# Shared Care Protocol

## Dronedarone for patients in adult services

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

## 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.
- 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.
- Adjust the dose prescribed as advised by the specialist.
- 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.

- Stop dronedarone and make an urgent referral to the specialist if ECG changes, hepatotoxicity, pulmonary toxicity or renal toxicity are suspected.
- 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

- Take dronedarone as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- 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 with their pharmacist before purchasing any OTC medicines.
- Avoid grapefruit juice while taking dronedarone.
- 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.

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| **1. Background** | Dronedarone is used in the treatment of severe cardiac rhythm disorders, as a second line option when other drugs are ineffective or contraindicated. It has potentially serious adverse effects and its use requires monitoring both clinically and via laboratory testing.<br>Due to the significant safety concerns, NHS England (NHSE) and NHS Improvement's guidance advises that prescribers should not initiate dronedarone in primary care for any new patients. In exceptional circumstances, if there is a clinical need for dronedarone to be prescribed, this must be initiated by a specialist and only continued under a shared care arrangement in line with NICE clinical guidance (Atrial fibrillation: NG 196 ). Dronedarone should be used as recommended in NICE TA 197 Dronedarone for the treatment of non-permanent atrial fibrillation<br>Where there is an existing cohort taking dronedarone, it is recommended that these patients be reviewed to ensure that prescribing remains safe and appropriate.<br>This document applies to adults aged 18 and over. |
| **2. Indication(s) covered by this SCP** | Licensed indication: maintenance of sinus rhythm after successful cardioversion in adult clinically stable patients with paroxysmal or persistent atrial fibrillation.<br>NICE TA 197 recommends dronedarone as an option in patients: |

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| **(Please state whether licensed or unlicensed)** | • whose atrial fibrillation is not controlled by first-line therapy (usually including beta-blockers), that is, as a second-line treatment option and after alternative options have been considered **and**<br>• who have at least 1 of the following cardiovascular risk factors:<br>  ○ hypertension requiring drugs of at least 2 different classes<br>  ○ diabetes mellitus<br>  ○ previous transient ischaemic attack, stroke or systemic embolism<br>  ○ left atrial diameter of 50 mm or greater **or**<br>  ○ age 70 years or older and<br>• who do not have left ventricular systolic dysfunction **and**<br>• who do not have a history of, or current, heart failure |
| **3. Locally agreed off-label use** | NA |
| **4. Contraindications and cautions**<br><br>Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. | **Contraindications:**<br>• Known hypersensitivity to dronedarone or any of the excipients<br>• Second- or third-degree atrio-ventricular block, complete bundle branch block, distal block, sinus node dysfunction, atrial conduction defects, or sick sinus syndrome (except when used in conjunction with a functioning pacemaker)<br>• Bradycardia less than 50 beats per minute<br>• Permanent atrial fibrillation (AF) with an AF duration ≥6 months (or duration unknown), and attempts to restore sinus rhythm no longer considered by the physician<br>• Unstable haemodynamic conditions<br>• History of or current heart failure, or left ventricular systolic dysfunction<br>• Patients with liver or lung toxicity related to previous use of amiodarone<br>• Co-administration with potent cytochrome P450 3A4 (CYP3A4) inhibitors, such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir (see section 7)<br>• Co-administration with medicinal products inducing torsades de pointes, including phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides (such as erythromycin), class I and III anti-arrhythmics (see section 7)<br>• Co-administration with dabigatran<br>• QTc Bazett interval  greater than 500 milliseconds<br>• Severe hepatic or renal impairment (CrCl <30 mL/min)<br><br>**Cautions:**<br>Please see SPC for comprehensive information. |

