NHS North East and North Cumbria

Shared Care Protocol

Melatonin

This SCP is approved and adopted by the NENC ICB and the following Trusts:

If not applicable to Trust state not applicable	North Cumbria Integrated Care Foundation Trust	Northumbria Healthcare NHS Foundation Trust	South Tyneside & Sunderland NHS Foundation Trust	County Durham & Darlington Foundation Trust	North Tees & Hartlepool Foundation Trust	South Tees Hospitals Foundation Trust	Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust	Tees, Esk & Wear Valleys Foundation Trust
Date	*N/A*	*N/A*	*N/A*	***29th June 2023***	***29th June 2023***	***29th June 2023***	*N/A*	***23rd March 2023***

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Assess the need and opportunity for deprescribing at each review, as outlined in appendix 2
- Reassume prescribing responsibilities if a patient becomes or wishes to become pregnant.

- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of melatonin with their pharmacist before purchasing any OTC medicines.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

1. Background	Melatonin is an endogenous hormone secreted by the pineal gland in a circadian manner. The evening rise in melatonin, enabled by darkness, precedes the onset of natural sleep by about 2 hours. Melatonin is involved in the induction of sleep and in synchronisation of the circadian system. Inadequate or irregular melatonin production can cause insomnia. Before starting treatment, traditional non-pharmacological methods must have been tried and failed. The aim is to establish healthy sleep habits with the lowest effective dose of melatonin. The patient / carers should understand that treatment is not intended to be lifelong and regular treatment breaks will be trialled.
2. Indication(s) covered by this SCP **(Please state whether licensed or unlicensed)**	1. Chronic sleep disturbance in the following conditions: ○ Neurological or behavioural disorders, for example Attention Deficit Hyperactivity Disorder *(licensed, exc.adults[a])* or Autistic Spectrum Disorders *(licensed, exc.adults[b])* ○ Neurodevelopment disabilities, for example Smith-Magenis syndrome *(licensed, exc.adults[b])*, delayed brain maturation, sensory dysfunction - especially visual, and dysfunction of sleep centres *(unlicensed)*

	For children / young people (in TEWV) – only where the patient / family and clinical team agree that application of the sleep CLiP (Clinical Link Pathway) has been unsuccessful or has insufficiently improved sleep T:\CAMHS\CAMHS PATHWAYS\8. CLiPs\Sleep CLiP\sleep flowchart v11.docx (access for TEWV staff only) For adults – only where sleep hygiene measures have been insufficient 2. REM sleep behavioural disorders associated with degenerative conditions such as Parkinson's disease or dementia *(unlicensed)* a) *Adaflex® (immediate release melatonin) is licensed for insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient. [use in adults is off-label]* b) *Slenyto® (prolonged release melatonin) is licensed for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient [use in adults is off-label]* N.B. this SCP does not cover the licensed indication for Circadin®/generic equivalents - "monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over"
3. Locally agreed off-label use	Adaflex® – doses above 5 mg daily (up to 10 mg daily) Circadin®/generic equivalents - established prescribing for above indications which pre-dates this SCP **DO NOT INITIATE FOR NEW PATIENTS** Melatonin oral solution, alcohol- and propylene glycol-free formulations (unlicensed specials)
4. Contraindications and cautions Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	**Contraindications:** Hypersensitivity to the active substance or any excipients **Cautions:** Autoimmune disease (limited information available – exacerbation reported occasionally), susceptibility to seizures (risk of increased seizure frequency) Please see SPC for comprehensive information.
5. Initiation and ongoing dose regime Note - •Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks •The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. •All dose or formulation adjustments will be the responsibility of the initiating	**Initial stabilisation and maintenance dose:** *(see appendix 1)* **Adaflex®**: starting dose = 1–2 mg, increase by 1 mg every week up to a maximum of 10 mg/day (licensed max. = 5 mg/day); lowest effective dose should be sought **Slenyto®**: starting dose = 2 mg; if an inadequate response has been observed, the dose should be increased to 5 mg, with a maximum dose of 10 mg. *[see "other important information" in section 6 regarding use of melatonin oral solution instead of Adaflex® or Slenyto®]* **Circadin®**/generic equivalents *(not to be initiated in new patients)*: starting dose = 2 mg; if no benefit after 2 weeks, increase by 2 mg increments up to a maximum dose of 10 mg (most patients should respond at doses of 6 mg or less). **The loading period must be prescribed by the initiating specialist.** **The initial maintenance dose must be prescribed by the initiating specialist.** If no response after 2 weeks at maximum dose – stop treatment.

