Agomelatine for the treatment of major depressive episodes – information for healthcare professionals working in primary care

This information aims to support healthcare professionals working in primary care who may be requested to continue prescribing of agomelatine in major depressive episodes, once it has been initiated and prescribed by specialist mental health service for at least 6 weeks.

Mechanism of action
Agomelatine is a melatonin receptor agonist.

Place in therapy
Agomelatine has been licensed in the UK for the treatment of depression in adults since 2008. It is relatively well tolerated, with network meta-analysis demonstrating the lowest dropout rates from side effects of all the reviewed antidepressants [1]. It may be considered an appropriate choice of drug in patients with specific comorbidities or who are at risk of particular side effects – see below.

The melatonergic mechanism of action of agomelatine gives it a unique place in therapy for patients with sleep disturbance (it has been shown to improve the sleep/wake cycle [2], sleep efficiency and quality [3, 4], and correct circadian rhythm abnormalities [5]).

Of particular importance is agomelatine's lack of serotonergic effects, which makes it an option to consider for patients who:

- Are at risk of serotonin syndrome [6, 7]
- Are at risk of bleeding [6, 8, 9]
- Are at risk of hyponatraemia [10, 11].

The efficacy of agomelatine has not been established in patients over the age of 75.

Dose
The recommended dose is 25mg once daily taken orally at bedtime [12].

After two weeks of treatment, if there is no improvement, or partial improvement of symptoms, the dose may be increased to 50mg once daily taken orally at bedtime.

Side effects and monitoring
Adverse reactions are usually mild or moderate and occur within the first two weeks of treatment. The most common adverse reactions are headache, nausea and dizziness. These side effects are usually transient and do not require cessation of therapy.

Some cases of liver injury have been reported, and for this reason the manufacturer stipulates monitoring criteria for liver function tests (LFTs).

LFTs must be monitored at:

- Baseline
- 3 weeks
- 6 weeks
- 12 weeks
- 24 weeks and thereafter if clinically indicated.

If the dose is increased, LFT monitoring should be carried out at the same frequency as when initiating treatment.

Treatment should be discontinued if transaminases exceed 3 x upper limit of normal, or if the patient develops signs or symptoms of potential liver injury (e.g. dark urine, light coloured stools, yellow skin/eyes, pain in the upper right belly, sustain new-onset and unexplained fatigue). LFTs should be repeated weekly after treatment discontinuation until return to baseline.

Please report any patient safety events associated with the use of agomelatine via the NHS Learn from patient safety events service which can be accessed here. Risk minimisation materials are available for this medication to support safer prescribing (prescriber guide to liver function monitoring and patient alert card). The risk minimisation materials can be accessed via the Electronic Medicines Compendium (EMC) website here (or please use this link: https://www.medicines.org.uk/emc/search?q=agomelatine)

Initiation and continuation of care

Agomelatine is an Amber 2 status drug. Prescribing must be initiated by a specialist.

Once treatment has been initiated in secondary mental health services, transfer of prescribing to primary care may be made after a minimum of 6 weeks. **Note that the LFT monitoring at baseline, 3 weeks, and 6 weeks must be carried out in secondary care prior to transfer**.

Clinical psychiatric advice can be sought from Consultant Connect and/or Medicines Information.

Contact details

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16.02.23

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Approval date: March 2023 **Review date:** March **2025 (or sooner if evidence or practice changes)**