BSW APC: BaNES, Swindon & Wiltshire (BSW) CCG, Avon & Wiltshire Mental Health Partnership NHS Trust (AWP), Royal United Hospitals Bath NHS Foundation Trust, Great Western Hospitals NHS Foundation Trust, Salisbury NHS Foundation Trust, Virgin Care, Swindon Community Health Services, Wiltshire Health & Care

SHARED CARE AGREEMENT

Sildenafil 25mg/50mg (*generic*) tablets for digital ulceration / management of severe Raynaud's phenomenon in patients with Connective Tissue Disease [unlicensed indication] – Adults

Amber TLS – 1 Month

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and in the patient's best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) concerned and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

Responsibilities of Secondary Care Specialist

- Initiate treatment and prescribe for the length of time agreed (1 months) – this should be a sufficient amount of time to allow optimisation of treatment and demonstrate that the patient's response is consistent.
- Discuss the benefits and side effects of treatment with the patient.
- Review concurrent medications for potential interactions prior to initiation.
- Undertake the clinical assessment and relevant monitoring at baseline and during the initiation period.
- Communicate details of treatment to GP (in writing or via secure email) within the first month of treatment and ask the GP whether he or she is willing to participate in shared care.
- Discuss shared care arrangements with the patient/carer, obtain their consent and explain their responsibilities.
- Review the patient's condition and monitor response to treatment regularly where indicated.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Supply GP with clinic letter or discharge summary within 14 days of an outpatient review or inpatient admission, and inform GP if patient does not attend scheduled clinic appointments.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Report adverse events to the MHRA.
- Stop treatment where appropriate or provide GP with advice on when to stop.

Responsibilities of GP/Primary Care Prescriber

- Reply to the request as soon as practicable if they are unable to support shared care (in writing or via secure email)
- Prescribe medicine at the dose recommended after the initiation period (1 month).
- Undertake ongoing clinical assessment and relevant monitoring following initiation period.
- Review any new concurrent medications for potential interactions.
- Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Report adverse events to the specialist and MHRA.
- Stop treatment on the advice of the specialist.

Responsibilities of Patient/Carer

- Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
- Share any concerns in relation to treatment with medicine.
- Report any adverse effects to the specialist or GP whilst taking the medicine.
- Attend appointments for clinical review and monitoring.

1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	Connective Tissue Disease (CTD) encompasses a range of uncommon systemic autoimmune conditions that are capable of causing a wide range of tissue damage due to microvascular injury and excessive fibrotic response. In Systemic sclerosis (SSc) the most common vascular manifestation is Raynaud's phenomenon due to excessive vasoconstriction. In SSc digital ulceration occurs in over 50% of patients at some point. Severe ulceration can lead to complications, including infections (including osteomyelitis), which may result in amputation and can contribute to lengthy spells of hospital treatment and have devastating effects on hand function and the independence of the individual. Standard medical treatments include; calcium channel blockers, ACE inhibitors, losartan and/or fluoxetine (although only immediate release nifedipine is licensed for Raynaud's management). Where standard medical treatment is ineffective and digital ulceration develops intravenous prostanoids (iloprost or epoprostenol) may be used but require administration on a day case basis, usually on 5 consecutive days. Bosentan, an endothelin receptor antagonist, is licensed to reduce the incidence of new digital ulcer formation in patients with active digital ulceration. Sildenafil, a phosphodiesterase type 5 inhibitor (PDE5i) is also a potent vasodilator which can be used instead of, or in combination with either prostanoids or bosentan. This is an unlicensed, but well established use with the evidence base discussed in NICE ESUOM42 (link below). Treatment with sildenafil aims to reduce severity of Raynaud's phenomenon and/or treat established, and prevent further, digital ulceration in SSc and associated CTD's. NICE ESUOM42 CCP: Sildenafil and bosentan for the treatment of digital ulceration in SSc in adults (see pg 14 for treatment pathway)
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	• Sildenafil (25mg, 50mg and 100mg) is licensed for use in adult men with erectile dysfunction. Revatio® brand (20mg) is specifically licensed for treatment of pulmonary arterial hypertension in defined patients. • For the purposes of this shared care policy sildenafil is being used outside of license (off-label) for the treatment and prevention of digital ulceration in patients with systemic sclerosis initiated on treatment as per the NHSE England Clinical Commissioning Policy (link above) and for management of severe Raynaud's phenomenon in Connective Tissues Disorders (CTDs) such as scleroderma.

