



Abbreviated prescribing information
Please consult the entire SPC

Name: Serdolect® sertindole.

Presentation: Tablets of 4, 12, 16 or 20 mg. **Indication:** Treatment of schizophrenia. Due to cardiovascular safety concerns, sertindole should only be used for patients intolerant to at least one other antipsychotic agent. Not for urgent relief of symptoms in acutely disturbed patients. **Switching from other antipsychotics:** Treatment can be initiated according to the recommended titration schedule concomitantly with cessation of other oral antipsychotics, or in place of the next depot injection. **ECG monitoring:** Mandatory prior to and during treatment with Serdolect®. ECG monitoring should be conducted at baseline, upon reaching steady state after approximately 3 weeks or when reaching 16 mg and again after 3 months of treatment. During maintenance therapy an ECG is required every 3 months. **Dosage and administration:** Once daily with or without meals. In patients where sedation is required, a benzodiazepine may be co-administered. **Adults:** All patients should be started on sertindole 4 mg/day. The dose should be increased by increments of 4 mg after 4-5 days on each dose until the optimal daily maintenance dose within the

range of 12-20 mg is reached. Only in exceptional cases should the maximum dose of 24mg be considered. **Elderly (> 65 years):** Treatment should only be initiated after a thorough cardiovascular examination. Slower titration and lower maintenance doses may be appropriate. **Children and adolescents (< 18 years):** Not recommended. **Re-titration:** Not required if patients have been without Serdolect® for less than a week. Otherwise the recommended titration schedule should be followed. **Contraindications:** Prescribing physicians should comply fully with the required safety measures. Hypersensitivity to sertindole or any of the excipients. Known uncorrected hypokalaemia or hypomagnesaemia. History of clinically significant cardiovascular disease, congestive heart failure, cardiac hypertrophy, arrhythmia, or bradycardia (<50 beats per minute). Congenital long QT syndrome (or family history of this disease), or known acquired QT interval prolongation. **Pregnancy.** Severe hepatic impairment. **Drugs known to significantly prolong the QT interval:** e.g. class Ia and III antiarrhythmics, antipsychotics, macrolides, antihistamines, quinolone antibiotics, cisapride, and lithium. **Drugs known to potentially inhibit hepatic cytochrome P450 3A enzymes:** e.g. 'azole' antifungal agents (systemic treatment), macrolide antibiotics, HIV protease inhibitors, calcium channel blockers, and cimetidine. **Special precautions:** Mild/moderate hepatic dysfunction. Risk of significant electro-

lyte disturbances: e.g. experiencing vomiting or diarrhoea, potassium depleting diuretic use. Parkinson's disease. Elderly > 65 years. Known poor metabolisers of CYP2D6. History of seizures. Breast-feeding. Dopamine agonists. Some SSRIs: e.g. fluoxetine, paroxetine (potent CYP2D6 inhibitors). Agents known to induce CYP isozymes: e.g. rifampicin, carbamazepine, phenytoin, phenobarbital. **Adverse events:** >10%: Rhinitis/nasal congestion. 1-10%: Decreased ejaculatory volume, dizziness, dry mouth, postural hypotension, weight gain, peripheral oedema, dyspnoea, paraesthesia, and prolonged QT interval. **Overdose:** Symptoms have included somnolence, slurred speech, tachycardia, hypotension, and transient prolongation of the QTc interval. Cases of Torsade de Pointes have been observed, often in combination with other drugs known to induce TdP. **Treatment:** There is no specific antidote to sertindole, and it is not dialysable, therefore appropriate supportive measures should be instituted. Adrenaline and dopamine should be used with caution (may worsen hypotension).

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The lifeline of
Serdolect®

“ Combined with its favourable tolerability and safety profiles and potential cognitive benefits, Serdolect® offers patients an effective and acceptable treatment option for managing their illness and restoring their ability to function. ”

Azorin et al. 2006

Trialed, tested and approved



Serdolect® is an oral antipsychotic treatment for schizophrenia that was first launched in 1996. It was withdrawn from the market in 1998 after a signal from the UK Adverse Drug Reactions On-line Information Tracking (ADROIT) database speculated it may be a causative of cardiac arrhythmia and sudden unexplained deaths (SUD).

What followed was eight years of extensive research that has conclusively unsubstantiated the suggestions. In 2005, the Committee for Human Medicinal Products (CHMP) issued a favourable opinion, and the European Commission lifted the Serdolect® marketing restrictions.

To date, the efficacy, tolerability and safety of Serdolect® has been evaluated in clinical and epidemiological studies including more than 17,000 patients with schizophrenia. They conclude:

Effective

Serdolect® improves the positive and negative symptoms of schizophrenia.

Improved cognitive function

Serdolect® significantly improves reaction time, working memory and executive function.

No sedation

Serdolect® improves social, recreational and vocational function by delivering effectiveness without the sedative characteristics of other leading treatments.

Placebo-level EPS

The EPS measure experienced by patients receiving Serdolect® has consistently been at placebo level.

No excessive weight gain

Weight gain reported in 8-, 12- and 52-week studies have been between 1.3 and 3 kg.

No change in libido

Prolactin is kept within normal limits, and patients generally do not experience reduced libido, erectile dysfunction or anorgasmia. 22% of male patients experience a decreased ejaculatory volume.

Cost efficiency

Serdolect® has a documented low re-hospitalisation rate.

Conclusion

Serdolect® is an antipsychotic with a unique clinical profile. The positive benefit/risk ratio of the compound was established in October 2001 and the current data from the post-marketing study support this assessment. There are no indications that the use of Serdolect® is associated with excess overall mortality.

* Conditions of marketing authorization

1. A stepwise approach with respect to the reintroduction of sertindole on the market. The elements are: stepwise introduction in countries, and initial approach to the users already familiar with the use of sertindole.
2. Promotional and educational material is reviewed and agreed by the individual National Competent Authorities.
3. A 'Dear Doctor' letter is used in the Concerned Member States (CMS), when sertindole is reintroduced.
4. Cardiac events and events with fatal outcome will be closely monitored.
5. Periodic safety update reports (PSURs) are submitted every 6 months to the Reference Member State (RMS).
6. Lundbeck agrees to continue the SCoP study until the CHMP decides otherwise.
7. Lundbeck agrees to provide the CHMP with the previously agreed interim analysis of the SCoP study, as described in the protocol.

Serdolect® lifeline

1996
Serdolect® receives marketing authorisation and launches in 17 European countries.

1998
Serdolect® is withdrawn following safety concerns regarding cardiac function and mortality. Eight years of extensive non-clinical, clinical and epidemiological studies commence to address key speculations.

2001
Expert group recommends to the CHMP that the Serdolect® marketing suspension is lifted based on its positive benefit-risk profile.

2002
The Commission Decision was issued in June, restricting the marketing activities, as patients treated with Serdolect® had to be included in the Sertindole Cohort Prospective (SCoP) study.

2004
More than 5,000 patients have participated in the SCoP study (equal to 3,000 patient years of exposure). Results are positive, concluding no excess in mortality. Furthermore, extensive non-clinical investigations have not been able to substantiate a link between the QT interval prolongation of Serdolect® and fatal cardiac arrhythmias. Lundbeck applies to the CHMP for Serdolect® to be reinstated with normal prescription rights.

2005
Lundbeck agree on CHMP marketing authorisation conditions.* CHMP issues a favourable opinion regarding the lifting of Serdolect® marketing restrictions to the European Commission, who officially lift them in December.

2006
Serdolect® is re-launched in Estonia in January and in Norway in February. Other countries will follow during 2006 and in the years to come.