**Name of Medicine / Class (generic and brand)**

| Trimipramine (Surmontil®) |

**Licensed indication(s)**

- Treatment of depressive illness, especially where sleep disturbance, anxiety or agitation are presenting symptoms. Sleep disturbance is controlled within 24 hours and true antidepressant action follows within 7 to 10 days.

**Licensed dose(s)**

- **Adults:** For depression 50-75 mg/day initially increasing to 150-300 mg/day in divided doses or one dose at night. The maintenance dose is 75-150 mg/day.
- **Elderly:** 10-25 mg three times a day initially. The initial dose should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.
- **Children:** Not recommended.

**Purpose of Document**

To review information currently available on this class of medicines, give guidance on potential use and assign a prescribing classification.

**Annual cost (FP10)**

- 10mg three times daily: £6,991
- 25mg three times daily: £7,819
- 150mg daily: £7,410
- 300mg daily: £14,820

**Alternative Treatment Options within Class**

<table>
<thead>
<tr>
<th>Tricyclic Antidepressant</th>
<th>CPCG Formulary Classification</th>
<th>Annual Cost (FP10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (75mg)</td>
<td>Formulary</td>
<td>£36</td>
</tr>
<tr>
<td>Lofepramine (140mg)</td>
<td>Formulary</td>
<td>£146</td>
</tr>
<tr>
<td>Imipramine (75mg)</td>
<td>Non-formulary</td>
<td>£37</td>
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<tr>
<td>Clomipramine (75mg)</td>
<td>Non-formulary</td>
<td>£63</td>
</tr>
<tr>
<td>Trimipramine (75mg)</td>
<td>TBC</td>
<td>£7,819</td>
</tr>
<tr>
<td>Nortriptyline (75mg)</td>
<td>Not Recommended (pain)</td>
<td>£276</td>
</tr>
<tr>
<td>Doxepin (150mg)</td>
<td>TBC</td>
<td>£6,006</td>
</tr>
<tr>
<td>Dosulepin (75mg)</td>
<td>Not Recommended (NICE DO NOT DO)</td>
<td>£19</td>
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</table>

Dosages are based on possible maintenance dose and are not equivalent between medications.

**Recommendation**

It is recommended to Cambridgeshire and Peterborough CCG JPG members and through them to local NHS organisations that the arrangements for use of trimipramine are in line with restrictions agreed locally for drugs designated as NOT RECOMMENDED: DO NOT PRESCRIBE TRIMIPRAMINE ON THE NHS IN CAMBRIDGESHIRE & PETERBOROUGH.

Trimipramine is a dibenzazepine tricyclic antidepressant with actions and uses similar to those of amitriptyline. It has marked antimuscarinic and sedative properties.

Tricyclic antidepressants have similar efficacy to selective serotonin re-uptake inhibitors (SSRIs) but are more likely to be discontinued because of side-effects; toxicity in overdosage is also a problem. SSRIs are less sedating and
Tricyclic antidepressant drugs can be roughly divided into those with additional sedative properties and those that are less sedating. Agitated and anxious patients tend to respond best to the sedative compounds, whereas withdrawn and apathetic patients will often obtain most benefit from the less sedating ones.

Those with sedative properties include amitriptyline hydrochloride, clomipramine hydrochloride, dosulepin hydrochloride, doxepin, mianserin hydrochloride, trazodone hydrochloride, and trimipramine. (italics indicates non-formulary)

Those with less sedative properties include imipramine hydrochloride, lofepramine and nortriptyline.

Tricyclic and related antidepressants also have varying degrees of antimuscarinic side-effects and cardiotoxicity in overdosage, which may be important in individual patients. Lofepramine has a lower incidence of side-effects and is less dangerous in overdosage but is infrequently associated with hepatic toxicity. Imipramine hydrochloride is also well established, but has more marked antimuscarinic side-effects than other tricyclic and related antidepressants.

Amitriptyline hydrochloride and dosulepin hydrochloride are effective but they are particularly dangerous in overdosage and are not recommended for the treatment of depression; dosulepin hydrochloride is not recommended for prescribing in primary care (NICE Do Not Do).

Where a tricyclic antidepressant is required, and depending on the indication, amitriptyline is currently 1st line formulary choice, and lofepramine 2nd line. Where a sedating tricyclic antidepressant is required, and amitriptyline is not a suitable treatment option, clomipramine could be considered (currently non-formulary CPCCG / formulary CPFT)

A review of the literature failed to identify any indications where trimipramine is considered the only pharmacological treatment available. Where trimipramine is indicated alternative cost effective treatment options should be considered.

In general, withdrawal effects may occur within 5 days of stopping treatment with antidepressant drugs; they are usually mild and self-limiting, but in some cases may be severe. The risk of withdrawal symptoms is also increased if the antidepressant is stopped suddenly after regular administration for 8 weeks or more. The dose should preferably be reduced gradually over about 4 weeks, or longer if withdrawal symptoms emerge (6 months in patients who have been on long-term maintenance treatment).

When changing from one antidepressant to another, abrupt withdrawal should usually be avoided. Cross-tapering is preferred, in which the dose of the ineffective or poorly tolerated drug is slowly reduced while the new drug is slowly introduced. The speed of cross-tapering is best judged by monitoring patient tolerability. No clear guidelines are available, so caution is required. If patients are not tolerating, cross taper more slowly.

Across C&PCCG over £164K is spent on trimipramine annually. Alternative cost effective pharmacological treatments are available.
| Local Hospital Formulary Status | NWAFT: Non-formulary  
CUHFT: Non-formulary  
Papworth: Non-formulary  
CPFT: Not listed  
CPCCG: Non-formulary (*under review*) |
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<tbody>
<tr>
<td>Status</td>
<td>Presented to CPJPG July 2017</td>
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| Prepared by                     | Cambridgeshire & Peterborough Medicines Optimisation Team  
[CAPCCG.prescribingpartnership@nhs.net](mailto:CAPCCG.prescribingpartnership@nhs.net) July 2017 |