IRISH JOURNAL OF
PSYCHOLOGICAL MEDICINE
VOL 27 NO 4 Dec 2010 ISSN 0790-9667

'Landscape' by AL. Reproduced with kind permission from the Art Therapy Group at the Central Mental Hospital, Dublin, Ireland

So many symptoms...

Treat the core of depression with Lexapro®

Lexapro®
escitalopram

The No.1 prescribed anti-depressant in Ireland [1]

Abbreviated Prescribing Information: Please refer to the Summary of Product Characteristics before prescribing. **Presentation:** Lexapro™ tablets 5 mg, 10 mg, 15 mg and 20 mg containing escitalopram as the oxalate. **Indications:** Treatment of major depressive episodes. Panic disorder with or without agoraphobia. Social Anxiety Disorder. Generalised Anxiety Disorder. Obsessive Compulsive Disorder. **Dosage: Treating depression:** ***Adults:*** Usual dosage is 10 mg once daily. The dose may be increased to a maximum of 20 mg/day. **Panic Disorder** ***with or without agoraphobia:*** An initial dose of 5 mg is recommended for the first week before increasing the dose to 10 mg/day. The dose may be further increased, up to a maximum of 20 mg/day. **Social Anxiety Disorder:** Usual dosage is 10 mg once daily. The dose may subsequently be decreased to 5 mg or increased to a maximum of 20 mg/day. **Generalised Anxiety Disorder:** Initial dosage is 10 mg once daily. The dose may subsequently be increased to a maximum of 20 mg/day. **Obsessive Compulsive Disorder:** Initial dosage is 10 mg once daily. The dose may be increased to a maximum of 20 mg daily. In known poor metabolisers of CYP2C19, 5 mg/day Lexapro is recommended for first 2 weeks, the dose can be increased to 10 mg after assessment. **Elderly (>65 yrs):** Initial treatment with half the usually recommended dose and a lower maximum dose should be considered. The efficacy of Lexapro in social anxiety disorder has not been studied in elderly patients. **Children and adolescents (<18 years):** Not recommended. **Reduced hepatic/renal function:** In mild/moderately impaired hepatic function an initial dose of 5 mg/day for the first two weeks of treatment is recommended, the dose may be increased to 10 mg/day. Caution and careful dose titration advised in patients with severely reduced hepatic function. Dosage adjustment is not necessary in patients with mild or moderate renal impairment. Caution is advised in patients with severely reduced renal function (CL_{cr}<30 ml/min). **Contraindications:** Hypersensitivity to escitalopram or to any of the excipients. Concomitant treatment with a nonselective, irreversible monoamine oxidase inhibitor (MAOI). Concomitant treatment with a reversible MAO-A inhibitor e.g. moclobemide or reversible non-selective MAO-inhibitors e.g. linezolid. Lexapro may be started 14 days after discontinuing treatment with an irreversible MAOI. At least 7 days should elapse after discontinuing Lexapro treatment, before starting a non-selective irreversible MAOI. **Pregnancy and Lactation:** Lexapro should not be used during pregnancy unless clearly necessary. Neonates should be observed if maternal use of Lexapro continues into the later stages of pregnancy, particularly the third trimester. Abrupt discontinuation should be avoided during pregnancy. Use of SSRIs during pregnancy may increase the risk of persistent pulmonary hypertension (PPHN) in the newborn. Refer to the full prescribing information for a list of serotonergic or discontinuation symptoms, which may occur in the neonate after maternal SSRI/SNRI use in later stages of pregnancy. Breast-feeding is not recommended during treatment. **Precautions:** Patients should be cautioned about the risk to their ability to drive a car and operate machinery. No pharmacokinetic or pharmacodynamic interactions are expected with concomitant alcohol intake, however the combination is not advised. Combination with serotonergic compounds is not recommended. Insulin and/or oral hypoglycaemic dosage may need to be readjusted in diabetics. Hyponatraemia has been observed rarely with SSRI use, caution required in patients at risk of hyponatraemia. Caution is advised with coadministration of ECT and in patients with a history of mania/hypomania. Caution advised with concomitant use of oral anticoagulants, products affecting platelet function and in patients with known bleeding tendencies. Avoid in patients with unstable epilepsy and monitor patients with controlled epilepsy. Stop treatment immediately if patient develops serotonin syndrome. Use at a low starting dose for panic disorders. Avoid abrupt discontinuation. Gradual discontinuation by dose tapering is advised. As with all SSRIs it is advisable to closely monitor patients for suicide and self-harm risk in the first few weeks of treatment and until significant remission occurs. Caution is advised in patients with coronary heart disease. The use of SSRIs/SNRIs has been associated with the development of akathisia, increasing the dose in these patients may be detrimental. **Drug Interactions:** MAO inhibitors (see Contraindications/ Precautions), advise caution in use with irreversible selective MAO-B inhibitors (selegiline). Caution in use with lithium, tryptophan, serotonergic medicinal products or with products capable of lowering the seizure threshold. Avoid concomitant use with St. John's Wort. Caution is advised with co-administration of drugs metabolised by enzymes CYP2C19, CYP3A4 and CYP2D6. Co-administration with CYP2C19 inhibitors, and general enzyme inhibitors e.g. cimetidine may require reduction of the Lexapro dose. Lexapro is an inhibitor of CYP2D6, caution is advised with concomitant use of drugs (particularly those with a narrow therapeutic index) mainly metabolized by CYP2D6. **Adverse Events:** Adverse reactions are most frequent during the first or second week of treatment and usually decrease in intensity and frequency with continued treatment. Frequencies are not placebo-corrected. ***Very Common*** (≥1/10): Nausea. ***Common*** (≥1/100 to <1/10): Weight increased, insomnia, somnolence, dizziness, paraesthesia, tremor, sinusitis, yawning, diarrhoea, constipation, vomiting, dry mouth, sweating increased, arthralgia, myalgia, decreased and increased appetite, fatigue, pyrexia, ejaculation disorder, impotence, anxiety, restlessness, abnormal dreams, male libido decreased, female anorgasmia. ***Uncommon*** (≥1/1,000 to <1/100): weight decreased, tachycardia, taste disturbance, sleep disorder, syncope, mydriasis, visual disturbance, tinnitus, epistaxis, gastrointestinal haemorrhages (incl. rectal), urticaria, alopecia, rash, pruritus, oedema, metrorrhagia, menorrhagia, bruxism, agitation, nervousness, panic attack, confusional state. ***Rare*** (≥1/10,000 to <1/1,000): Bradycardia, serotonin syndrome, anaphylactic reaction, aggression, depersonalisation, hallucination. ***Not known*** (cannot be estimated from the available data): Liver function test abnormal, thrombocytopenia, dyskinesia, movement disorder, convulsion, urinary retention, ecchymosis, angioedemas, inappropriate ADH secretion, hyponatraemia, orthostatic hypotension, hepatitis, galactorrhoea, male priapism, mania, suicidal ideation, suicidal behaviour. Others: psychomotor restlessness/akathisia, anorexia, QT-prolongation, discontinuation symptoms, increased risk of bone fractures (patients ≥50 years). **Overdosage:** Clinical data on escitalopram overdose is limited and many cases involve concomitant overdoses with other drugs. Doses between 400-800 mg of Lexapro alone have been taken without any severe symptoms. Symptoms seen in reported overdose of Lexapro mainly relate to the central nervous system, the gastrointestinal system, the cardiovascular system and electrolyte/fluid balance conditions. There is no specific antidote. Treatment is symptomatic and supportive with monitoring of cardiac and vital signs. Gastric lavage and the use of activated charcoal should be considered. **Legal Category:** POM. **Product Licence Holder:** H. Lundbeck A/S, Ottiliavej 9, DK-2500, Copenhagen – Valby, Denmark. **PA Numbers:** 5 mg PA805/2/1; 10 mg PA805/2/2; 15 mg PA805/2/3; 20 mg PA805/2/4. Further information is available upon request from Lundbeck (Ireland) Ltd., 7 Riverwalk, Citywest Business Campus, Citywest, Dublin 24. 'Lexapro' is a registered trademark ® 2002 Lundbeck Ltd. **Date of preparation:** September 2010 **Reference:** 1. Combined IMS Hospital & Retail Data (Unit Sales) YTD July 2010

Lundbeck

LX3/7/10

https://doi.org/10.1017/S0790966700001440 Published online by Cambridge University Press

Submissions & correspondence to:
The Editor,
Irish Journal of Psychological Medicine,
25 Adelaide Street, Dun Laoghaire,
Co Dublin, Ireland.

Telephone: 00-353-1-2803967
Fax: 00-353-1-2807076
Email: psychological@medmedia.ie
Website: www.ijpm.org

Publisher
MedMedia Ltd,
25 Adelaide Street,
Dun Laoghaire, Co Dublin, Ireland.
www.medmedia.ie

Printing: W&G Baird Ltd

Subscriptions
Rates per volume of four issues (Mar, Jun, Sept, Dec): €170
Incl. airmail postage internationally.

Subscription enquiries, orders and cheques made payable to:
MedMedia Ltd,
25 Adelaide St, Dun Laoghaire,
Co Dublin, Ireland
Tel: + 353 1 280 3967
Email: psychological@medmedia.ie
www.medmedia.ie

Circulation
2,200 to 54 countries. The Journal participates in the World Health Organisation project to improve distribution of scientific materials on mental health. Publication does not imply endorsement.

IRISH JOURNAL OF **PSYCHOLOGICAL MEDICINE**

Vol 27 No 4 December 2010 ISSN 0790-9667

Indexed and abstracted by BIOLOGICAL ABSTRACTS (BIOSIS Previews); CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE/INIST: PASCAL; EXCERPTA MEDICA/EMBASE; INSTITUTE FOR SCIENTIFIC INFORMATION: CURRENT CONTENTS/ Social & Behavioural Sciences (Social Science CITATION INDEX, Research Alert); PSYCHOLOGICAL ABSTRACTS (PsycINFO/PsycLIT); Cumulative Index to Nursing & Allied Health Literature, Current AIDS Literature (CAB Abstracts), International Pharmaceutical Abstracts, Linguistics & Language Behaviour Abstracts, Nutrition Abstracts and Reviews, (CAB Abstracts), Referativnyi Zhurnal, Social Planning/Policy & Development Abstracts, Social Work Research & Abstracts, Sociological Abstracts.

Microfilm, microfiche & article copies from **University Microfilms International**, 300 North Zeeb Rd., Ann Arbor, MI 48106, USA. Journal included in the **Adonis** service, whereby article copies can be printed out from compact disks (CD-ROM) on demand; explanatory leaflet available from ADONIS BV, PO Box 639, 1000 AV Amsterdam, The Netherlands. Journal listed in **Ulrich's** International Periodicals Directory (**Bowker** International Serials Database), **EBSCO's** Selected Periodicals for the Medical and Health Sciences, & EBSCO's Librarians' Handbook.

Valdoxan®

Agomelatine

The first melatonergic antidepressant

TREATING THE UNMET NEEDS AT EACH STEP OF DEPRESSION [1-5]

73% of Patients achieve Remission [4]

78% of Patients remain Relapse-free

NEW IN DEPRESSION

Week 12 — Week 24

Week 6

76% of Patients achieve Response [3]

Week 1-2

Early improvement in mood and daytime functioning [1,2]

Valdoxan (agomelatine) abbreviated prescribing information: *Please refer to the Summary of Product Characteristics before prescribing.* **Presentation and composition:** Valdoxan 25 mg film-coated tablets. **Indication:** Treatment of major depressive episodes in adults. **Dosage: Adults:** The recommended dose is 25 mg once daily taken orally at bedtime. After two weeks of treatment, if there is no improvement of symptoms, the dose may be increased to 50 mg once daily, i.e. two 25 mg tablets, taken together at bedtime. Liver function tests should be performed in all patients at initiation of treatment and then periodically after around six weeks (end of acute phase), after around twelve and twenty four weeks (end of maintenance phase) and thereafter when clinically indicated. **Elderly (>65y):** Efficacy has not been clearly demonstrated in the elderly (≥ 65 years). Only limited clinical data is available on the use of Valdoxan in elderly patients ≥ 65 years old with major depressive episodes. Therefore, caution should be exercised when prescribing Valdoxan to these patients. **Children and adolescents (<18y):** Not recommended. **Administration:** taken as a single dose at bedtime. Patients with depression should be treated for a sufficient period of at least 6 months to ensure that they are free of symptoms. **Properties:** Agomelatine is a melatonergic agonist (MT1 and MT2 receptors) and 5-HT_{2C} antagonist. Agomelatine resynchronises circadian rhythms in animal models of circadian rhythm disruption. Agomelatine increases noradrenaline and dopamine release specifically in the frontal cortex and has no influence on the extracellular levels of serotonin. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients, Hepatic impairment (eg cirrhosis or active liver disease), Concomitant use of potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin). **Pregnancy and lactation:** For Valdoxan, no clinical data on exposed pregnancies are available. Caution should be exercised when prescribing Valdoxan in pregnancy. It is not known whether Valdoxan is excreted into human milk. If treatment with Valdoxan is considered necessary, breastfeeding should be discontinued. **Precautions:** Valdoxan should not be used in elderly patients with dementia with depressive symptoms as safety and efficacy has not been established in this group. Valdoxan should be used with caution in patients with a history of mania or hypomania and should be discontinued if a patient develops manic symptoms. Valdoxan contains lactose. The combination of Valdoxan and alcohol is not advisable. Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. If any patient develops symptoms suggesting hepatic dysfunction liver function tests should be performed. The decision whether to continue the patient on therapy with Valdoxan should be guided by clinical judgement pending laboratory evaluations. If jaundice is observed therapy should be discontinued. **Drug Interactions:** Agomelatine is metabolised mainly by cytochrome P450 1A2 (CYP1A2) (90%) and by CYP2C9/19 (10%). Medicinal products that interact with these isoenzymes may decrease or increase the bioavailability of agomelatine. Fluvoxamine, a potent CYP1A2 and moderate CYP2C9 inhibitor markedly inhibits the metabolism of agomelatine resulting in a 60-fold (range 12-412) increase of agomelatine exposure. Consequently, co-administration of Valdoxan with potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin) is contraindicated. Combination of agomelatine with oestrogens (moderate CYP1A2 inhibitors) results in a several fold increased exposure of agomelatine. While there was no specific safety signal in the 800 patients treated in combination with oestrogens, caution should be exercised when prescribing agomelatine with other moderate CYP1A2 inhibitors (e.g. propranolol, grepafloxacine, enoxacine) until more experience has been gained. *In vivo*, agomelatine does not induce CYP450 isoenzymes. Agomelatine inhibits neither CYP1A2 *in vivo* nor the other CYP450 *in vitro*. Therefore, agomelatine will not modify exposure to medicinal products metabolised by CYP 450. **Adverse Events:** In clinical trials, over 3,900 depressed patients have received Valdoxan. Adverse reactions were usually mild or moderate and occurred within the first two weeks of treatment. The most common adverse reactions were nausea and dizziness. These adverse reactions were usually transient and did not generally lead to cessation of therapy. Adverse reactions are listed below using the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), Common: headache, dizziness, somnolence, insomnia, migraine, nausea, diarrhoea, constipation, upper abdominal pain, hyperhidrosis, back pain, fatigue, increases (*>3 times the upper limit of the normal* range) in ALAT and/or ASAT (i.e. 1.1% on agomelatine 25/50 mg vs. 0.7 % on placebo), anxiety. Uncommon: paraesthesia, blurred vision, eczema. Rare: erythematous rash, hepatitis. Frequency not known: suicidal thoughts or behaviour **Overdosage:** There is limited experience with agomelatine overdose. During the clinical development, there were a few reports of agomelatine overdose, taken alone (up to 450 mg) or in combination (up to 525 mg) with other psychotropic medicinal products. Signs and symptoms of overdose were limited and included drowsiness and epigastralgia. No specific antidotes for agomelatine are known. Management of overdose should consist of treatment of clinical symptoms and routine monitoring. Medical follow-up in a specialised environment is recommended. **Presentation:** Pack of 28 tablets of Valdoxan 25 mg **See Summary of Product Characteristics for further details. Legal Category:** POM. **Marketing Authorisation Numbers and Holders:** EU/1/08/499/003 Les Laboratoires Servier, 22 rue Garnier, 92200 Neuilly-sur-Seine, France. **Date of Preparation or Last Review:** February 2010. **Full prescribing information is available from:** Servier Laboratories, Block 2, West Pier Business Campus, Old Dunleary Road, Dun Laoghaire, Co Dublin. Tel: (01) 6638110, Fax (01) 6638120. **Date of preparation of item:** February 2010.

1. Kasper L et al. Eur Neuropsychopharmacol. 2008;18(suppl 4), Abstract P.2.c.022. **2.** Lemoine P, Guilleminault C, Alvarez E. 2007; J Clin Psychiatry. 2007 ; 68 :1723-32. **3.** Kennedy SH, Guilleminault C. Eur Neuropsychopharmacol. 2006;16(suppl 4):S319. Abstract P2.013. **4.** Kennedy S, Rizvi S, Fulton K and Rasmussen J. J Clin Psychopharmacol. 2008;28(3):329-333. **5.** Goodwin GM, Rouillon F, Emsley R. Eur Neuropsychopharmacol. 2008;17(suppl.4):S361-362. Abstract P2.c.038.

SERVIER

1 tablet at bedtime

SI/DTC - 09 AG 061 IA

www.valdoxan.com