**INDICATION**

“Off-label” use for secondary severe Raynaud’s phenomena associated with systemic sclerosis/scleroderma. Treatment must be initiated and monitored by a specialist experienced in the diagnosis and treatment of Raynaud’s disease in accordance with national and international best practice, when the following criteria apply:

- Patient has severe Raynaud’s causing digital ischaemia & ulceration
- Patient is following lifestyle management (proper body insulation, avoidance of cold exposure, smoking cessation support, avoidance of sympathomimetic drugs); and
- Patient has persisting severe symptoms despite standard treatment with calcium channel blockers, ACE inhibitors and fluoxetine (unless contraindicated or not tolerated)


**AREAS OF RESPONSIBILITY FOR SHARED CARE**

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of sildenafil can be shared between the specialist setting and the patient’s GP (if different). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

**REFERRAL AND INITIATION**

**Specialist Responsibilities**

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<table>
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<tr>
<td>1</td>
<td>The specialist will diagnose and co-ordinate the long-term management of patients with systemic sclerosis</td>
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<td>2</td>
<td>The specialist will ensure that patients have tried first line measures for secondary Raynaud’s symptoms</td>
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<td>3</td>
<td>The specialist will initiate sildenafil therapy in secondary care</td>
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<td>4</td>
<td>The specialist team will ensure adequate blood pressure monitoring is undertaken at initiation and dose adjustment</td>
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<tr>
<td>5</td>
<td>The specialist will provide on-going review and monitoring of patients receiving sildenafil to enable assessment of response to treatment</td>
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<td>6</td>
<td>The specialist will discontinue sildenafil in cases where benefit is not demonstrated</td>
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<td>7</td>
<td>The specialist will establish the patient on a stable dose of sildenafil prior to asking the GP to take on long-term prescribing</td>
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General Practitioner Responsibilities

1. The GP will be asked to continue to prescribe generic sildenafil at the dose recommended by the specialist.
2. Identify & report any adverse events to the specialist & MHRA and take appropriate action.
3. Report any worsening of the condition to the specialist.

Patient's role (or that of carer)

1. The patient will report any adverse events to their GP and rheumatology specialist team.
2. The patient will report worsening of digital ulceration to their specialist so that treatment can be intensified appropriately.

SUPPORTING INFORMATION

Monitoring

Unless otherwise advised by the specialist:
GP practice to monitor patient’s blood pressure after stabilisation. If hypotensive seek advice from specialist.

Dosage and Administration

Sildenafil tablets 25 – 50mg three times daily according to response.

- Treatment is usually initiated at 25mg three times a day as per national guidance.
- If the patient has renal or hepatic impairment, low baseline blood pressure or judged to be at risk of hypotension, the specialist may advise the patient to introduce treatment cautiously.
- The specialist will prescribe at least the first month of sildenafil treatment and ensure the patient understands their treatment, including which side effects to report promptly and advise the patient to stop treatment if they experience hypotensive side effects.
- The specialist will arrange for the patient to book an appointment for a BP check before starting treatment and to take the first tablet 2 hours before the appointment.
- Once stabilised the dose may be further increased (by the specialist) to 50mg three times a day in accordance with response and tolerability.
- No dose reduction is required for patients >65yrs.
- Clearance may be reduced in renal impairment (creatinine clearance <30 mL/min) or hepatic impairment (such as cirrhosis) - start with 25 mg and titrate cautiously.

Contraindications

- Co-administration with nitric oxide donors (such as amyl nitrite) or nitrates in any form - potentiates the hypotensive effects of nitrates due to effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway.
- 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.
- Severe hepatic impairment
- Hypotension (blood pressure <90/50 mmHg)
- Recent history of stroke or myocardial infarction
Dorset Medicines Advisory Group

- known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases)
- Pregnant or breastfeeding women - no adequate and well-controlled studies available
- Rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption due to lactose content of tablet.
- Pulmonary hypertension secondary to sickle cell anaemia

Cautions

- Patients with increased susceptibility to vasodilators, including those with postural hypotension, fluid depletion, left ventricular outflow obstruction (e.g., aortic stenosis, hypertrophic obstructive cardiomyopathy).

Side effects

- Dizziness. Advise patients to be aware of how they react to sildenafil, before driving or operating machinery
- Priapism. Advise patients to seek immediate medical assistance if an erection persists longer than 4 hours.
- Visual defects. Advise patients to stop taking Sildenafil and seek medical attention immediately in the event of any sudden visual defect or loss of vision.
- Headaches, flushing, night sweats - Very Common.
- Diarrhoea, dyspepsia - Very Common.

Interactions

- Alpha Blockers -Caution. May lead to symptomatic hypotension in a few susceptible individuals. Most likely to occur within 4 hours post sildenafil dosing.
- 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.
- Anti-retrovirals -Avoid. Substantially increases serum concentrations of sildenafil

This list is not exhaustive. The manufacturer’s summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.
Drug costs:

£197 pa for 25mg TDS; £197 pa for 50mg TDS (Drug Tariff Aug 2017)

References


References drawn from Clinical Commissioning Policy


Developed by Rheumatology Working Group, March 2017
Approved by Dorset Medicines Advisory Group, July 2017
Review date March 2019 or before, in light of new evidence or recommendations.