence to support the rationale for a prescribing algorithm and a new process for initiating SGA LAIs.

New initiations for SGA LAIs will now be subject to approval by local clinical director.

Any new request to initiate a SGA LAI should be made in writing to the respective CD for the service with a clear rationale for the choice of a SGA LAI over a first line choice of a FGA LAI.

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 first generation antipsychotic depots.[1]

Shajahan et al[2] 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 al[3] studied prescribing patterns and outcomes for zuclopenthixol, paliperidone and risperidone LAIs and found poorer outcomes for paliperidone over zuclopenthixol or risperidone.

A recent local study[4] 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. (Note: Paliperidone LAI over risperidone LAI should be considered for people who have responded well to oral risperidone and fit the exception criteria).

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.

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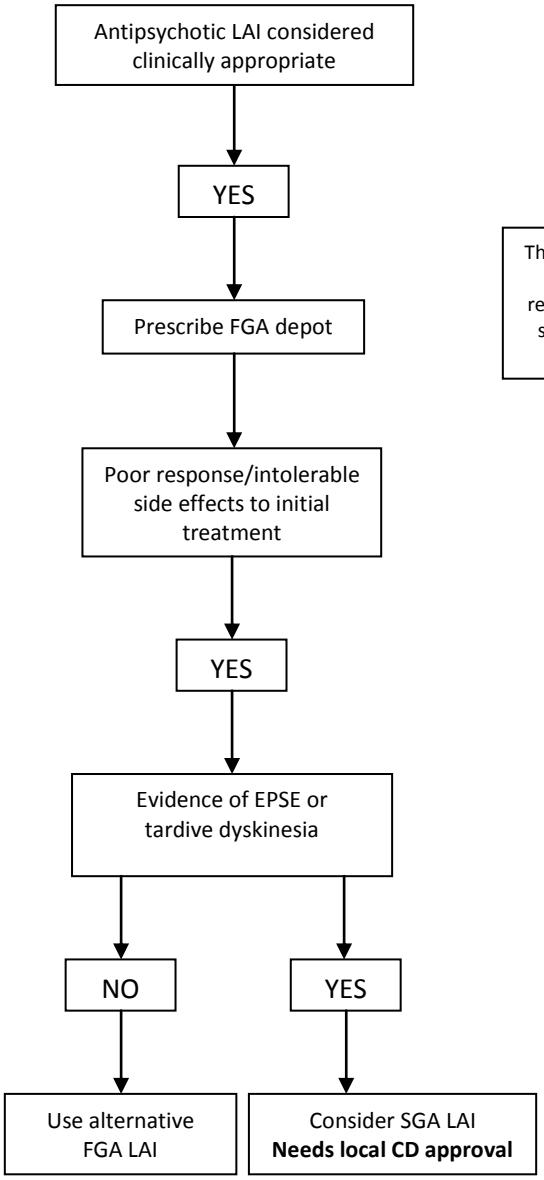
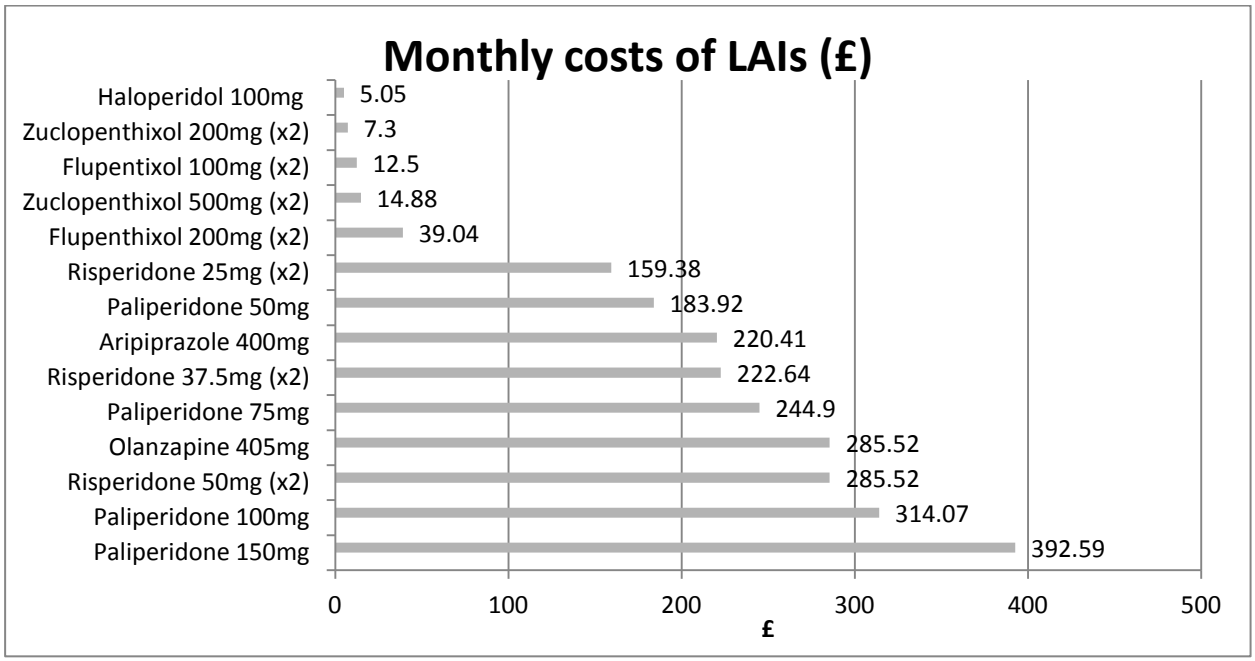
Antipsychotic Long-Acting Injection Prescribing Algorithm: Flowchart



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:
Olanzapine LAI injection is non-formulary and requires a full IPTR3 request submitted to PMG-MH for consideration and approval.

Paliperidone three monthly prolonged injection (Trevicta®) requires an IPTR2 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. Zuclopenthixol 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 Zuclopenthixol 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