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| | Dronedarone can cause serious adverse reactions; clinical monitoring for development of congestive heart failure, left ventricular systolic dysfunction, QTc prolongation, liver injury, and respiratory disease are required (see also section 8 & section 9). | |
| **5. Initiation and ongoing dose regime**<br><br>Note -<br>•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<br>•The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.<br>•All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician<br>•Termination of treatment will be the responsibility of the specialist. | **Initial stabilisation and maintenance dose:**<br>400mg twice daily, with the morning and evening meals.<br>**The starting and initial maintenance dose must be prescribed by the initiating specialist. Treatment should be initiated and monitored only under specialist supervision.** | |
| **6. Pharmaceutical aspects**<br><br>*Please include relevant details such as:*<br>*- if the SCP covers specific formulations or presentations of a medicine (e,g. particular brands, particular strengths, pre-filled syringes vs. vials etc.)*<br>*- whether the medicine should be taken with food or on an empty stomach*<br>*- any safety precautions (e,g. must be swallowed whole, cannot be crushed etc.)* | Route of administration: | Oral |
| | Formulation: | 400 mg film-coated tablets |
| | Administration details: | Tablets should be swallowed whole with a drink of water during a meal. The tablet cannot be divided into equal doses and should not be split.<br>If a dose is missed, patients should take the next dose at the regular scheduled time and should not double the dose. |
| | Other important information: | Grapefruit juice should be avoided during treatment with dronedarone (see section 7). |
| **7. Significant medicine interactions**<br><br>For a comprehensive list consult the BNF or Summary of Product Characteristics. SPC<br><br>*Please detail any key contraindications/ cautions as per BNF or product information e.g. live vaccines.* | **The following list is not exhaustive; please see SPC for comprehensive information and recommended management.**<br>**Dronedarone is associated with a large number of interactions, some of which are significant enough to contradict concurrent use, require dose adjustment and/or additional monitoring.**<br>Dronedarone is contraindicated when co-administered with potent cytochrome P450 3A4 (CYP3A4) inhibitors, medicinal products inducing torsades de pointes, and dabigatran (see section 4).<br>Dronedarone is an enzyme inhibitor and can increase exposure to a number of medicines including:<br>• P-glycoprotein (PgP) substrates (e.g. digoxin, dabigatran, apixaban, rivaroxaban, edoxaban).<br>• CYP3A4 substrates (e.g. ciclosporin, statins, fentanyl, sildenafil, tacrolimus, sirolimus, everolimus, apixaban, rivaroxaban, edoxaban).<br>• CYP2D6 substrates (e.g. metoprolol).<br>Dronedarone interacts with other medicines that: | |

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| | • Induce Torsade de Points or prolong qtc (e.g. Phenothiazines, cisapride, bepridil, tricyclic antidepressants, certain oral macrolides (such as clarithromycin and erythromycin), terfenadine and Class I and III anti-arrhythmics). Concomitant use is contraindicated.<br>• Lower heart rate (e.g. Beta-blockers, calcium channel blockers).<br>• Induce hypokalaemia (e.g. Diuretics, stimulant laxatives).<br>• Induce hypomagnesaemia (e.g. Diuretics).<br>Other interactions include:<br>• CYP3A4 inhibitors – may increase exposure to dronedarone (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, clarithromycin, grapefruit juice). Concomitant use is contraindicated.<br>• Potent CYP3A4 inducers – may reduce exposure to dronedarone and are not recommended (e.g. rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort).<br>• Anticoagulants – vitamin K antagonist and direct oral anticoagulant (DOAC) exposure may be increased by dronedarone (e.g. warfarin, rivaroxaban, edoxaban). |
| **8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist** | **Baseline investigations:**<br>• Liver function tests (LFTs)<br>• Urea and electrolytes (U&Es), including potassium, magnesium, and serum creatinine<br>• Electrocardiogram (ECG)<br>**Initial monitoring:**<br>• Liver function tests: after 7 days of treatment, after 1 month of treatment, then monthly for 6 months, at 9 and 12 months and annually thereafter (NB GP also monitoring annually, at intervening 6 month interval).<br>• Urea and electrolytes: after 7 days of treatment, and after a further 7 days if any elevation is observed. If serum creatinine continues to rise then consideration should be given to further investigation and discontinuing treatment. Thereafter annually (NB GP also monitoring annually, at intervening 6 month interval).<br>• Monitor concurrent medicines as appropriate, e.g. anticoagulants, digoxin.<br>**Ongoing monitoring:**<br>• ECG, at least every six months<br>• Chest X-ray and pulmonary function tests, if respiratory symptoms or toxicity suspected<br>• 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. |

| | Monitoring | Frequency |
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| **9. Ongoing monitoring requirements to be undertaken by primary care**<br><br>See section 10 for further guidance on management of adverse effects/ responding to monitoring results. | Urea and electrolytes (including magnesium and potassium) and creatinine clearance.<br><br>Liver function tests<br><br>Symptoms of heart failure, e.g. development or worsening of weight gain, dependent oedema, or dyspnoea | Annually (NB specialist also monitoring annually, at intervening 6 month interval)<br><br>Annually (NB specialist also monitoring annually, at intervening 6 month interval)<br><br>Ongoing |
| **10. Adverse effects and management**<br><br>**Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme** www.mhra.gov.uk/yellowcard<br><br>For information on incidence of ADRs see relevant summaries of product characteristics. | Result | Action for primary care |
| | **As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance** | |
| | **Renal function:**<br>Electrolyte deficiency: hypokalaemia / hypomagnesaemia | Continue dronedarone. Correct deficiency as per local guidelines. |
| | Creatinine elevated from baseline | **Stop dronedarone** for any elevations of serum creatinine which occur after transfer to primary care. Discuss urgently with specialist |
| | Creatinine clearance <30 mL/minute/ 1.73m$^2$ | **Stop dronedarone** and refer urgently to the specialist. |
| | **Cardiovascular:**<br>Bradycardia:<br>Heart rate 50 - 60bpm without symptoms | Continue dronedarone. Repeat monitoring. No action required if hear rate remains >50 without symptoms. |
| | Heart rate ≤ 50bpm or ≤ 60bpm with symptoms | Discuss with specialist team; dose reduction may be required. |
| | Worsening of arrhythmia, new arrhythmia, or heart block | **Stop dronedarone.** Urgent referral to specialist team. |
| | Recurrence of atrial fibrillation | Refer to specialist team; discontinuation should be considered.<br><br>Discontinue dronedarone if patient develops permanent AF with a duration of six months or more. |
| | Signs or symptoms of congestive heart failure, e.g. weight gain, dependent oedema, or increased dyspnoea. | **Stop dronedarone** if congestive heart failure is suspected and refer urgently to specialist team. |
| | **Hepatotoxicity**:<br>Serum transaminases >5xULN or any symptoms of hepatic injury | **Stop dronedarone**. Urgent referral to initiating specialist and hepatologist. |
| | ALT elevated >3xULN but no symptoms of hepatic injury | Continue dronedarone and repeat LFTs in 48-72 hours. If still elevated **stop dronedarone** and discuss with specialist urgently. |

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| | Symptoms of hepatic injury (e.g. hepatomegaly, weakness, ascites, jaundice) | Check LFTs urgently; proceed as above. |
| | **Pulmonary toxicity**: new/worsening cough, shortness of breath or deterioration in general health (e.g. fatigue, weight loss, fever) | Continue dronedarone**.** Urgent referral to initiating specialist and respiratory specialist. |
| | **Gastrointestinal disturbance**: diarrhoea, nausea, vomiting, abdominal pain, dyspepsia | Continue dronedarone. May require dose reduction; discuss with specialist if persistent. |
| | **General disorders**: fatigue, asthenia | Continue dronedarone. May require dose reduction; discuss with specialist. |
| | **Dermatological disorders**: rashes, pruritus, photosensitivity | Continue dronedarone. Reinforce appropriate self-care, including sun avoidance and purchasing of a broad spectrum sunscreen (at least SPF30) if photosensitivity occurs.<br>May require dose reduction; discuss with specialist. |

## 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.

**The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:**

- **Signs or symptoms of pulmonary toxicity**, e.g. breathlessness, non-productive cough or deterioration in general health (e.g. fatigue, weight loss, fever)
- **Signs or symptoms of liver injury**, e.g. abdominal pain, loss of appetite, nausea, vomiting, fever, malaise, fatigue, itching, dark urine, or yellowing of skin or eyes
- **Signs or symptoms of heart failure**, e.g. development or worsening of weight gain, dependent oedema, or dyspnoea
- **Signs or symptoms of bradycardia,** e.g. dizziness, fatigue, fainting, shortness of breath, chest pain or palpitations, confusion or trouble concentrating

**The patient should be advised:**

- Avoid grapefruit and grapefruit juice while taking dronedarone.
- If taking a statin and dronedarone, to report any signs of unexplained muscle pain, tenderness, weakness or dark coloured urine.
- Photosensitivity is an uncommon side effect of dronedarone (less than 1 in 100 people). If it occurs, patients should be advised on appropriate self-care: e.g. sun avoidance, protective clothing, avoiding tanning (including tanning beds) and to purchase and use of a wide broad spectrum sunscreen (at least SPF30). These measures should be continued for the duration of therapy.

Patient information:

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| | **British Heart Foundation – Anti-arrhythmics:**<br>https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/drug-cabinet/anti-arrhythmics |
| **12. Pregnancy, paternal exposure and breast feeding**<br>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. | **Pregnancy:**<br>There are limited data on the use of dronedarone in pregnant women. Studies in animals have shown reproductive toxicity. Use is not recommended during pregnancy and in women of childbearing potential not using contraception.<br>**Breastfeeding:**<br>Low levels of dronedarone are anticipated in breast milk. Use is cautioned while breast feeding; infants should be monitored for adverse events such as diarrhoea, vomiting, weakness, bradycardia.<br>Information for healthcare professionals:<br>https://www.sps.nhs.uk/medicines/dronedarone/ |
| **13. Specialist contact information** | Name: **Northumbria HC FT Cardiology team**<br>Telephone number: Consultant's secretary via switch or if urgent on-call cardiologist via switch – 0344 8118111<br><br>Name: **Newcastle upon Tyne FT Cardiology team**<br>Telephone number: Consultant's secretary via switch or if urgent on-call cardiologist via switch – 0191 2336161 |
| **14. Additional information** | Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. |
| **15. References** | • eBNF accessed via www.medicinescomplete.com on 12/04/2021<br>• Dronedarone hydrochloride 400 mg film-coated tablets (Multaq®). Sanofi. Date of revision of the text: 02/06/2020. Accessed via https://www.medicines.org.uk/emc/product/497/ on 09/04/2021.<br>• Dronedarone hydrochloride 400 mg film-coated tablets (Dronedarone Aristo). Aristo Pharma. Date of revision of the text: 14/10/2020. Accessed via https://www.medicines.org.uk/emc/ on 09/04/2021<br>• NHS England and NHS Clinical Commissioners. Aug 2019. https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/ Accessed 09/04/2020<br>• MHRA. Drug Safety Update volume 5 issue 3: A1. October 2011. Dronedarone (Multaq▼): cardiovascular, hepatic and pulmonary adverse events – new restrictions and monitoring requirements. Accessed via https://www.gov.uk/drug-safety-update/dronedarone-multaq-cardiovascular-hepatic-and-pulmonary-adverse-events-new-restrictions-and-monitoring-requirements on 09/04/2021 |

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| | • NICE. TA197: Dronedarone for the treatment of non-permanent atrial fibrillation. Last updated December 2012. Accessed via https://www.nice.org.uk/guidance/ta197 on 12/04/2021.<br>• NICE. NG196: Atrial fibrillation: diagnosis and management. Last updated June 2021. Accessed via https://www.nice.org.uk/guidance/ng196 on 28/04/21.<br>• Specialist Pharmacy Service- Medicines Monitoring. Published July 2021 Accessed via Dronedarone monitoring – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice on 24/06/2022.<br>• Specialist Pharmacy Service. Lactation Safety Information: dronedarone. Last reviewed 05/08/20. Accessed via https://www.sps.nhs.uk/medicines/dronedarone/ on 12/04/2021.<br>• LiverTox. Dronedarone. Last updated 05/01/2018. Accessed via https://www.ncbi.nlm.nih.gov/books/NBK548208/ 12/04/2021.<br>• CredibleMeds. QTDrugs List. Clarithromycin. Last updated 31st March 2021. Accessed via https://crediblemeds.org/ on 26/04/21 |
| **16. To be read in conjunction with the following documents** | • Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/<br>• NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/<br>• General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care<br>• NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/. |
| **17. Local arrangements for seeking specialist advice**<br>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:**<br>• If pregnancy occurs or if the patient is planning to become pregnant or breastfeed.<br>• 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)<br>• 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<br>• |
| **18. Version Control** | Date of Issue / Review: January 2023<br>Date for next Review: January 2026<br>Approved by: |

## Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear

Patient name:
Date of birth:
NHS Number*:*
Diagnosis:

As per the agreed North of Tyne, Gateshead and North Cumbria APC shared care protocol for Dronedarone 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** |
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| 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 | No |
| The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care | No |
| The risks and benefits of treatment have been explained to the patient | No |
| The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed | No |
| The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments | 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) | No |
| I have included with the letter copies of the information the patient has received | No |
| I have provided the patient with sufficient medication to last until | No |
| I have arranged a follow up with this patient in the following timescale | No |

Treatment was started on and the current dose is .

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

The next blood monitoring is due on and should be continued in line with the shared care guideline.

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:
Role and specialty:
Daytime telephone number:
Email address:
Alternative contact:
Out of hours contact details:

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

**Primary Care Prescriber Response**

Dear

Patient

NHS Number

Identifier

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 |
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I can confirm that

☐ I am willing to take on this responsibility from 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: