

Escitalopram (Lexapro) for major depressive disorder

Summary

PBS listing

Restricted benefit: Major depressive disorders.

Reason for listing

Escitalopram was listed on the basis of cost-minimisation compared to citalopram. Escitalopram was considered to have similar — not superior — efficacy to citalopram.

Place in therapy

Escitalopram is not a new concept; it is merely the active isomer of the antidepressant, citalopram. On existing evidence, little difference to citalopram is expected.

For patients whose depression is well-managed on citalopram or another selective serotonin re-uptake inhibitor (SSRI) there is no reason to change to escitalopram. Similarly, patients who have a poor response or adverse effects with citalopram are unlikely to do any better with escitalopram.

Safety issues

The safety profile of escitalopram appears to be similar to that of citalopram. No unexpected adverse events have occurred in the short-term studies of escitalopram conducted to date.

Escitalopram is an SSRI, and has similar drug interactions. In particular, do not prescribe with: other serotonergic agents, including tramadol and sumatriptan; or MAO inhibitors. Using other antidepressants concurrently is not recommended and a washout period may be required. This includes complementary medicines used for depression such as St John's Wort.

Dosing issues

- Escitalopram 10 mg is the usual effective dose, and is equivalent to citalopram 20 mg.
- Escitalopram doses should not exceed 20 mg. As with any SSRI, trial at the minimum effective dose for at least 4 to 6 weeks before changing treatment.
- Adverse effects are dose-related.

PBS Listing

Restricted benefit Major depressive disorders.

Reason for PBS Listing

Efficacy of escitalopram and citalopram were similar — superiority was not demonstrated. Therefore, the PBAC recommended listing escitalopram on the basis of cost-minimisation compared with citalopram. At the proposed pricing, escitalopram would cost the PBS slightly less than citalopram. However if prescribing of higher doses increases with escitalopram, the cost to the PBS will increase compared to citalopram.

Place in therapy

Escitalopram is listed for the treatment of major depressive disorder only.

Evidence for the effectiveness of antidepressant medication in less severe depression is lacking. (See *Therapeutic Guidelines: Psychotropic* for diagnostic criteria for major depression.)

Escitalopram does not have a novel mechanism of action, but is merely the active isomer of the SSRI antidepressant, citalopram (See *Isomer drugs below*). To date, no significant advantage over citalopram has been shown.¹

Compared to existing therapy

For patients well managed on citalopram or another SSRI, there is no reason to change to escitalopram. Similarly, patients with a poor response or adverse effects on citalopram are unlikely to benefit from escitalopram.

There is no evidence to suggest greater efficacy of escitalopram compared with equipotent doses of citalopram. Evidence of superiority was not presented to PBAC and was not the basis of PBS listing.

All SSRIs have similar efficacy,^{2,3} and there is no reason to expect escitalopram to be any different. Like citalopram, escitalopram does not affect uptake of noradrenaline, dopamine or GABA — hence it is a highly selective serotonin inhibitor.⁴ However, this has not resulted in a therapeutic advantage over other SSRIs and as stated in the Cipramil product information, the clinical relevance of this *in vitro* finding has not been established.

Role of non-drug therapy

Cognitive behavioural therapy or supportive psychotherapy can be considered for patients with mild-to-moderate major depression and medication may not be required.

However in severe or melancholic major depression, psychological treatment alone is not recommended as first-line treatment.³

Isomer drugs

What is an active isomer?

Some drug molecules are made up of pairs of isomers or stereoisomers. Like left and right hands, stereoisomers are mirror images of identical structures and are referred to as the 'S' (left) and 'R' (right) isomers. Hence **escitalopram** is the **S**-isomer of citalopram. S and R isomers can have different properties — in citalopram, the S-isomer is responsible for most of the serotonergic activity.⁴

How to assess the value of an 'isomer' drug

Creating medicines from single isomers of known drugs is an expanding area of pharmaceutical development — e.g. esomeprazole and omeprazole. The relationship between the parent drug and its isomers differs from drug to drug. Frequently one of the isomers has most of the activity. In theory, isolating the active isomer may potentially improve a drug by reducing adverse effects or interactions. However isomer derivatives can also cause more adverse effects.⁵

Commercial advantages include the ability to create a new product with lower than usual development costs,⁵ and to protect market share when a medicine nears patent expiry, by patenting a "new" drug.⁶

Evaluating 'isomer' drugs^{5,6}

Question	Answer for escitalopram
Does selecting one isomer	
• Eliminate any adverse effects?	No adverse effects eliminated.
• Remove important drug interactions?	No drug interactions eliminated.
• Enhance the clinical effect?	Not better than citalopram.
Have equipotent doses been used in comparison trials?	Yes. ^{1,7}
Is there good evidence that the isomer drug has any therapeutic advantage over equipotent doses of the parent drug?	Comparisons of escitalopram and citalopram show similar efficacy. ^{1,7} There is no good evidence of a therapeutic advantage.
Does the isomer drug cost more, and is the cost justified by projected benefits?	Escitalopram is similarly priced to generic citalopram, which is reasonable since there is no proven advantage.

Potency and the dose in milligrams — 10 is not less than 20

Escitalopram 10 mg is equivalent to citalopram 20 mg. There is no advantage in prescribing a smaller escitalopram dose, because the dose of the active isomer is the same as with citalopram 20 mg.

Within the citalopram molecule, the S-isomer is more active and therefore more 'potent' than the R-isomer, but this bears no relation to the clinical comparison of escitalopram and citalopram. One comparative trial found no difference in effectiveness between escitalopram 20 mg and the equipotent dose of citalopram.¹

As with any SSRI, the likelihood of adverse events increases with higher doses. (See Adverse Drug Reactions)

Safety issues

Assumptions about long-term safety for escitalopram are based on experience with citalopram. The safety profiles of escitalopram and citalopram appear to be similar.

Adverse Drug Reactions

Adverse effects can be expected to be similar for escitalopram and citalopram at equipotent doses. No unexpected adverse events have occurred in the short-term 8-week trials conducted to date,^{1,7,8} but there are no long-term safety data for escitalopram.

The most common adverse events in patients taking escitalopram included nausea, increased sweating, insomnia, ejaculatory disorder, diarrhoea, dry mouth and somnolence.^{1,7}

Higher doses of most SSRIs increase the likelihood of adverse effects. The increase in adverse events with higher doses is shown in Table 2.

Table 2: Adverse events with citalopram and escitalopram¹

	Placebo	Escitalopram 10 mg/day*	Escitalopram 20 mg/day*	Citalopram 40 mg/day*
Discontinued due to adverse events:	3%	4%	10%	9%
		No different to placebo	Significantly higher than placebo ($p \leq 0.05$)	
Rate of adverse events	71%	79%	86%	86%
		No different to placebo	Significantly higher than placebo ($p \leq 0.01$)	

* Note: 20 mg citalopram was not tested in this trial

Drug interactions

Serotonergic drugs such as tramadol, sumatriptan, and other SSRIs can increase serotonergic effects and should be avoided while using escitalopram. St John's Wort (*Hypericum perforatum*) interacts with a number of prescription medicines including antidepressants. SAMe (S-adenosylmethionine), a complementary medicine for depression and arthritis, is also thought to interact with tricyclic antidepressants and may have serotonergic properties.⁹

As with any SSRI, monoamine oxidase inhibitors are contraindicated and a washout period is required when changing between these drugs and escitalopram. See the Australian Medicines Handbook,² or the Lexapro product information for more information on interactions.

Dosing issues

Dose-equivalence for escitalopram and citalopram

Escitalopram		Citalopram
10 mg	equivalent to	20 mg
20 mg	equivalent to	40 mg*

*Note that higher doses of SSRIs are not necessarily more effective and carry an increased risk of adverse events.

Based on experience with citalopram, escitalopram 10 mg should be sufficient to manage most depression. A small proportion of patients with particularly severe depression may require the higher dose (20 mg). However, as with any SSRI, trial at the minimum effective dose for at least 4–6 weeks before changing treatment. Allow 2–4 weeks between dose increases and taper doses gradually when reducing doses or discontinuing.³

Remember that most adverse effects are dose-related. Doses of escitalopram should not exceed 20 mg, or 10 mg for the elderly.

Information for patients

For more detailed information, suggest or provide the Lexapro Consumer Medicine Information (CMI).

References

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the individual clinical circumstances of each patient.

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