Prescribing Protocol SESLHDPR/646
Agomelatine in major depression

Prescribing Protocol	
Title	Agomelatine in major depression
Areas where Protocol/Guideline applicable	District
Areas where Protocol/Guideline not applicable	Paediatrics
Authorised Prescribers	Psychiatrists
Indication for use	Treatment of major depression in adults including prevention of relapse.
Clinical condition Patient selection: Inclusion criteria (list investigations necessary and relevant results)	Major depression where the patients meet the following 4 inclusion criteria: • Experienced sexual dysfunction from other antidepressants such as SNRIs or SSRIs or have not responded to these classes of medication. • Experienced weight gain from mirtazapine, or where weight gain would be a significant negative outcome for the patient (e.g. metabolic issues or would greatly negatively affect self-esteem) • Where medication interactions with concurrent medications (e.g. antiretroviral therapy) prevent the use of other antidepressants • Aged 18 to 75 years Treatment with agomelatine should only be initiated after careful consideration of the benefits and risk in patients with hepatic injury risk factors. Treatment with agomelatine should not be initiated if serum transaminase levels are > 3 times the upper limit of the normal range. Baseline liver function tests (LFTs) should be performed in all patients before initiation of treatment. Subsequent LFT monitoring is required at 3 & 6 weeks and at 3 & 6 months post-initiation. The same monitoring schedule should occur prior to dose increases.
Contra-indications	• Patients with a history of previous hypersensitivity to the active ingredient or any of the excipients • Patients with hepatic impairment (i.e. cirrhosis or active liver disease) or transaminases exceeding 3 times the upper limit of normal • Patients taking potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin)
Precautions	• Hepatic impairment • Suicide ideation/suicidality • Elderly – avoid using in patients >75 years • Pregnancy and breastfeeding • Lactose intolerance

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Place in Therapy State whether drug to be used as first, second or third line. When not first line, describe therapies to be used first.	First, second or third line depending on the opinion of the psychiatrist and the patient meeting the proposed criteria (see above)
If part of combination therapy, list other drugs	May be used in combination with other antidepressants: SSRIs (fluoxetine, sertraline, escitalopram, citalopram), SNRIs (venlafaxine, duloxetine), MAO-Is, TCAs, mirtazapine.
Dosage (Include dosage adjustment for specific patient groups)	25mg orally once daily, at bedtime. After two weeks of treatment, if there is no improvement in symptoms, the dose may be increased to 50 mg once daily, at bedtime.
Duration of therapy	12 months or longer depending on the opinion of the psychiatrist
Important Drug Interactions	• Potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin) - **contraindicated** • Moderate CYP1A2 inhibitors (e.g. propranolol, combined oral contraceptives) • Rifampicin, ritonavir (CYP1A2, CYP2C9 & CYP2C19 inducer) – may reduce bioavailability of agomelatine
Administration instructions	Take once daily at bedtime. Tablets may be taken with or without food.
Monitoring requirements Safety Effectiveness (state objective criteria)	Baseline LFTs prior to initiation, at 3 & 6 weeks, at 3 & 6 months, and prior to dose escalations. Efficacy monitoring: patient response
Management of complications	Agomelatine should be discontinued immediately if any of the following are observed: • Increase in serum transaminases > 3 times the upper limit of normal • Signs or symptoms of potential liver injury (such as dark urine, light coloured stools, yellow skin/eyes, pain in the upper right abdomen, new-onset and unexplained fatigue). LFTs should continue to be performed regularly following discontinuation until serum transaminases return to normal
Basis of Protocol/Guideline (including sources of evidence, references)	Valdoxan® Product Information, last amended 04/09/17 (accessed 18/12/18) Australian Medicines Handbook – Agomelatine monograph (accessed 18/12/18) Laux, G., Huttner, N. A., & VIVALDI Study Group. (2014). Subgroup analysis of the non-interventional study VIVALDI: agomelatine in treatment-naïve patients, in combination therapy and after treatment switch. *International journal of psychiatry in clinical practice*, *18*(2), 86-96
Groups consulted in development of this protocol	Department of Consultation Liaison Psychiatry, POWH Pharmacy, The Albion Centre

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AUTHORISATION	
Author (Name)	Dr Duncan George
Position	Consultant Psychiatrist
Department	Prince of Wales Hospital & The Albion Centre
Department Contact (for ongoing maintenance of Protocol/Guideline)	Duncan.George@health.nsw.gov.au
GOVERNANCE	
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