specialist unless directions have been discussed and agreed with the primary care clinician •Termination of treatment will be the responsibility of the specialist.	Melatonin is not intended to be a lifelong treatment. Efficacy is generally sustained in long term use, but in some specific patient groups the benefits of melatonin may diminish after a 6-12 month period of continuous treatment. The British Association of Psychopharmacology states that intermittent dosing may reduce the risk of tolerance with hypnotics. If response is achieved, consider continuing for at least 6 months, then review and consider for a trial without treatment. There are no withdrawal or discontinuation symptoms associated with melatonin. Melatonin can be safely stopped at any point or can be gradually reduced if this is considered more acceptable. The preferred method of discontinuation should be discussed and agreed with the patient and/or carers. See appendix 2. **Conditions requiring dose adjustment:** Use with caution in patients with renal or hepatic impairment. Patients with reduced elimination rates (e.g., hepatic impairment) may have extended supraphysiological plasma levels (>10h), which may increase the risk of daytime drowsiness.	
6. Pharmaceutical aspects	Route of administration:	Oral
	Formulation:	Tablet or oral solution
	Administration details:	**Adaflex®** - should be taken 30-60 minutes before bedtime, at least 2 hours before or after food. Tablet can be crushed and mixed with water directly before administration (licensed) if the patient is unable to swallow tablets or has swallowing difficulties. **Slenyto®** - should be taken 30-60 minutes before bedtime and with/after food. The tablet should not be broken, crushed or chewed because it will lose the prolonged release properties. Tablets can be put into food such as yoghurt, orange juice or ice-cream to facilitate swallowing and improve compliance (licensed). If the tablets are mixed with food or drink, they should be taken immediately, and the mixture not stored. **Circadin®/generic equivalents** - should be taken 1–2 hours before bedtime and after food. Tablets should be swallowed whole for prolonged-release effect but can be crushed for immediate-release effect. *[N.B. crushing Circadin®/generic equivalent tablets to achieve an immediate-release profile is "off-label", but supported in patients established on treatment prior to this SCP; Adaflex® should be prescribed instead ® for new patients who require an immediate-release preparation]*
	Other important information:	For patients unable to swallow tablets[1] and/or if crushing tablets is inappropriate (e.g., administration via PEG tube), an **oral solution** may be prescribed – an oral solution containing 1 mg/ml [5 mg in 5 ml] is the recommended strength. Products which do not contain alcohol[2] or propylene glycol are recommended – the preferred product is "Melatonin Consilient Health 1 mg/ml oral solution"[3] Review the need for the oral solution on a regular basis and if circumstances change, e.g., no longer needs enteral feeding or able to swallow tablets

		1. *Offer the parent/carer the Kidzmed resource to optimise swallowing of tablets prior to considering the oral solution* 2. *Kidnaps oral solution, a well-known unlicensed special, contains alcohol* *Licensed for "insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient" – use for other indications covered by this SCP would be off-label*
7. Significant medicine interactions For a comprehensive list consult the BNF or Summary of Product Characteristics. SPC	**The following list is not exhaustive; please see SPC for comprehensive information and recommended management.** The following drugs must not be prescribed without consultation with the specialist: • Fluvoxamine – increases melatonin levels by inhibiting its metabolism. The manufacturer advises that this combination should be avoided. • Benzodiazepines/non-benzodiazepine hypnotics - melatonin may enhance the sedative properties. Manufacturer advises to avoid this combination. The following drugs may be prescribed with caution. Dose adjustment may be required • Cimetidine, oestrogens - inhibit melatonin metabolism and therefore increases plasma melatonin levels. • CYP1A2 inducers, such as ciprofloxacin, carbamazepine and rifampicin - may reduce plasma levels of melatonin. Alcohol and cigarette smoking may also affect plasma melatonin levels.	
8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist	**Baseline investigations:** Assess suitability of patient for treatment. Discuss benefits and side-effects of treatment with the patient/carer, including any off-label prescribing or use of unlicensed products. **Initial monitoring:** Monitor for response and adverse reactions during the initiation period Monitoring at baseline and during initiation is the responsibility of the specialist, only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care **Ongoing monitoring:** Specialist review to include assessment of continuing benefit and need (every 6-12 months), utilising treatment breaks to inform deprescribing decisions and advice to primary care; specialist to measure height & weight if not done recently and include in clinic review letter	
9. Ongoing monitoring requirements to be undertaken by primary care See section 10 for further guidance on management of adverse effects/ responding to monitoring results.	Monitoring	Frequency
	Height and weight (children)	Annually (unless monitored by specialist at annual review)

