

lurasidone, 18.5mg, 37mg, 74mg film-coated tablets (Latuda[®])

SMC No. (994/14)

Sunovion

05 September 2014

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in Scotland. The advice is summarised as follows:

ADVICE: following a full submission

lurasidone (Latuda[®]) is accepted for restricted use within NHS Scotland.

Indication under review: For the treatment of schizophrenia in adults aged 18 years and over.

SMC Restriction: as an alternative treatment option in patients in whom it is important to avoid weight gain and metabolic adverse effects.

Lurasidone demonstrated benefit over placebo in mean change from baseline in Positive and Negative Syndrome Scale (PANSS) total score after six weeks of treatment and was non-inferior to another second generation antipsychotic medicine for time to relapse over 12 months.

Overleaf is the detailed advice on this product.

**Chairman,
Scottish Medicines Consortium**

Indication

For the treatment of schizophrenia in adults aged 18 years and over.

Dosing Information

The recommended starting dose of lurasidone is 37mg once daily. No initial dose titration is required. Lurasidone is effective in a dose range of 37 to 148mg once daily. Dose increase should be based on physician judgement and observed clinical response. The maximum daily dose should not exceed 148mg.

Patients on doses higher than 111mg once daily who discontinue their treatment for longer than three days should be restarted on 111mg once daily and up-titrated to their optimal dose. For all other doses patients can be restarted on their previous dose without need for up-titration.

Lurasidone tablets should be taken with a meal because it is anticipated that if taken without food its exposure would be significantly lower. The tablets should be swallowed whole, to mask the bitter taste, and should be taken at the same time every day to aid compliance.

(In this document lurasidone doses are expressed as lurasidone base. Equivalent doses of lurasidone base and the hydrochloride salt are 18.5mg=20mg, 37mg=40mg, 74mg=80mg, 111mg=120mg and 148mg=160mg).

Product availability date

11 August 2014

Summary of evidence on comparative efficacy

Lurasidone is a second generation (atypical) antipsychotic agent that inhibits the effects of dopamine and 5-hydroxytryptamine.¹ The submitting company initially requested that the Scottish Medicines Consortium (SMC) assesses lurasidone when positioned for the treatment of adults with schizophrenia who have previously failed treatment with other atypical antipsychotics due to metabolic side effects, and who are at risk of metabolic adverse events.

The evidence is from four studies in patients with an acute exacerbation of schizophrenia: three 6-week double-blind randomised controlled studies (one of which included a 12-month blinded extension study) and a double-blind randomised controlled withdrawal study; and one active-controlled study in clinically stable schizophrenic patients primarily to investigate safety.^{2,3,4,5,6,7,8}

The three 6-week studies (D1050233, D1050231 and D1050229) had similar designs and inclusion criteria.^{3,4,5} Patients were aged 18 to 75 years and had recently been admitted to hospital for an acute exacerbation of psychotic symptoms starting within the previous two months; with a primary diagnosis of schizophrenia of duration >1 year; Clinical Global Impression, Severity (CGI-S) score ≥ 4 (moderate or greater) and a Positive and Negative Syndrome Scale (PANSS) total score ≥ 80 , including a score ≥ 4 (moderate) on two or more of the following PANSS items: delusions, conceptual disorganisation, hallucinations, unusual thought content and suspiciousness.

After screening and placebo washout, patients were randomised equally to receive daily doses of lurasidone 74mg, lurasidone 148mg, quetiapine XR 600mg or placebo in D1050233; lurasidone 37mg; lurasidone 111mg; olanzapine 15mg (initially 10mg daily for one week) or placebo in D1050231 and lurasidone 37mg, lurasidone 74mg, lurasidone 111mg or placebo in D1050229. The main reason for inclusion of the quetiapine XR and olanzapine groups was to test for assay sensitivity.

The primary outcome in all three studies was least squares (LS) mean change from baseline in PANSS total score at week 6 analysed in the intention to treat (ITT) population. PANSS is a validated 30-item scale (range 30 to 210, higher scores indicate worsening) to assess symptoms of schizophrenia.¹

Table 1 Primary outcomes in 6-week studies^{3,4,5}

PANSS total score LS mean change	Lurasidone 37mg	Lurasidone 74mg	Lurasidone 111mg	Lurasidone 148mg	Quetiapine XR 600mg	Olanzapine	Placebo
D1050233 (n=488)		-22.2**		-26.5**	-27.8*		-10.3
D1050231 (n=478)	-25.7*		-23.6*			-28.7**	-16.0
D1050229 (n=500)	-19.2	-23.4*	-20.5				-17.0

PANSS=Positive and Negative Symptoms Scale; LS=least squares; SE=standard error

*p<0.05 versus placebo; **p<0.001 versus placebo

There was a statistically significant improvement over placebo for all active treatments in all three 6-week studies in the key secondary outcome of CGI-S, except for the lurasidone 37mg and 111mg groups in D1050229. In D1050233 and D1050231, all active treatments showed significantly greater improvement over placebo at six weeks in the PANSS positive and negative sub-scores.^{3,4,5}

Patients who successfully completed the D1050233 6-week study (treatment responders) could enter a double-blind extension study, D1050234, in which the primary outcome was to demonstrate non-inferiority of lurasidone to quetiapine XR for probability of relapse over 12 months.⁶ The primary analysis population comprised patients who had been randomised to active drug in the initial study and who met clinical response criteria on Day 42, defined as $\geq 20\%$ reduction in PANSS total score from acute study baseline and a CGI-S ≤ 4 at Day 42. Relapse was defined as the earliest occurrence of any of the following 3 criteria: (1) worsening of $\geq 30\%$ in the PANSS total score from Day 42 of the initial acute treatment study and a CGI-S ≥ 3 ; (2) re-hospitalisation for worsening of psychosis; or (3) emergence of suicidal ideation, homicidal ideation and/or risk of harm. Of the 353 patients who completed the initial 6-week study, 292 (83%) entered the extension study: 151 patients continued to receive lurasidone, 85 patients continued to receive quetiapine XR, and 56 patients treated with placebo in the initial study started treatment with lurasidone. In the extension study, flexible doses of lurasidone (37 to 148mg daily) and quetiapine XR (200 to 800mg daily) were used. Kaplan–Meier estimates of the probability of relapse at 12 months were 24% for the lurasidone group and 34% for the quetiapine XR group; hazard ratio (HR) 0.73 (95% confidence interval [CI]: 0.41 to 1.30). As the upper limit of the 95% CI of the HR was below the pre-specified margin (1.93), non-inferiority of lurasidone to quetiapine XR was concluded. The secondary outcome of PANSS total score continued to decrease throughout the extension study in the group that had received lurasidone in the acute study; -5.0, (95% CI: -7.8 to -2.1), while it increased in the quetiapine XR group; 1.7 (95% CI: -2.4 to 5.9). The PANSS positive subscale showed a similar pattern. There was no significant difference in CGI-S, PANSS negative subscale or negative symptom assessment (NSA)-16 in the group that received lurasidone throughout both studies compared with the group that received quetiapine XR.⁶

D1050238 was a double-blind, randomised, placebo-controlled withdrawal study with a screening/washout and open-label stabilisation phase (up to 24 weeks), a double-blind, randomised withdrawal phase (up to 28 weeks) and a follow-up 12-week open-label extension.² Patients were aged between 18 and 75 years with a primary diagnosis of schizophrenia and experiencing an acute episode of schizophrenia; had ≥ 1 prior episode of psychotic exacerbation (investigator evaluated) in the previous two years; had a PANSS total score ≥ 80 with a score ≥ 4 on at least one PANSS positive subscale item and a CGI-S score of ≥ 4 ; had good physical health and stable living arrangements and agreed not to take prior antipsychotic medication throughout the study. In the open-label stabilisation phase, patients received flexibly-dosed lurasidone 37mg to 74mg daily. Patients who responded and remained clinically stable for at least 12 weeks could enter the double-blind phase and be randomised (1:1 ratio) to receive the same dose of lurasidone as at the end of the open-label period, or matching placebo. Inclusion criteria for the double-blind phase were: PANSS total score ≤ 70 ; CGI-S score < 4 , and a score of ≤ 4 on all PANSS positive subscale items over ≥ 12 weeks although two excursions were permitted. Patients also had a PANSS item score of ≤ 4 on item G8 (uncooperativeness) and were taking a stable dose of lurasidone for the last four weeks of the open-label phase.²

Discontinuation rates were extremely high. Of the 676 patients who entered the open-label stabilisation phase, 42% (285/676) entered the double-blind withdrawal phase and were randomised to receive lurasidone (n=144) or placebo (n=141). Only 19% of patients receiving lurasidone and 14% of patients receiving placebo completed the double-blind phase.²

The primary outcome (ITT population) was the time to the first relapse event defined as at least one of the following during the double-blind phase:

- An increase from double-blind phase baseline in both PANSS total score of $\geq 25\%$ and a CGI-S worsening of ≥ 1 point, for two consecutive visits, occurring ≤ 10 days apart.
- At any single visit, a PANSS item score of ≥ 5 (moderately severe) on hostility or uncooperativeness, or PANSS item score ≥ 5 on ≥ 2 items of unusual thought content, delusions, conceptual disorganisation, or hallucinatory behaviour.
- Protocol-specified treatment interventions

Fewer patients relapsed in the lurasidone group, 30% (43/144), than in the placebo group, 41% (58/141). Kaplan-Meier estimates of the probability of relapse by week 28 were 0.42 and 0.51 for lurasidone and placebo, respectively, and overall there was a statistically significant increase in the time to relapse for lurasidone compared with placebo (p=0.039).² During the double-blind phase, there were smaller increases in PANSS total score and in CGI-S scores for lurasidone versus placebo which were both statistically significant.²

D1050237 was a 12-month randomised, double-blind safety study comparing lurasidone with risperidone in 629 clinically stable adult outpatients with schizophrenia.⁸ Efficacy outcomes were secondary endpoints, however the study was powered to test the non-inferiority of lurasidone relative to risperidone on the basis of the assumption of expected relapse rates of PANSS and CGI-S scores.¹⁴ After a screening/washout period, patients were randomised in a 2:1 ratio to receive lurasidone (74mg daily for 7 days then flexibly dosed 37mg to 111mg daily) or risperidone (2mg daily for 2 days then 4mg daily for five days then flexibly dosed 2mg to 6mg daily). Study medication was taken once daily within 30 minutes of breakfast although patients who experienced sedation could take the study medication with their evening meal.⁸

A numerically, but not statistically significantly, higher proportion of patients receiving lurasidone than risperidone experienced relapse (defined as for D1050238): 20% (82/410) of patients versus 16% (32/198), respectively. As the number of relapses was much lower than anticipated, it was not possible to interpret the non-inferiority test. There was no significant difference between the groups in PANSS total score: lurasidone group – 4.7 (95% CI: – 6.4 to – 3.0) and risperidone group – 6.5 (95% CI: – 8.8

to – 4.3); or in CGI-S score: lurasidone group – 0.4 (95% CI: – 0.5 to – 0.3) and risperidone group – 0.4 (95% CI: – 0.5 to – 0.2); or in Montgomery-Asberg Depression Rating Scale (MADRS) total score: lurasidone group – 0.8 (95% CI – 1.6 to – 0.0) and risperidone group – 2.4 (95% CI: – 3.4 to – 1.4).⁸

Summary of evidence on comparative safety

In the 6-week D1050233 study and its 12-month open-label extension, D1050234, comparable proportions of patients receiving lurasidone and quetiapine reported adverse events.^{3,6} During the extension study higher rates of adverse events in the lurasidone versus quetiapine groups included akathisia (13% versus 2.4%) and parkinsonism (6.0% versus 0). Clinically significant weight gain ($\geq 7\%$) was reported in similar proportions of patients receiving lurasidone and quetiapine; (12% versus 15%).⁶

After 12-months treatment in the D1050237 study, similar proportions of patients in the lurasidone and risperidone groups reported adverse events and serious adverse events. Discontinuations due to adverse events were higher in patients receiving lurasidone than risperidone; 17% versus 11%, respectively. Higher rates of adverse events in the lurasidone versus risperidone groups included nausea (17% versus 11%); akathisia (14% versus 7.9%); vomiting (10% versus 3.5%). Weight gain was reported in fewer patients in the lurasidone than risperidone groups (9.3% versus 20%).⁸

In the 6-week D1050231 study, similar proportions of patients in the lurasidone and olanzapine groups reported adverse events. Higher rates of adverse events reported in the lurasidone 37mg and 111mg groups compared with the olanzapine 15mg group included akathisia (12% and 23% versus 7.4%) and parkinsonism (9.2% and 11% versus 4.9%). Lower rates of weight gain were reported in the lurasidone groups than in the olanzapine group (1.7% and 1.7% versus 20%).⁴

Overall lurasidone appears to have a favourable safety profile in terms of metabolic parameters such as glucose and lipids. Treatment with lurasidone produced higher rates of akathisia than quetiapine, risperidone and olanzapine and higher rates of parkinsonism than quetiapine and olanzapine. Nausea was more common with lurasidone than with the other three drugs.

Summary of clinical effectiveness issues

Schizophrenia is a severe, debilitating psychiatric illness that affects approximately 1% of the global population. It is the fourth leading cause of disability in the developed world for ages 15 to 44 years, inclusive. Schizophrenia reduces life expectancy by approximately 10 years, mostly as a consequence of suicide.² The submitting company initially requested that SMC assesses lurasidone when positioned for the treatment of adults with schizophrenia who have previously failed treatment with other second generation antipsychotics due to metabolic side effects, and who are at risk of metabolic adverse events. Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area, namely drugs that do not cause metabolic adverse events.

The submission included study evidence versus placebo and active comparators in several acute and longer term studies. In the short-term studies, lurasidone demonstrated benefit over placebo in the primary efficacy outcome of mean change from baseline to Week 6 in PANSS total score which is a validated symptom scale in schizophrenia studies.⁹ European Medicines Agency guidance states that a reduction of $\geq 30\%$ on the PANSS total score compared to baseline is generally considered to be clinically relevant.⁹ Mean baseline PANSS total scores were 96 to 97 for the three 6-week studies, therefore the treatment effect over placebo was slightly less than 30% in all the studies. The European Assessment Report (EPAR) concluded that the short term efficacy of lurasidone had been sufficiently

justified and did not differ by an important margin from that of the other antipsychotics. It also noted that no consistent dose-response was observed in the short-term studies.² The long-term withdrawal study showed that lurasidone slowed relapse compared with placebo.² Non-inferiority to quetiapine XR for time to relapse was shown in the long-term extension study, D1050234, despite the limitation that the study was not fully randomised.⁶ Study D1050237 failed to demonstrate that lurasidone was non-inferior to risperidone.⁸

No evidence of efficacy was provided specifically in the population relevant for the company's proposed positioning, i.e. patients who have previously failed treatment with other second generation antipsychotics due to metabolic side effects, and who are at risk of metabolic adverse events. However, after the New Drugs Committee meeting, the company requested that SMC consider lurasidone in a revised positioning, namely as a treatment alternative when it is important to avoid weight gain and metabolic adverse events among adults with schizophrenia.

The submitting company considers aripiprazole to be the main comparator to lurasidone for the revised positioning. This concurs with advice from clinical experts. There was no direct study evidence comparing lurasidone with aripiprazole. An indirect comparison of lurasidone with aripiprazole in the acute treatment of schizophrenia (6-week studies) came from an independent, recently published Bayesian mixed treatment comparison (MTC) of 15 antipsychotic drugs and placebo.¹⁰ It included 212 blinded, randomised controlled studies with a total of 43,049 patients with schizophrenia or related disorders. The primary outcome was efficacy as measured by mean overall change in symptoms (PANSS or Brief Psychiatric Rating Scale). A random effects model was used.¹⁰ In terms of overall change in symptoms, or all-cause discontinuation, after six weeks of treatment, there was no significant difference between lurasidone and aripiprazole and both were better than placebo. Weight gain with lurasidone was not significantly different to placebo or aripiprazole; however, due to the short treatment duration, this result should be viewed cautiously. Treatment with lurasidone resulted in significantly more extrapyramidal symptoms and significantly larger increases in prolactin than aripiprazole.¹⁰

The submitting company also commissioned an indirect comparison of several antipsychotic drugs in the longer term treatment of schizophrenia.¹¹ Although described in the submission as an adjusted multi-step indirect comparison between lurasidone and aripiprazole, the only data used from this indirect comparison in the economic case were hazard ratios of aripiprazole versus quetiapine for long term discontinuation and relapse. No data from this indirect comparison relating to lurasidone were included in the economic case.

The proportions of white patients in the main studies in the clinical programme were much lower than in the Scottish population: 36% to 60% in the studies described above. This may be relevant as the prevalence of diabetes is higher in some ethnic groups.¹² The number of elderly (>65 years) patients in the clinical program was low, and certain patient groups, including patients with clinically significant cardiovascular disease, active epilepsy or Parkinson's disease, were excluded from the clinical studies which limits the generalisability of the results.

The chronic nature of schizophrenia necessitates long-term treatment with antipsychotic medications. Up to 80% of outpatients with schizophrenia discontinue their treatment due to lack of efficacy, side effects, or non-adherence, so there is a need for additional treatments that are effective and well tolerated.² Lurasidone is associated with more extrapyramidal symptoms and prolactin increase but with lower weight gain than some second generation antipsychotics. Clinical experts consulted by SMC considered that the place in therapy of lurasidone is as an alternative choice when it is important to avoid weight gain and metabolic adverse events.

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis comparing lurasidone with aripiprazole as a primary comparison and quetiapine as a secondary comparison, for its initial positioning for the treatment of adults with schizophrenia who have previously failed treatment with other atypical antipsychotics due to metabolic side effects, and who are risk of metabolic adverse events. Based on SMC expert clinical feedback the comparators are appropriate for current clinical practice in Scotland; however, the experts did also highlight that other treatments may be used in clinical practice such as olanzapine.

A Markov model was used with two phases: an acute phase and a maintenance phase. Initially, the patient enters the acute phase where the patient has relapsed and is trying a new treatment. After the cycle length of 6 weeks, the patient may enter the stable health state. Patients who have discontinued treatment at this point switch treatment and re-enter at the beginning of the model. If patients discontinue treatment at a later date after the first 6 weeks it is assumed the patient will not receive treatment until they relapse and they enter the stable/non adherent state. Transition to death can happen from all of the health states. In addition, health-related quality of life and the costs associated with weight gain, extrapyramidal symptoms and diabetes were included in the model.

The clinical evidence to support the economic model in the acute phase for the comparison with quetiapine was taken from the short-term (D1050233) placebo controlled and the long-term (D1050234) comparator controlled studies, as described above. Clinical evidence for the acute phase for the comparison with aripiprazole was drawn from an independent, Bayesian MTC of 15 antipsychotic drugs and placebo. As noted above the results of the MTC showed no significant difference in efficacy or weight gain for the comparison with aripiprazole, however numerical differences were included in the model. The results did show a significant difference in weight gain in favour of lurasidone for the comparison with quetiapine, but no significant difference in efficacy outcomes. The submitting company performed and presented an indirect comparison of several antipsychotics, as described above which were included for outcomes past 6 weeks. Only data comparing aripiprazole versus quetiapine were used in the economic model. The data from the indirect comparison for the primary comparison with aripiprazole and patient level data used for the secondary comparison with quetiapine were extrapolated using parametric functions for the efficacy outcomes of relapse and all-cause discontinuation over the 10 year time horizon. For the comparison with aripiprazole, there was a lack of a common definition of relapse identified from the studies included in the indirect comparison so all-cause hospitalisation was used as a proxy for relapse in the model.

The utility values were combined from two published studies which used standard gamble and visual analogue scale techniques to elicit utility values for relapse, stable, weight gain and extrapyramidal symptoms. Another source was used to determine the disutility for diabetes. A range of costs was included such as drug acquisition costs, adverse events costs, cost of residential care, costs associated with relapse and costs for outpatient, primary and community care.

The submitting company estimated that in the base case analysis for the primary comparison with aripiprazole, lurasidone was dominant (i.e. more effective and less costly). This was based on a small increase in quality-adjusted life-years (QALYs) of 0.005 and a cost saving of £3,864. For the secondary comparison with quetiapine, lurasidone was also dominant. This was based on a QALY gain of 0.01 and a cost saving of £2,509 compared with quetiapine. The main area driver of the costs savings for both comparisons is reduced relapse with lurasidone, for both inpatient and Crisis Resolution Home Treatment Team (CRHTT) relapse.

A range of sensitivity analyses was performed. The results for the primary comparison of lurasidone and aripiprazole showed that the only scenario where the results were sensitive and aripiprazole became dominant was when no difference in relapse rates was assumed. For the comparison of lurasidone and quetiapine, lurasidone remained dominant in all scenarios.

The following weaknesses were noted:

- As noted above there is a lack of evidence to support the use of lurasidone in the company's initial proposed positioning. To address this concern, following NDC, the company suggested an alternative positioning where lurasidone would be considered as an alternative choice when it is important to avoid weight gain and metabolic adverse events among adults with schizophrenia.
- There is some uncertainty associated with the clinical data used in the economic model as there are weaknesses with the MTC showing comparable efficacy to the primary comparator which underpins the economic case. The additional analysis provided by the company which removed the non-significant differences was more appropriate, and in this analysis, for the primary comparison of lurasidone versus aripiprazole, lurasidone is £72 cheaper but no more effective. For the comparison with quetiapine, the incremental cost-effectiveness ratio (ICER) is £143,950 with an incremental cost of £1,003 and a QALY gain of 0.007, with the QALY gain being driven by a significant difference in weight gain, but the change in positioning by the company suggests that the comparison with aripiprazole is the more relevant analysis. Despite these issues, the economic case has been demonstrated.

Summary of patient and public involvement

A Patient Interest Group Submission was not made.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published national clinical guideline SIGN 131, Management of schizophrenia, in March 2013.¹³ It states:

In service users with an acute exacerbation or recurrence of schizophrenia, prescribers should consider amisulpride, olanzapine or risperidone as the preferred medications with chlorpromazine and other low-potency first-generation antipsychotics providing suitable alternatives. Individuals with schizophrenia which is in remission should be offered maintenance treatment with antipsychotic medication for a minimum of two years. Haloperidol, aripiprazole or amisulpride should be considered for service users who are particularly concerned about weight gain, or who may be at the greatest risk of weight gain.

Following initiation of an antipsychotic medication for service users in the first episode of psychosis, the medication should be continued for at least two weeks unless there are significant tolerability issues. Assessment of dose and response should be monitored during the early phase of prescribing. Where there is poor response to medication there should be an assessment of medication adherence and inter-current substance misuse before the lack of response can be definitively established. If there is no response to medication after four weeks, despite dose optimisation, a change in antipsychotic should be considered. Where there is partial response, this should be re-assessed after eight weeks unless there are significant adverse effects.

Individuals with schizophrenia which is in remission should be offered maintenance treatment with an antipsychotic medication. This should usually be with the medication that was used during their last acute episode, assuming efficacy and tolerability. For maintenance treatment, prescribers should consider amisulpride, olanzapine or risperidone as the preferred medications with chlorpromazine and other low-potency first-generation antipsychotics providing suitable alternatives. Individuals with schizophrenia which is in remission should be offered maintenance treatment with antipsychotic medication for a minimum of two years.

The decision to switch antipsychotic medication should take into account the risk of destabilisation and adverse effects and the dose of medications should be gradually cross tapered.

People with schizophrenia will benefit from reduced relapse rates if they remain on antipsychotic medication. This benefit may only apply to one third to two thirds of people, however, and there is no reliable method of distinguishing between those who will benefit and those who will relapse in any case. The clinical factors which tend to be associated with an increased chance of relapse, such as illness severity, lack of insight, and substance misuse are also those which predict poor adherence to medication. No particular drug or class is conclusively better in terms of efficacy, overall adverse effect burden, or at reducing relapse rates, than any other.

The National Institute for Health and Care Excellence (NICE) published Psychosis and schizophrenia in adults: a Treatment and management National Clinical Guideline Number 178 in 2014.¹⁴

The British Association for Psychopharmacology (BAP) published Evidence-based guidelines for the pharmacological treatment of schizophrenia in 2011. They note that amongst all of the available antipsychotic drugs none has emerged as superior in preventing relapse. In practice, choice of maintenance treatment for the individual patient may be more a question of the correct dose and formulation than of drug group.¹⁵

Additional information: comparators

Experts consulted by SMC indicate that aripiprazole is the relevant comparator as it would be used where avoidance of weight gain/metabolic adverse events is important.

Cost of relevant comparators

Drug	Dose Regimen (after initial titration if required)	Cost per year (£)
Lurasidone	Orally 37 to 148mg once daily	1,180 to 2,359
Paliperidone	Orally 3 to 12mg daily	1,265 to 2,529
Aripiprazole	Orally 10 to 30mg once daily	1,249 to 2,497
Amisulpride	Orally up to 1,200mg daily in two divided doses	Up to 360
Quetiapine	Orally 300 to 750mg daily in two divided doses	92 to 170
Olanzapine	Orally 5 to 20mg daily	23 to 61
Risperidone	Orally 4 to 6mg once daily or in two divided doses	15 to 26

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 19.06.14 except for paliperidone from MIMS online on 25.06.14 and cost of lurasidone from the submitting company.

Additional information: budget impact

The submitting company estimated the population eligible for treatment with lurasidone to be 18,417 patients in year 1 rising to 19,800 in year 5, with an estimated uptake rate of 0.3% in year 1 and 2.5% in year 5.

The gross impact on the medicines budget was estimated to be £63k in year 1 increasing to £688k in year 5. As other drugs were assumed to be displaced, the net medicines budget impact was estimated to be £38k in year 1 increasing to £412k in year 5. The net medicines budget impact reflected displacement of both aripiprazole and quetiapine. It should be noted that these estimates are based on the original positioning proposed by the submitting company.

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

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13. SIGN 131 • Management of schizophrenia A national clinical guideline March 2013
14. The National Institute for Health and Care Excellence (NICE) Psychosis and schizophrenia in adults: a Treatment and management National Clinical Guideline Number 178 2014.

15. Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology Thomas RE Barnes and the Schizophrenia Consensus Group of the British Association for Psychopharmacology Journal of Psychopharmacology 25 (5) 567–620 2011

This assessment is based on data submitted by the applicant company up to and including 15 August 2014.

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.