Lurasidone (Latuda®) Guidelines for Prescribing and Administration
(Version 3 – September 2018)

1. Key Points.

1.1 Lurasidone (oral tablets) is only licensed / indicated for the treatment of schizophrenia in patients aged 18 years and over.

1.2 The NICE Evidence Summary for lurasidone considered it an additional treatment option alongside existing antipsychotics, but considered its place in therapy unclear from the evidence reviewed.

1.3 Lurasidone is approved for third-line use after two previous antipsychotics have been tried, one of which must be aripiprazole, and at least one was effective but not tolerated. Lurasidone must not be used in place of clozapine third-line if two previous antipsychotics have been tolerated and are both ineffective as this is indicative of treatment resistance.

1.4 Alternatively, lurasidone is approved for second-line use in patients identified as having significant metabolic risk factors, e.g. diabetes, obesity. In such circumstances aripiprazole must be tried before lurasidone.

1.5 Lurasidone is not indicated for treatment-resistant schizophrenia, or for bipolar disorder. It must not be used for unlicensed indications.

1.6 Lurasidone may only be newly prescribed by doctors of specialist staff grade or above. Other grades must not initiate therapy or adjust dose without direct instruction from their consultant.

1.7 Lurasidone is intended for once-daily administration, at the same time each day, with a meal. (Note that if taken without food the plasma levels achieved per dose will be significantly lower than intended and this may precipitate reduced efficacy and possibly treatment failure).

1.8 The usual recommended starting dose of lurasidone is 37mg once daily with a meal. (See section 3 for recommendations on dose reduction). Any dose increases should be in 37mg increments (if tolerated) and based on clinical judgement, observed clinical response and tolerability. (Note: increments of 18.5mg are possible, but greatly increase cost).

1.9 The usual recommended maintenance dose range of lurasidone is 37mg to 74mg once daily with a meal. (See section 3 for recommendations on dose reduction). Note that many lurasidone side effects are dose dependent and more likely at higher doses.

1.10 The licensed maximum dose of lurasidone is 148mg once daily with a meal. However, there is limited evidence to support the use of higher doses in the licensed range. (See section 3 for recommendations on dose reduction).

If you require this document in an alternative format, ie, easy read, large text, audio, Braille or a community language please contact the Pharmacy Team on 01243 623349. (Text Relay calls welcome).
2. Prescribing Treatment.

2.1 Lurasidone must not be prescribed as a first-line antipsychotic.

2.2 Lurasidone is approved for third-line use after two previous antipsychotics have been tried. One of them must have been aripiprazole and at least one of them must have been effective but not tolerated, (i.e. the patient is not treatment resistant as defined by NICE). Alternatively, it can be used second-line in patients identified as having significant metabolic risk factors, eg. diabetes, obesity, etc. In such circumstances aripiprazole must have been tried before lurasidone.

2.3 Switching from other oral antipsychotics. There is no specific guidance available regarding switching antipsychotics to or from lurasidone and therefore particular caution should be used whatever method of switching is used. Titrating down and stopping drug 1 and leaving a short interval before starting drug 2 is always considered the safest method although it is recognised that this may increase the risk of loss of symptom control in some patients. Leaving no gap or using cross titration are also common methods of switching and may prove more suitable with close monitoring. If in doubt, advice should be sought from the pharmacy team.

2.4 Switching from long-acting antipsychotic injections (LAIs). There is no specific guidance available regarding switching to lurasidone from an LAI. The potential best method will be dependent on the pharmacokinetics of the LAI and advice should be sought from the pharmacy team.

2.5 Missed doses. Patients on doses higher than 111mg daily that discontinue their treatment or miss doses for more than 3 days should be restarted at 111mg once daily and up-titrated to their optimal dose over a period based on tolerability and observed clinical response. For doses of 111mg daily or lower, patients can be restarted on their previous dose without the need for any titration.

3. Other Dosing Recommendations / Considerations.

3.1 The elderly: Dose recommendations for elderly patients with normal renal function are the same as for younger adults. There are limited data available to support the use of higher doses of lurasidone in the elderly and no data for the 148mg dose. Caution is required if treating elderly patients with higher doses. Lurasidone has not been studied in elderly patients with dementia and therefore should not be used.

3.2 Children & Adolescents: The product is not licensed for use in patients less than 18 years of age as efficacy and safety has not been established.

3.3 Renal impairment: No dosage adjustment is needed in patients with mild renal impairment. In moderate and severe renal impairment, the recommended starting dose is 18.5mg and the maximum dose should not exceed 74mg once daily.

3.4 Hepatic impairment: No dosage adjustment is needed patients with mild hepatic impairment. In moderate and severe hepatic impairment, the recommended starting dose is 18.5mg. In moderate impairment the maximum dose should not exceed 74mg once daily and in severe impairment should not exceed 37mg once daily.