<table>
<tr><td rowspan="2">10. Adverse effects and management

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme
www.mhra.gov.uk/yellowcard</td><td>Result</td><td>Action for primary care</td></tr>
<tr><td>Daytime drowsiness</td><td>Use with caution if the effects of drowsiness are likely to be associated with a risk to safety. Inform secondary care, may need dose reduction</td></tr>
<tr><td colspan="2">Melatonin is generally well tolerated. Common side effects include headaches, abnormal dreams, nausea and dizziness. All suspected reactions (including those not considered to be serious and even where the causal link is uncertain) should be reported to the specialist and the MHRA.</td></tr>
<tr><td>11. Advice to patients and carers
The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.</td><td colspan="2">Patient information on this medicine can be found here
Inform patient/carers that treatment will be subject to regular assessment of ongoing need</td></tr>
<tr><td>12. Pregnancy, paternal exposure and breast feeding
It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.</td><td colspan="2">Pregnancy: Avoid during pregnancy due to lack of data
Breastfeeding: Melatonin is excreted into milk and therefore should not be prescribed when breast feeding</td></tr>
<tr><td>13. Specialist contact information</td><td colspan="2">Name: [insert name]
Role and specialty: [insert role and specialty]
Daytime telephone number: [insert daytime telephone number]
Email address: [insert email address]
Alternative contact: [insert contact information, e.g. for clinic or specialist nurse]
Out of hours contact details: [insert contact information, e.g. for duty doctor]</td></tr>
<tr><td>14. Additional information</td><td colspan="2">Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.
If a dose is missed at the usual time, then it can be taken up until bedtime. Melatonin should not be taken at any time during the day.</td></tr>
<tr><td>15. References</td><td colspan="2">• Adaflex, Summary of Product Characteristics
• Slenyto, Summary of Product Characteristics
• Circadin, Summary of Product Characteristics
• Melatonin Consilient Health 1 mg/ml oral solution. Summary of Product Characteristics
• BNF
• Melatonin Deprescribing Guidelines for Adults in Primary Care, South Tyneside and Sunderland APC. December 2021</td></tr>
<tr><td>16. To be read in conjunction with the following documents</td><td colspan="2">• RMOC Shared Care Guidance
• NHSE/NHSCC guidance – items which should not be routinely prescribed in primary care: guidance for CCGs
• NHSE policy- Responsibility for prescribing between Primary & Secondary/Tertiary Care</td></tr>
</table>

17. Local arrangements for seeking specialist advice Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.	**The following circumstances/ changes in the patient's condition require discussion with the specialist team:** • If pregnancy occurs or if the patient is planning to become pregnant or breastfeed. • If non-compliance is suspected or the patient fails to attend monitoring appointments and the primary care prescriber considers it no longer safe to continue prescribing. (All appropriate steps must first be taken by primary care to reinforce the importance of attendance to the patient) • The patient's clinical condition deteriorates such that the primary care prescriber feels a dose change is required/ the patient no longer appears to be benefiting from therapy
18. Version Control	Prepared by: Maymouna Haider, Advanced Clinical Pharmacist, TEWVFT Checked by: Richard Morris, Deputy Chief Pharmacist, TEWVFT Version: 5.2 Date of Issue / Review: 23rd March 2023 (amended 28th September 2023) Date for next Review: 1st April 2026 Approved by: TEWV D&T Committee; CDTV Area Prescribing Committee

