Lancashire & South Cumbria Medicines Management Group

NHS Midlands and Lancashire Commissioning Support Unit

Zuclopenthixol Decanoate RAG Status

Recommendation: RAG rating Amber 0

- Suitable for prescribing in primary care following recommendation or initiation by a specialist.
- Little or no specific monitoring required.
- Patient may need a regular review, but this would not exceed that required for other medicines routinely prescribed in primary care.
- Brief prescribing document or information sheet may be required.
- Primary care prescribers must be familiar with the drug to take on prescribing responsibility or must get the required information.

When recommending or handing over care, specialists should ask primary care prescribers to take over prescribing responsibility, and should give enough information about the indication, dose, monitoring requirements, use outside product licence and any necessary dose adjustments to allow them to confidently prescribe.

Summary of evidence

Martindale: The Complete Drug Reference, online

A systematic review comparing zuclopenthixol decanoate with other depot antipsychotics considered that although it may induce more adverse effects, limited data suggested it might offer advantages such as lower relapse rates and increased acceptability in the treatment of schizophrenia and similar serious mental illnesses. Similar reviews of the use of the acetate or hydrochloride found, however, that evidence of additional benefit over other antipsychotics was lacking (monograph last updated October 2011)

The Maudsley Prescribing Guidelines in Psychiatry, 14th Edition:

There are few differences between individual first generation antipsychotic depot injections. Cochrane reviews have been completed for pipotiazine, flupentixol, zuclopenthixol, haloperidol and fluphenazine. With the exception of zuclopenthixol, these preparations are equally effective with respect to each other. Standard doses are said to be as effective as high doses for flupentixol. Two differences that possibly do exist between FGA LAIs are:

- Zuclopenthixol may be more effective in preventing relapses than others, although this may be at the expense of an increased burden of adverse effects.

Zuclopenthixol decanoate for schizophrenia and other serious mental illnesses, The Cochrane Collaboration (July 1999):

Four studies relating to zuclopenthixol decanoate were included. All compared zuclopenthixol decanoate with other depot preparations. Zuclopenthixol decanoate prevented or postponed relapses when compared to other depots (NNT 8, CI 5-53). However, zuclopenthixol decanoate may induce more adverse effects (NNH 5, CI 3-31) although it decreases need for anticholinergic medication when compared to a group of other depot preparations (NNT 9, CI 5-38). For the risk of leaving the study early, there was also a trend for benefit to those allocated to zuclopenthixol decanoate. None of the studies reported outcomes on service utilisation, costs, or quality of life.

Authors' conclusions

Choice of which depot to use must always take into account clinical judgement and the preferences of the recipients of care and their carers. Limited trial data suggests, however, that there are real differences between zuclopenthixol decanoate and other depots and these differences largely favour the former. This review highlights the need for good controlled clinical trials to fully address the effects of zuclopenthixol decanoate for those with schizophrenia. Future studies should report service utilisation data, as well as satisfaction with care and economic outcomes. Duration of such trials should be of a longer duration than the included studies (12 months or more).

Additional evidence

Limited additional evidence upon reviewing the literature.

BNF cautions of first generation depots listed as Amber 0 on LSCMMG vs. zuclopenthixol decanoate (additional to those listed for all antipsychotics):

Flupentixol decanoate	Haloperidol decanoate	Zuclopenthixol decanoate
An alternative antipsychotic may be necessary if symptoms such as aggression or agitation appear; hyperthyroidism; hypothyroidism; phaeochromocytoma; when transferring from oral to depot therapy, the dose by mouth should be reduced gradually	Bradycardia; electrolyte disturbances (correct before treatment initiation); family history of QTc-interval prolongation; history of heavy alcohol exposure; hyperthyroidism; hypotension (including orthostatic hypotension); prolactin-dependent tumours; prolactinaemia; risk factors for stroke; when transferring from oral to depot therapy, the dose by mouth should be reduced gradually	Hyperthyroidism; hypothyroidism; QT interval prolongation; when transferring from oral to depot therapy, the dose by mouth should be reduced gradually

Side effect of first generation depots listed as Amber 0 on LSCMMG vs. zuclopenthixol decanoate (additional to those listed for all antipsychotics):

Frequency	Flupentixol decanoate	Haloperidol decanoate	Zuclopenthixol decanoate
Very common or common	Appetite abnormal; asthenia; concentration impaired; depression; diarrhoea; dyspnoea; gastrointestinal discomfort; headache; hyperhidrosis; hypersalivation; myalgia; nervousness; palpitations; sexual dysfunction; skin reactions; urinary disorder; vision disorders	Depression; hypersalivation; sexual dysfunction	
Uncommon	Flatulence; hot flush; nausea; oculogyration;	Eye disorders; headache;	

	photosensitivity reaction; speech disorder	neuromuscular dysfunction; vision disorders	
Rare or very rare	Glucose tolerance impaired; jaundice; thrombocytopenia		
Frequency not known	Suicidal behaviours	Angioedema; breast abnormalities; cardiac arrest; dyspnoea; gait abnormal; hepatic disorders; hyperhidrosis; hypersensitivity vasculitis; hypoglycaemia; menstrual cycle irregularities; muscle complaints; musculoskeletal stiffness; nausea; oedema; pancytopenia; photosensitivity reaction; psychotic disorder; respiratory disorders; restlessness; rhabdomyolysis; SIADH; skin reactions; temperature regulation disorders; thrombocytopenia; trismus; weight decreased	Anxiety; appetite abnormal; asthenia; concentration impaired; depression; diarrhoea; dyspnoea; eye disorders; fever; flatulence; gait abnormal; gastrointestinal discomfort; glucose tolerance impaired; headaches; hepatic disorders; hot flush; hyperacusia; hyperhidrosis; hyperlipidaemia; hypersalivation; hypothermia; malaise; memory loss; myalgia; nasal congestion; nausea; neuromuscular dysfunction; pain; palpitations; paraesthesia; photosensitivity reaction; reflexes increased; seborrhoea; sexual dysfunction; skin reactions; sleep disorders; speech disorder; syncope; thirst; thrombocytopenia; tinnitus; urinary disorders; vertigo; vision disorders; vulvovaginal dryness; weight decreased; withdrawal syndrome

Discussion

The Maudsley prescribing guideline does single out zuclopenthixol decanoate against other first generation long anting antipsychotics as having a more burdensome side effect profile but appears to be more effective than other agents at preventing relapse. The main source of evidence for the conclusion made in Maudsley is a 1999 Cochrane review. This conclusion is also supported by Martindale. There is limited recent additional evidence in the literature.

The side effect profile, as listed in the BNF, specific to zuclopenthixol decanoate appears to have less certainty in the frequency that patients will experience them compared to the other depots RAG rated Amber 0 on LSCMMG.