HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

PALIPERIDONE PALMITATE LONG ACTING INJECTION FOR THE TREATMENT OF SCHIZOPHRENIA

RECOMMENDED FOR RESTRICTED USE

<table>
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<th>Name: generic (trade)</th>
<th>What it is</th>
<th>Indication</th>
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<td>Paliperidone palmitate (Xeplion®)</td>
<td>Antipsychotic depot injection</td>
<td>maintenance treatment of schizophrenia</td>
<td>June 2013</td>
<td>Final</td>
<td>NICE - No Guidance SMC – accepted for use</td>
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**HMMC Recommendation:**

**RECOMMENDED FOR RESTRICTED USE AS AN ANTIPSYCHOTIC DEPOT INJECTION OPTION:**
as an alternative to risperidone long-acting injection (LAI) (*Risperdal Consta®*) within licensed indications when one or more of the following advantages of paliperidone (over risperidone) would be of significant benefit: monthly administration, quicker onset of action, 7 day flexibility to avoid missed doses, smaller administration volume, fewer drug interactions, wider dosing range, no dose adjustment required in mild to moderate hepatic impairment.

To be initiated by specialists within Hertfordshire Partnership University NHS Foundation Trust (HPFT). Prescribing responsibility to be retained in most cases by HPFT. GP practices that already prescribe antipsychotic depot injections may consider taking on prescribing responsibility for stable patients under shared care guidelines.

**Efficacy**

- Short-term studies have demonstrated that paliperidone LAI is a more effective antipsychotic than placebo.
- Out of 3 non inferiority studies of paliperidone LAI vs risperidone LAI only 2 demonstrated non inferiority. It has been suggested that the study that failed to demonstrate non-inferiority may have been be due to the use of a lower loading dose than the licensed dose.

**Safety**

- The overall adverse effect profile of paliperidone LAI appears similar to that of risperidone LAI.
- Common adverse reactions include injection site reactions, insomnia, headache, somnolence, extrapyramidal movement disorders, weight gain and tachycardia.

**Cost**

- Total annual ongoing treatment costs are similar for approximate equivalent doses of paliperidone LAI (£2,207-£4,711) and risperidone LAI. Paliperidone LAI cost is more in the 1st year due to the loading dose regime.
- The patent for risperidone LAI expires in 2014. Due to the complexity of the technology it is unlikely that lower cost generic products will then become available.
- Paliperidone LAI is approved for use by SMC and AWMSG following economic evaluation.

**Patient Factors**

- Paliperidone LAI is administered monthly compared to every 2 weeks for risperidone LAI which would reduce clinic visits.
- There is no published data to evaluate the effect of injection frequency on patient adherence.

This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.
Assessment against Ethical Framework

Evidence of Clinical Effectiveness
• Refer to efficacy, safety and patient factors boxes.
• Paliperidone is the active metabolite of risperidone and an antagonist of serotonin 5-HT₂ and dopamine D₂ receptors.
• Paliperidone LAI appears to have the following advantages over risperidone LAI:
  o may be given 7 days before or after usual date of administration allowing flexibility to avoid missed doses.
  o does not require oral supplementation on initiation of therapy.
  o available as a pre-filled syringe with a smaller administration volume that does not require refrigeration
  o faster onset of action
  o less drug interactions as not as extensively metabolised in the liver as risperidone
  o wider licensed dosing range
• There is no long-term data regarding the use of the licensed dosage regimen.
• The comparator trials excluded patients with a history of treatment resistance.

Cost of treatment and Cost Effectiveness
• Refer to cost box.

The needs of the population
The needs of the population appear to be low as there are available alternative treatment options recommended within local guidelines and by NICE as treatment options. However, schizophrenia is a condition with profound consequences for the affected person, their social environment and society as a whole. The average cost of a relapse event in schizophrenia has been estimated to be approximately £25,000 of which a small proportion is due to drug acquisition costs. Appropriate choice of antipsychotic medication may increase adherence and reduce risk of relapse and risk of suicide. Paliperidone LAI would provide another treatment choice with some apparent advantages over risperidone LAI.

The needs of the community
The needs of the community appear to be low. Paliperidone LAI costs more than risperidone but if restricted to appropriate patients these costs may be offset.

Equity
No impact anticipated. Reduced clinic visits may be advantageous for certain patient groups.

Policy Drivers
• NICE CG 82: Schizophrenia states ‘consider offering depot/long-acting injectable antipsychotic medication to people with schizophrenia: who would prefer such treatment after an acute episode; where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan’. NICE did not include specific advice on depot/LAI choice. The only 2nd generation agent included in the NICE evaluation was risperidone LAI. An update to this CG is expected to be published February 2014.
• CQC Standards for medicines Outcome 9 (Regulation 13) – providing personalised care through effective use of medicines. Provide evidence to demonstrate that people who use services receive medicines which are deemed appropriate for them as individuals including monitoring the effect of their medicines and action if necessary if their condition changes, including side effects and adverse reactions.

Implementability
No issues identified.

References
• Scottish Medicines Consortium (SMC) Oct 2011 – includes health economic evidence
• All Wales Medicines Strategy Group (AWMSG) Oct 2012 – includes health economic evidence
• Cochrane Review paliperidone palmitate for schizophrenia (June 2012)
• SPC Paliperidone palmitate (Xeplion®)
  http://www.medicines.org.uk/emc/medicine/24403/SPC/XEPLION+50+mg%2c+75+mg%2c+100+mg+and+150+mg+p+prolonged+release+suspension+for+injection/
• NICE Clinical Guideline for Schizophrenia (CG 82) (March 2009) http://www.nice.org.uk/CG82

Produced by Hertfordshire Pharmacy and Medicines Optimisation Team
Hertfordshire, Bedfordshire and Luton Commissioning Support
NHS Central Eastern Commissioning Support Unit

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