**HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE**

**TOLVAPTAN FOR THE TREATMENT OF HYPONATRAEMIA**

**RECOMMENDED FOR RESTRICTED USE**

<table>
<thead>
<tr>
<th>Name:</th>
<th>What it is</th>
<th>Indication</th>
<th>Date Decision last revised</th>
<th>Decision Status</th>
<th>NICE / SMC Guidance</th>
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<tbody>
<tr>
<td>Tolvaptan (Samsca®)</td>
<td>Selective vasopressin V2 receptor antagonist</td>
<td>Treatment of hyponatraemia secondary to SIADH</td>
<td>November 2010</td>
<td>Final</td>
<td>NICE - No Guidance SMC - Not recommended (absence of submission)</td>
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</tbody>
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**HMMC Recommendation (following further clarification from specialists):**

**RECOMMENDED FOR RESTRICTED USE** as a treatment option for the short-term treatment of hyponatraemia secondary to SIADH in the non-emergency in-patient setting in accordance with the East and North Herts NHS Trust Guidelines for Emergency Management of Adult Inpatients with Hyponatraemia (to be adapted and adopted Hertfordshire wide) in patients:

- who fail to respond to fluid restrictions **AND**
- when demeclocycline is ineffective or contra-indicated

**Initiation, monitoring, titration and prescribing responsibility to remain with secondary care Consultant Endocrinologists as this is a short term specialist treatment.**

- NHS Hertfordshire funding application approval pro-forma to be completed and submitted to NHS Hertfordshire when tolvaptan has been used

**NOT RECOMMENDED FOR:**

- Primary care prescribing (prescribing responsibility NOT to be transferred to GPs)
- Unlicensed indications
- Long-term use (the Samsca® Formulary Pack states that the anticipated average duration of treatment is 4-10 days)

For any long-term use or use for a different indication then a business case will need to be submitted to HMMC

### Efficacy

- Place in therapy is unclear
- Studies demonstrated effectiveness at increasing serum sodium concentrations compared to placebo during the first 4 days and up to 30 days
- Lack of long-term controlled efficacy data
- Limited evidence on comparative effectiveness to fluid restriction and none to possible alternatives

### Safety

- Lack of controlled long-term safety data
- Most common side effects seen in studies were thirst and dry mouth
- Serious adverse events included rash / exanthema, nocturia, urinary frequency, muscle weakness and hypernatraemia

### Cost

- No cost-effectiveness analysis is available
- Significantly more expensive than demeclocycline

### Patient Factors

**Assessment against Ethical Framework**

**Evidence of Clinical Effectiveness:**

- The place in therapy is unclear and there is limited controlled long-term efficacy and safety data
- The main randomised controlled trials showed that tolvaptan was effective in the studied patient population at increasing serum sodium concentrations compared to placebo during the first 4 days and up to 30 days of therapy
- Comparative effectiveness to fluid restriction is limited to one small study
- There is a lack of evidence compared to the possible alternatives demeclocycline, urea or lithium
- The most common side effects seen with tolvaptan were thirst and dry mouth. Serious adverse events leading to withdrawal included rash / exanthema, nocturia, urinary frequency, muscle weakness and hypernatraemia

**Cost of treatment and Cost Effectiveness**

- No cost-effectiveness analysis is available
- Cost of Tolvaptan = £866 per patient (comparative cost of demeclocycline £40) for 12 day treatment period
- The manufacturer’s model anticipates that for the Hertfordshire population 40 patients per year will be treated with tolvaptan. **Therefore total cost for 12 day treatment = £34,652** (cf demeclocycline = up to £1,600)
- The manufacturer suggests possible cost offsets (shorter titration period and reduced inpatient stay) but these assumptions have not been considered by a health economist and were not assessed in the main studies

**The Needs of the population**

- The needs of the population are potentially high as there are only limited alternatives.

**The Needs of the community**

- Needs of the community are low (according to specialists) as specialists expect very few patients to need treatment.
- The cost pressures could be significant depending on duration of therapy.

Evidence considered by the Group: Included London New Drugs Group APC/DTC Briefing Document September 2009