South West Yorkshire Area Prescribing Committee

Agomelatine

Introduction	
General Statements	• The patient will receive supplies of the drug from secondary care until the transfer of shared care is agreed between the Consultant and GP. • The GP must reply in writing to the request for shared care as soon as practicable if unwilling to participate • The responsibility for prescribing and monitoring must be clearly documented in the patient's hospital and GP notes • The use of a shared care guideline is only considered when the patient's clinical condition is stable or predictable • Refer to the BNF and SmPC www.medicines.org.uk for further details before prescribing • *Agomelatine is a **red drug** following a terminated NICE appraisal: this shared care guideline applies only to those prescribed the medicine prior to the change in classification. **Prescribing for new patients remains the responsibility of the consultant psychiatrist.***
Indication	Agomelatine is indicated and licensed for the treatment of major depressive episodes in adults. Initiation is recommended by a specialist and after an adequate trial of at least two other antidepressants, where these treatments have not been tolerated due to weight gain, sexual dysfunction or sleep disturbance.

Individuals' Responsibilities	
Hospital Specialist's Responsibilities	• Prescribing until maintenance regime established • **Prescribing for new patients remains the responsibility of the specialist** • Ensure that the patient has an adequate supply of medication until GP supply can be arranged. • Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP. • Baseline monitoring of clinical parameters including liver function at initiation, at six weeks and at twelve weeks. • Discussion of risks and benefits of medication with patients and carers • Communication to GP of treatment regime, monitoring to be done, recommended treatment duration and criteria for referral. Highlight particularly monitoring of liver function. **PATIENT INFORMATION TO BE RECEIVED BY THE GP FROM THE CONSULTANT** • Diagnosis • Concurrent medication prescribed via secondary care • Details of patient follow up including care plan • Details of mental health key worker if appropriate • Details of prescribed dose and frequency • Details of referral criteria and review by secondary care specialist

Agomelatine

General Practitioner's Responsibilities	• Continued discussion of risks and benefits of medication with patients and carers as required • Prescribing once maintenance doses established • Continued monitoring as agreed with secondary care **including liver function tests at 24 weeks** and subsequently if signs and symptoms of liver impairment are identified. Only continue prescription if compliance with monitoring and results satisfactory. • Referral back to secondary care if patient stops the medication without medical advice, if mental state deteriorates or if you have concerns over patient compliance. • Follow guidance in the event of reaction or abnormality, record it and report back to the specialist • Ensure no drug interactions with concomitant medicines • To inform Psychiatry Team if patient repeatedly does not attend routine blood monitoring. **PATIENT INFORMATION TO BE RECEIVED BY THE CONSULTANT FROM THE GP** • Details of concurrent medication • Details of any identified problems eg compliance with treatment
Monitoring Required	• Liver function tests are required prior to initiation or dose increase, then at three weeks, six weeks, twelve weeks and twenty-four weeks of treatment. Subsequently these should be performed as clinically indicated if signs and symptoms of liver impairment are identified. • The Hospital Specialist must confirm to the GP which stages of the maintenance monitoring have already been completed at the point when prescribing and monitoring are transferred to the GP
When and How to Discontinue Treatment	Gradual discontinuation is generally recommended for antidepressants to avoid the risk of acute withdrawal syndromes or rapid relapse. If patient stops the medication without medical advice please refer to secondary care. Licensing studies have not shown agomelatine to induce a discontinuation syndrome
Information given to the patient	• The patient will be involved in the choice of medication and verbal information given. Patient information leaflets from the manufacturer and the Choice and medication website will be given to the patient. • Tell patients and carers to watch out for the symptoms and signs of liver injury (e.g. jaundice, dark urine, bruising). Explain the importance of regular liver function monitoring. • Advise patients to stop taking agomelatine and get medical help immediately if they have signs or symptoms of liver injury.
Contact Details	Telephone, bleep, email and fax numbers, out of hours and contact details of hospital medicines information department to be included in specialist's letter.

Product Information

The information in this Shared Care Guideline should be used in conjunction with the

Agomelatine

latest edition of the BNF and Summary of Product Characteristics	
Dosage	The starting dose is 25mg daily at bedtime. For most patients this is the recommended dose. The SmPC advises that if a patient has shown **no** response after two weeks then the dose may be increased to 50mg at bedtime. Patients showing partial response at this stage should be maintained at the 25mg dose There is limited data in the elderly (>65yrs), so caution is recommended. Do not start treatment if serum transaminases exceed three times the upper limit of normal.
Adverse Effects	In clinical studies an elevation of liver function tests of up to three times the reference value was seen in some patients. However elevations were also seen in some patients in the placebo group, and the difference between the two groups did not reach statistical significance. However, liver function tests are required at commencement of therapy and at six, twelve and twenty-four weeks. Adverse effects reported from clinical trials are described as mild or moderate, and seem to occur in the first two weeks of treatment. Common side effects reported in these trials include headache, dizziness, somnolence, insomnia, migraine, nausea, diarrhoea, upper abdominal pain, hyperhidrosis, fatigue and anxiety. Refer to the BNF and SmPC for full details.
Precautions and Contra-indications	• Hepatic impairment • Stop treatment immediately if LFTs are raised more than 3 times the upper limit of the reference range, i.e. treatment is **contraindicated**. • Concomitant use of potent CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin)
Clinically relevant Drug Interactions and their management	• Co-administration with potent inhibitors of cytochrome P450 1A2 (CYP1A2) such as fluvoxamine and ciprofloxacin is contra-indicated. • Some caution is advised when agomelatine is used with moderate inhibitors of CYP1A2 such as propranolol and oestrogens. The SmPC describes increased exposure to agomelatine resulting from this combination, but at this stage it does not seem to be clinically relevant.