Appendix 1 – Cost comparison / optimisation of melatonin products

Product	Price per unit (Drug Tariff, May 2023)	Cost per day							
		1mg	2 mg	3mg	4mg	5mg	6mg	8mg	10mg
Adaflex 1mg tablets	44p	**44p**	**88p**				**£1.18** (2mg + 4mg) **£1.32** (2 x 3mg)		
Adaflex 2mg tablets	51p		**51p**		**£1.02**				
Adaflex 3mg tablets	66p			**66p**					
Adaflex 4mg tablets	67p				**67p**			**£1.34**	
Adaflex 5mg tablets	78p					**78p**			**£1.56**
Circadin 2mg tablets	51p		**51p**		**£1.02**		**£1.53**	**£2.04**	**£2.55**
Melatonin oral solution 1mg/ml	£0.96 per mg	**£0.96**	**£1.92**	**£2.88**	**£3.84**	**£4.80**	**£5.76**	**£7.68**	**£9.60**
Slenyto[1] 1mg tablets	69p	**69p**	**£1.38p**	**£2.07**	**£2.86**		**£4.12**	**£5.50**	
Slenyto[1] 5mg tablets	£3.43					**£3.43**			**£6.86**

1. Licensed / used for different indication to Adaflex

Appendix 2: Deprescribing Melatonin

(Adapted with thanks to South Tyneside and Sunderland APC, Melatonin Deprescribing Guideline for Adults in Primary Care)

Step 1: Education and Discussion

- Discuss the pros and cons of melatonin with patients, carers and family as appropriate, to encourage reflection on the appropriateness of continued treatment. Consider if the patient has mental capacity, and ensure discussions are held with the relevant person(s).
- Evaluate sleep quality by asking:
    - Did you sleep well last night?
    - How many nights have you slept well in the last week/month?
    - Do you have difficulty falling asleep, and/or staying asleep?
    - Do you feel refreshed when you wake up?

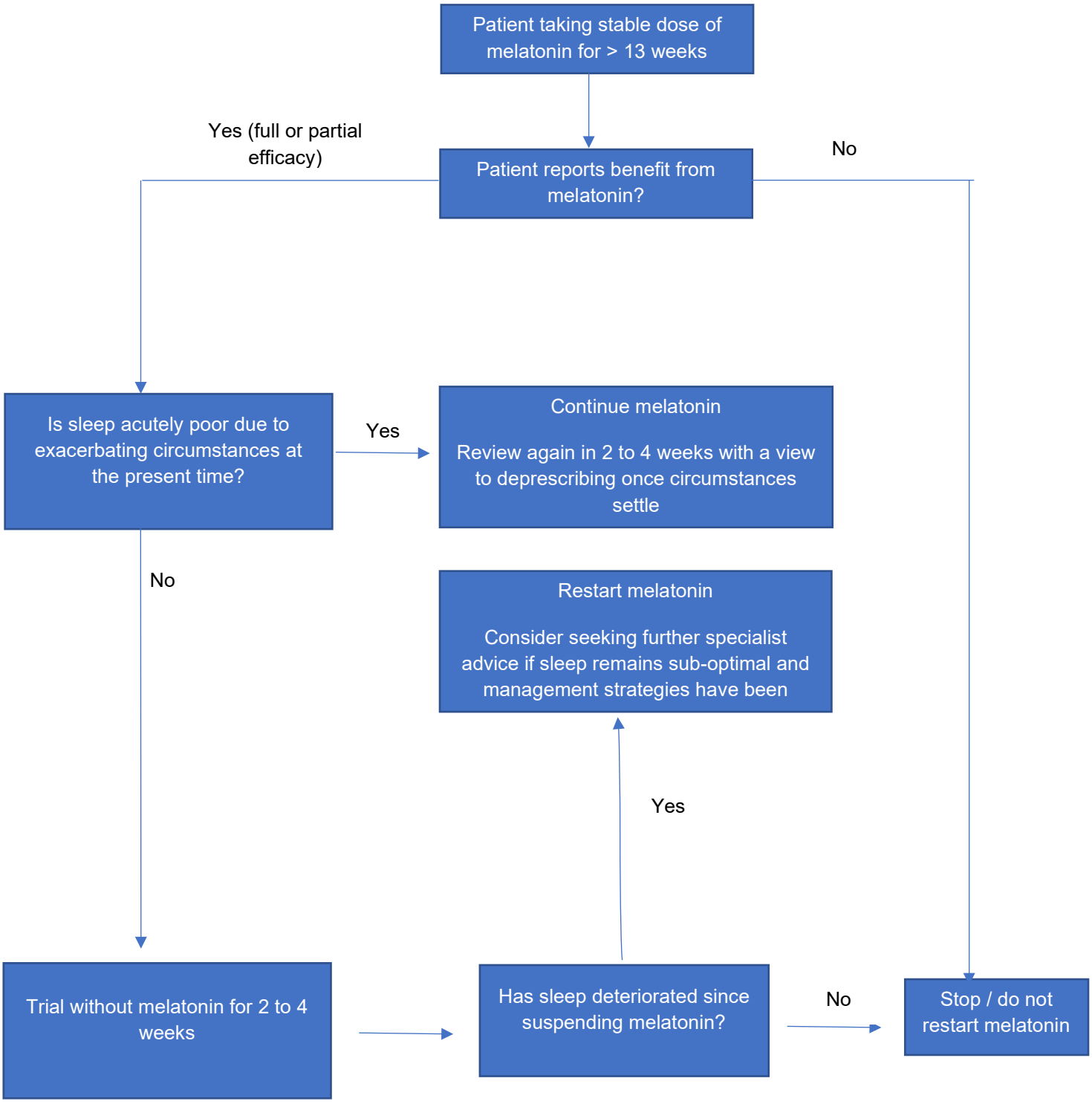
  The most convincing evidence for melatonin supports its use to reduce the time taken from shutting eyes until falling asleep (sleep onset latency). Evidence does not support using melatonin to induce feelings of relaxation or calm.
- If possible, aim to objectively measure sleep patterns using a sleep tracking chart or making use of any data from wearable technology if available to the patient.
- Before proceeding to step 2, identify (and attempt to resolve as far as possible) factors which may contribute to sleep disturbance such as stress, anxiety, sleep apnoea/snoring, nightmares/night terrors/sleep walking, poor sleep hygiene

