REGIONAL DRUG AND THERAPEUTICS CENTRE

NEW DRUG EVALUATION

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ZOTEPINE

Zotepine is an atypical antipsychotic licensed for the treatment of schizophrenia. Clinical trials suggest that it is as effective as conventional antipsychotics for the treatment of positive symptoms but causes fewer extrapyramidal side effects. At present atypical agents should be reserved for patients resistant to, or unable to tolerate conventional antipsychotics. They should be initiated only under specialist supervision.

What is it?

Zotepine (Zoleptil®, Orion Pharma UK Ltd) is an atypical antipsychotic licensed for the treatment of schizophrenia. The recommended dose range is 25-100 mg three times daily (maximum 150 mg daily in the elderly).

How effective is it?

Data on the efficacy of zotepine for the treatment of schizophrenia are limited; many of the studies involve small patient numbers[1-3] or are available in abstract form only.[4,5]

In randomised controlled studies lasting between six and eight weeks conducted in hospitalised patients with an acute exacerbation of schizophrenia, zotepine (150-450 mg daily) or haloperidol (10-20 mg daily) produced similar improvements in positive symptoms.[1,6] A further comparative study reported greater efficacy for zotepine (150-300 mg daily) than for chlorpromazine (300-600 mg daily), however this is available in abstract form only and cannot be fully evaluated.[4]

The effect of zotepine in patients with predominantly negative symptoms is unclear. A comparative study, completed in just 16 patients, found a benefit for zotepine (50-150 mg daily) compared with haloperidol (2-6 mg daily).[2] Other studies which report benefits for zotepine over conventional antipsychotics contain methodological flaws which make interpretation difficult.[4,6,7]

In the only comparative study with another atypical agent no difference in efficacy was detected between zotepine (150-450 mg daily) and clozapine (150-450 mg daily) in the 26 treatment resistant patients for whom results are presented.[3]

There are no comparative studies with other antipsychotics for maintenance therapy. However, in a double-blind placebo controlled study in 121 patients fewer relapses were reported in those receiving zotepine 150-300 mg daily compared with placebo (4 vs 21).[5]

How safe is it?

In the largest published comparative study extrapyramidal side effects (EPS) were less frequent with zotepine than with haloperidol (8% vs 19%).[6]

Elevations of liver enzymes have been reported in more than 10% of patients and zotepine should be used with caution in patients with established hepatic impairment.[8]

Dose-related QT_c prolongation and abnormal ECG have been reported occasionally (1-10%); an ECG should be performed prior to initiation of therapy in patients at risk. Zotepine lowers the seizure threshold and the seizure rate associated with the maximum daily dose of 300 mg is approximately 1%.[8]

Anticholinergic adverse events, such as blurred vision, dry mouth, and constipation have been reported frequently (> 10%). Other frequently reported adverse events include headache, hypotension, leucocytosis, leucopenia, agitation, anxiety, dizziness, insomnia, and weight gain.[8]

What other options are there?

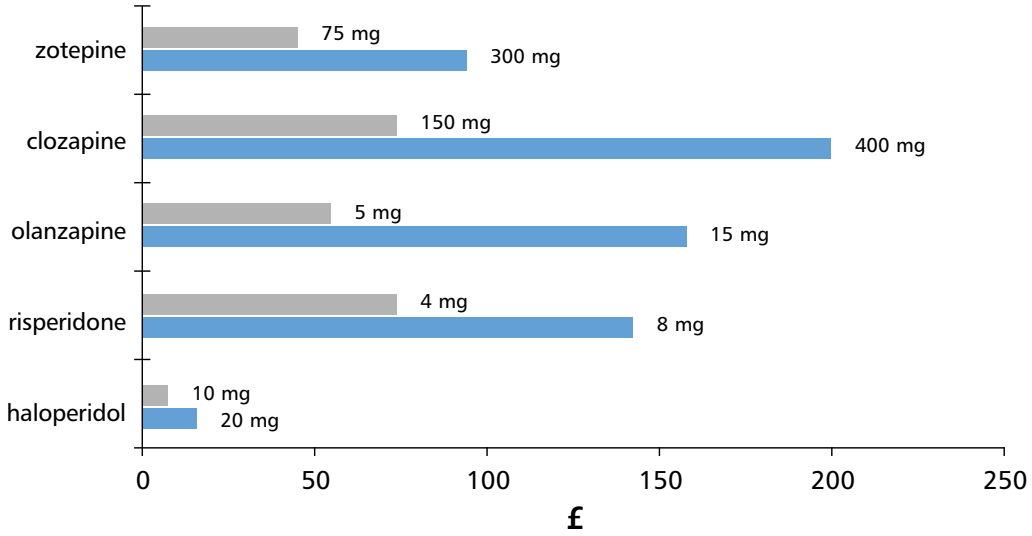
Conventional antipsychotics, e.g., haloperidol or chlorpromazine, have been the mainstay of treatment for schizophrenic patients for many years. Atypical agents e.g., olanzapine, clozapine and risperidone are also available.[9]

When should it be used?

Zotepine appears to be as effective as conventional agents for the treatment of positive symptoms but causes fewer extrapyramidal side effects. Atypical antipsychotics should, at present, be reserved for patients resistant to, or unable to tolerate conventional antipsychotics. They should only be initiated under specialist supervision.

How much does it cost?

Cost for 28 days treatment for total oral daily doses (prices from MIMS/Drug Tariff September 1999)



NB doses shown are for general comparison only and do not imply therapeutic equivalence

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KEY RCT-randomised controlled trial, CT-controlled trial, O-open study, MA-meta analysis, R-review, U-unpublished, Abs- abstract, E - editorial

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