3. Pharmaceutical aspects		
	Route of administration:	Oral
	Formulation:	25mg & 50mg tablets
	Administration details:	25 – 50mg three times a day
	Other important information:	Used outside of product license

<table>
<tr><td>4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy
Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results.
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.
The duration of treatment will be determined by the specialist, based on clinical response and tolerability.
Termination of treatment will be the responsibility of the specialist.</td><td colspan="2">Sildenfil 25 – 50mg three times a day with dose titrated by specialist to tolerance and response.

If on established treatment the patient develops symptomatic hypotension then consider stepwise reduction from 50mg three times a day > 25mg three times a day > 25mg twice a day.
If symptomatic hypotension persists at 25mg twice daily then stop sildenafil and seek advice from specialist.

No routine monitoring required.

May benefit from opportunistic review of hepatic and renal function (if test undertaken for another reason).

Periodic/routine assessment of blood pressure. Assessment of blood pressure if signs/symptoms suggestive of hypotension.</td></tr>
<tr><td rowspan="3">5. Baseline investigations and initial monitoring to be undertaken by specialist</td><td colspan="2">Baseline investigations</td></tr>
<tr><td colspan="2">• Assessment of blood pressure</td></tr>
<tr><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>6. Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td></td><td>• Blood pressure assessment</td><td>• Opportunistically / in response to reports of symptoms suggestive of symptomatic hypotension</td></tr>
<tr><td>7. Action(s) to be taken by primary care if abnormal result(s)</td><td colspan="2">• Stepwise dose reduction as per section 4.</td></tr>
<tr><td>8. Cautions and contraindications
Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.</td><td colspan="2">Cautions
• Co-administration with nitrates in any form (including amyl nitrate, glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate) due to significant potentiation of hypotensive effects.
• Patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure.
• Hypotension (blood pressure < 90/50 mmHg).
• Recent history of stroke or myocardial infarction.</td></tr>
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<tr><td></td><td colspan="2">Contraindications
Precaution in patients with increased susceptibility to vasodilators, including those with postural hypotension, fluid depletion, left ventricular outflow obstruction (such as aortic stenosis, hypertrophic obstructive cardiomyopathy).</td></tr>
<tr><td>9. Significant medicine and food interactions and management
For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)</td><td colspan="2">See BNF for full list (https://bnf.nice.org.uk/interaction/sildenafil-2.html). Of note;
• Alpha Blockers – Caution. May lead to symptomatic hypotension in a few susceptible individuals. Most likely to occur within 4 hours post sildenafil dosing. Patients should be haemodynamically stable on an alpha blocker prior to initiating sildenafil.
• Bosentan – Caution. May decrease exposure to sildenafil and higher doses required for therapeutic effect. NOTE: Secondary Care Specialists potentially need to titrate dose of sildenafil when stopping or starting bosentan.
• Clarithromycin – Caution. Increases serum concentrations of sildenafil. Reduce dose of sildenafil if symptoms of hypotension develop.
• Disopyramide – Avoid. Risk of ventricular arrhythmias. Erythromycin - Caution. Increases serum concentrations of sildenafil. Reduce dose of sildenafil if symptoms of hypotension develop.
• Grapefruit juice – Avoid. May increase serum concentrations of sildenafil
• Itraconazole – Avoid. Increases serum concentrations of sildenafil, consider dose reduction if unavoidable.
• Ketoconazole – Avoid. Increases serum concentrations of sildenafil, consider dose reduction if unavoidable.
• Nicorandil – Avoid. Potentiates the hypotensive effect of nicorandil.
• Nitrates – Avoid. Potentiates the hypotensive effect of nitrates.
• Pulmonary Arterial Hypertension Drugs - Avoid. Potentiation likely.
• Ritonavir – Avoid. Substantially increases serum concentrations of sildenafil
• Saquinavir – Avoid. Increases serum concentrations of sildenafil.</td></tr>
<tr><td rowspan="5">10. Adverse effects and management
Include details of incidence, identification, importance and management.</td><td>Adverse Effect</td><td>Action to be taken if detected</td></tr>
<tr><td>• Any sudden visual defect</td><td>• Stop taking sildenafil and seek medical advice immediately (cases of non-arteritic anterior ischaemic optic neuropathy, although rare, have been reported with sildenafil and other PDE5 inhibitors)</td></tr>
<tr><td>• Feeling of dizziness</td><td>• May be indicative of a drop in blood pressure. Arrange assessment of blood pressure in appropriate setting.
• Do not drive or operate machinery if experiencing dizziness.</td></tr>
<tr><td>• Symptomatic hypotension</td><td>• Dose reduction (see above)</td></tr>
<tr><td>• Priapism</td><td>• Seek immediate medical assistance if an erection persists for 4 or more hours</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">• To stop taking and seek advice if any visual defects
• To seek advice if feeling of dizziness
• (In male patients) to seek immediate medical assistance if an erection persists for 4 or more hours
• Do not use nitrates in any form (including amyl nitrate, glyceryl trinitate, isosorbide mononitrate or isosorbide dinitrate) due to potentiation of hypotensive effects</td></tr>
<tr><td>12. Pregnancy and breast feeding</td><td colspan="2">• Pregnancy – seek specialist advice and not suitable for continuation under Shared Care Agreement. See BUMP for additional information.</td></tr>
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<tr><td>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 GP and the specialist.</td><td colspan="4">https://www.medicinesinpregnancy.org/Medicine--pregnancy/Sildenafil/
• Breastfeeding - Limited data indicate that sildenafil and its active metabolite in are poorly excreted into breastmilk. Amounts ingested by the infant are small and would not be expected to cause any adverse effects in breastfed infants.</td></tr>
<tr><td rowspan="9">13. Specialist contact information</td><td colspan="4"></td></tr>
<tr><td rowspan="2">GWH</td><td>Rheumatology advice line</td><td>01793 604 323</td><td>gwh.rheumatologyadvice@nhs.net</td></tr>
<tr><td>GP Consultant Secretaries</td><td></td><td>gwh.rheumatologysecretaries@nhs.net</td></tr>
<tr><td rowspan="2">RUH</td><td>Rheumatology advice line (for patients)</td><td>01225 428 823</td><td></td></tr>
<tr><td>GP queries</td><td>07747 630 875</td><td></td></tr>
<tr><td rowspan="2">SFT</td><td>Rheumatology advice line</td><td>01722 429 137</td><td></td></tr>
<tr><td>Consultant Secretaries</td><td>01722 345 556</td><td></td></tr>
<tr><td colspan="4">Other Specialist Contact Information</td></tr>
<tr><td colspan="4">• N/A</td></tr>
<tr><td>14. Additional information
For example, process for when Specialist or GP changes roles; specific issues related to patient age/ capacity/ specific monitoring.</td><td colspan="4">• Shared Care Agreement only relates to 25mg and 50mg preparation (do not prescribe different strengths)
• It is recommended that the indication (Raynaud’s / Digital ulceration) is clarified on the prescribing system to avoid confusion over use.</td></tr>
<tr><td>15. References</td><td colspan="4">• Summary of Product Characteristics for via https://www.medicines.org.uk/emc
• BNF online via https://bnf.nice.org.uk/</td></tr>
<tr><td>16. To be read in conjunction with the following documents</td><td colspan="4">• NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/</td></tr>
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Shared Care Agreement template adapted with agreement from AWP by Rachel Hobson, October 2020.