Step 2: Determine if a trial period without medication would be appropriate – see flow chart overleaf

Exercise caution where patients:

- Have severe learning disabilities or autism (may be more sensitive to medication routine changes)
- Have mental health conditions which are currently unstable
- Have Smith-Magenis syndrome, or a circadian rhythm disorder (sleep cycle can be highly disturbed)
- Are taking concomitant medication which may cause sleep disturbance e.g. SSRIs
- Other significant medication changes have occurred recently or are ongoing
- Have been taking melatonin for > 2 years

The flow chart below can be used to guide decisions about deprescribing melatonin during patient reviews:



Step 3: How to stop melatonin

- Seek and document consent for any change to melatonin from patient, or from the relevant person(s), where the patient does not have mental capacity
- Ensure time is available to educate the patient/carer to fully understand the reasons behind medication changes. Emphasise a flexible approach to deprescribing, to ensure the patient feels comfortable
- Discuss the preferred approach to stopping melatonin with the patient / carer. There are no withdrawal or discontinuation symptoms associated with melatonin; it can be safely stopped abruptly at any point or can be gradually reduced if this is considered more acceptable. For a gradual reduction, taper the dose down at increments and intervals which the patient/carer feels comfortable with. An example regimen could be reducing the dose by 2 mg every month.
- Reinforce the management of good sleep hygiene to reduce sleep disturbance.
- Review patients, ideally with reference to data from a sleep chart to assess the impact of the change.

If sleep disturbance recurs upon discontinuation, consider reinstating melatonin at the previously prescribed dose, and/or seeking advice if clinically appropriate.

Appendix 3: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*: [insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]*shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened regarding this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	Yes / No
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	Yes / No
The risks and benefits of treatment have been explained to the patient	Yes / No
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	Yes / No
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	Yes / No
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	Yes / No
I have included with the letter copies of the information the patient has received	Yes / No
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Name: *[insert name]*
Role and specialty: *[insert role and specialty]*
Daytime telephone number: *[insert daytime telephone number]*
Email address: *[insert email address]*
Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]*
Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

Appendix 4: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that

☐ I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

☐ I am NOT willing to take on this responsibility due to the following reason/s (please specify):

……
……
……
……
……

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp: