

# Agomelatine in Major Depression

SESLHDMG/122

## Medicine Guideline



**Health**  
South Eastern Sydney  
Local Health District

<b>Areas where Protocol/Guideline applicable</b>	<b>SESLHD Outpatients only</b>  Agomelatine is NOT listed on the Medicines Formulary for inpatient initiation. Individual Patient use (IPU) approval must be sought prior to prescribing for inpatient initiation.
<b>Authorised Prescribers:</b>	Psychiatrists
<b>Indication for use</b>	Treatment of major depression in adults including prevention of relapse for SESLHD Outpatients.
<b>Clinical condition</b> Patient selection: Inclusion criteria (list investigations necessary and relevant results)	<p>Major depression where the patients meet the following 4 inclusion criteria:</p> <ul style="list-style-type: none"><li>• Experienced sexual dysfunction from other antidepressants such as SNRIs or SSRIs or have not responded to these classes of medication.</li><li>• 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)</li><li>• Where medication interactions with concurrent medications (e.g. antiretroviral therapy) prevent the use of other antidepressants</li><li>• Aged 18 to 75 years. No evidence of benefit in people &gt; 75 years with major depression.</li></ul> <p>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 &gt; 3 times the upper limit of the normal range.</p> <p>Baseline liver function tests (LFTs) should be performed in all patients before initiation of treatment.</p> <p>Subsequent LFT monitoring is required at 3 and 6 weeks and at 3 and 6 months post- initiation. The same monitoring schedule should occur prior to dose increases.</p>
<b>Proposed Place in Therapy</b>	First, second or third line depending on the opinion of the psychiatrist and the patient meeting the proposed criteria (see above)
<b>Contra-indications</b>	<ul style="list-style-type: none"><li>• Patients with a history of previous hypersensitivity to the active ingredient or any of the excipients</li><li>• Patients with hepatic impairment (i.e. cirrhosis or active liver disease) or transaminases exceeding 3 times the upper limit of normal</li><li>• Patients taking potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin)</li></ul>
<b>Precautions</b>	<ul style="list-style-type: none"><li>• Hepatic impairment</li><li>• Suicide ideation/suicidality</li><li>• Elderly – avoid using in patients &gt;75 years</li></ul>

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	<ul style="list-style-type: none"><li>• Pregnancy and breastfeeding</li><li>• lactose intolerance</li></ul>
<b>Important Drug Interactions</b>	<ul style="list-style-type: none"><li>• Potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin) - <b>contraindicated</b></li><li>• Moderate CYP1A2 inhibitors (e.g. propranolol, combined oral contraceptives)</li><li>• Rifampicin, ritonavir (CYP1A2, CYP2C9 &amp; CYP2C19 inducer) – may reduce bioavailability of agomelatine</li></ul>
<b>Dosage</b> (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.
<b>Duration of therapy</b>	12 months or longer depending on the opinion of the psychiatrist
<b>Prescribing Instructions</b>	Outpatient prescription
<b>Administration Instructions</b>	Take once daily at bedtime. Tablets may be taken with or without food.
<b>Adverse effects</b>	Adverse effects appear to be dose-dependent. <b>Common (&gt;1%):</b> increased aminotransferases, dizziness, abdominal pain <b>Infrequent (0.1–1%):</b> nausea, diarrhoea, anxiety, blurred vision, somnolence, fatigue, excessive sweating, rash, itch <b>Rare (&lt;0.1%):</b> hepatitis, hepatic failure (may be fatal), delirium
<b>Monitoring requirements</b>	Baseline LFTs prior to initiation, at 3 and 6 weeks, at 3 and 6 months, and prior to dose escalations.  Efficacy monitoring: patient response
<b>Management of Complications</b>	Agomelatine should be discontinued immediately if any of the following are observed: <ul style="list-style-type: none"><li>• Increase in serum transaminases &gt; 3 times the upper limit of normal</li><li>• 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).</li></ul> LFTs should continue to be performed regularly following discontinuation until serum transaminases return to normal
<b>Basis of Protocol/Guideline:</b> (including sources of evidence, references)	<a href="#">Valdoxan Product Information</a> . Last updated 16 May 2022. Australian Medicines Handbook – <a href="#">Agomelatine monograph</a> . Last updated <a href="#">January 2025</a> . 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. <i>International journal of psychiatry in clinical practice</i> , 18(2), 86-96

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<b>Groups consulted in development of this guideline</b>	Department of Consultation Liaison Psychiatry, POWH Pharmacy, The Albion Centre
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<b>AUTHORISATION</b>	
Author (Name)	Dr Duncan George
Position	Consultant Psychiatrist
Department	Prince of Wales Hospital & The Albion Centre
Position Responsible (for ongoing maintenance of Protocol)	<a href="mailto:Duncan.George@health.nsw.gov.au">Duncan.George@health.nsw.gov.au</a>
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