3.5 Concomitant treatment with a potent CYP3A4 inducer or inhibitor: ie. carbamazepine, phenytoin, rifampicin, St John’s Wort, clarithromycin, telithromycin, ketoconazole, itraconazole, posaconazole, protease-inhibitors. **Lurasidone is contraindicated.**

3.6 Concomitant treatment with a moderate CYP3A4 inhibitor: eg. amiodarone, diltiazem, erythromycin, fluconazole, verapamil. Starting dose should be reduced to 18.7mg and the maximum dose should not exceed 74mg once daily. (List of drugs is not exhaustive).
3.7 **Pregnancy and breast-feeding.**
There are limited data regarding the use of lurasidone during pregnancy. Therefore it should not be used unless the potential benefits are assessed as clearly outweighing the risks. It is not known whether lurasidone is excreted in human milk. Therefore it should not be used unless the potential benefits are assessed as clearly outweighing the risks.

4. **Administration.**

4.1 Lurasidone tablets are film-coated and should be swallowed whole in order to mask the bitter taste.

4.2 They should be taken once daily, with a meal, at or around the same time each day to aid compliance. (Lurasidone may not be suitable for patients known to have erratic eating patterns or who are unwilling to take the tablets with a meal).

4.3 Lurasidone tablets must be taken with a meal otherwise levels of absorption are reduced, optimal plasma levels will not be reached and efficacy may be compromised.

5. **Pricing.**

Lurasidone is very expensive when compared to generic oral antipsychotics.

Comparison Prices. (Note: example doses only. No equivalence implied).

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
<th>Cost per 28 days</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>(NHS Drug Tariff: Sep ’18)</td>
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<tr>
<td><strong>Lurasidone</strong></td>
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<tr>
<td>Available as:</td>
<td>37mg once daily</td>
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<tr>
<td></td>
<td>55.5mg once daily</td>
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<td></td>
<td>74mg once daily</td>
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<td></td>
<td>111mg once daily</td>
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<tr>
<td></td>
<td>148mg once daily</td>
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<tr>
<td>Aripiprazole (plain tablets)</td>
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<td></td>
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6. **References.**


**Guidelines prepared by:**

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Chief Pharmacist – Governance & Professional Practice.

Approved by the Drugs & Therapeutics Group (v1): January 2015  
Updated to Version 2: January 2017  
Updated to version 3: September 2018  
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Lurasidone (Latuda®) Information Sheet for GPs

Indication

Lurasidone is a lesser used antipsychotic, currently only licensed for the treatment of schizophrenia in adults. The CCG has approved its use for patients with schizophrenia, (not treatment resistant), if initiated by a specialist. It will normally only be prescribed third-line after two first-line antipsychotics, one of which will have been aripiprazole and one of which must have been effective but not tolerated. In patients with an identified metabolic risk, e.g. diabetes, it can be considered for second-line use. In such situations, aripiprazole should have been tried before lurasidone unless there are compelling reasons not to do so.

Dosing and administration

Lurasidone is taken orally as a tablet after a meal or snack that contains a minimum of 350 calories. Studies have shown that if taken on an empty stomach, the amount of drug absorbed is reduced by around 50%. Lurasidone tablets are film-coated and should be swallowed whole in order to mask the bitter taste.

The dose range is 37mg to 148mg daily. 18.5mg, 37mg and 74mg tablets are available.

Missed doses: Patients on doses higher than 111mg daily that discontinue their treatment or miss doses for more than 3 days should be restarted at 111mg once daily and up-titrated to their optimal dose over a period based on tolerability and observed clinical response. For doses of 111mg daily or lower, patients can be restarted on their previous dose without the need for any titration.

The elderly: Dose recommendations for elderly patients with normal renal function are the same as for younger adults. There are limited data available to support the use of higher doses of lurasidone in the elderly and no data for the 148mg dose. Caution is required if treating elderly patients with higher doses. Lurasidone has not been studied in elderly patients with dementia and therefore should not be used.

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Concomitant treatment with a potent CYP3A4 inducer or inhibitor: i.e. carbamazepine, phenytoin, rifampicin, St John’s Wort, clarithromycin, telithromycin, ketoconazole, itraconazole, posaconazole, protease-inhibitors. Lurasidone is contraindicated.

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Evidence summary

This is based on the two randomised controlled trials (Meltzer et al. 2011 and Citrome et al. 2012) that provide the best published evidence for lurasidone for treating schizophrenia.

Effectiveness

From these two studies, both of which have limitations, lurasidone appears to be statistically significantly more effective than placebo and of similar effectiveness to olanzapine and risperidone.

Adverse effects

Lurasidone, olanzapine and risperidone appear to have broadly similar rates of adverse events, although the adverse event profiles of the drugs differ. Meltzer et al. 2011 found that in a 6 week study, the proportion of participants experiencing at least one adverse event was broadly similar across all groups (around 78%). Akathisia and Parkinsonism were more commonly seen with lurasidone, and weight gain and dry mouth were more commonly seen with olanzapine. Citrome et al. 2012 found that the proportion of participants reporting one or more adverse events over 12 months was very similar in the lurasidone and risperidone groups (84.5% and 84.7% respectively). More participants in the lurasidone group reported nausea, vomiting and akathisia, while more participants in the risperidone group reported constipation and weight gain. In both studies, lurasidone appeared to have a low potential for causing adverse weight and metabolic effects.

Mechanism of action

Lurasidone is a second-generation antipsychotic. Although its mechanism of action in schizophrenia is unknown, lurasidone is thought to work by binding to dopamine and serotonin receptors in the brain, mostly as an antagonist (US Food and Drug Administration [FDA]).

References


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