DOXAZOSIN FOR TRAUMA- RELATED NIGHTMARES

TARGET AUDIENCE	Secondary care, mental health specialist prescribers.
PATIENT GROUP	All mental health patients under specialist care.

Clinical Guidelines Summary

- Doxazosin is the preferred alpha-receptor blocker in treating trauma-related nightmares
- It has a risk of hypotension; therefore, a baseline blood pressure should be measured prior to recommending/ initiating treatment.
- It should be titrated according to response and tolerability.
- It is for specialist initiation only.
- A “Form C PC” must be completed to by the recommending specialist to acknowledge the off-label nature of the prescribing request and to ensure continuity of prescribing in community.
- Duration of treatment is not well defined. As such, discontinuation can be considered after a period of stability or if ineffective after appropriate treatment trial. It is advisable to avoid abrupt withdrawal of alpha blockers due to risk of rebound hypertension.

DOXAZOSIN FOR TRAUMA- RELATED NIGHTMARES

Indication:

Doxazosin is indicated for distress / functional impairment in individuals experiencing trauma-related nightmares. This is not a licensed indication for doxazosin.

Mechanism of action:

Doxazosin is an alpha-receptor blocker. It blocks the brain's response to the neurotransmitter norepinephrine. Trauma nightmares appear to arise during light (non-REM) sleep or disruption in REM sleep and blocking norepinephrine has been shown to normalise and increase REM sleep, making trauma nightmares less likely and improving sleep quality.

Choice of alpha-receptor blocker for trauma-related nightmares

Doxazosin is the preferred alpha-blocker for this indication

Doxazosin has a long half-life which allows for once daily dosing. Standard and modified-release preparations have a similar half-life, allowing the immediate release preparation of doxazosin to be used for once daily dosing. There is no therapeutic benefit to using the modified release preparation (and is currently non-formulary).

The evidence suggests a dose range of 4-16mg. It is possible a response can be seen at lower doses. Therefore, titrate according to response/ tolerability and use the minimum effective dose.

Suggested Dose Schedule
Doxazosin: 2mg for 3 nights → 4mg for 3 nights → 6mg for 3 nights → 8mg (maintenance).
If there are issues with tolerance, patients can go back to their previous dose.
While there is not necessarily a clinical need, doxazosin if often prescribed at night.

Further dose increments of 2-4mg up to max 16 mg per day may be considered if response is positive but partial. It is worth noting that a response may be also be seen at doses lower than 2mg.

Duration of treatment is not well defined. As such, discontinuation can be considered after a period of stability or if ineffective after appropriate treatment trial. It is advisable to avoid abrupt withdrawal of alpha blockers due to risk of rebound hypertension.

<u>Prazosin</u> (for information only – Not currently recommended for use)
Prazosin has a shorter half-life and may require multiple doses in comparison to doxazosin. Effects may wear off, leading to disturbance in the latter period of sleep. Some evidence suggests a maintenance dose of 2-6mg, whereas other ranges go to 16mg. Treatment resistant cases can require maintenance of 25-45mg and above. Doses should be titrated according to response / tolerability and the minimum effective dose should be used. High maintenance doses present a practical issue as prazosin is only available in 500 micrograms tablets.

Please refer to SPC for full prescribing information.

Contraindications:

Doxazosin is contraindicated in:

- Hypersensitivity to the active substance or other types of quinazolines (e.g. prazosin, terazosin, doxazosin), or to any of the excipients listed in section 6.1 of product SPC.
- Patients with a history of orthostatic hypotension
- Patients with hypotension
- Patients with benign prostatic hyperplasia and concomitant congestion of the upper urinary tract, chronic urinary tract infection or bladder stones

Cautions:

Care with initial dose (postural hypotension, particularly where there are other concomitant antihypertensives); cataract surgery (risk of intra-operative floppy iris syndrome); elderly; heart failure; pulmonary oedema due to aortic or mitral stenosis

Interactions:

Antihypertensive medication including diuretics and beta-blockers and other alpha-blockers may result in additive hypotensive effects. This may be more severe in congestive heart failure.

Phosphodiesterase type-5 inhibitors (eg: Sildenafil, Tadalafil, etc) – Postural hypotension

CYP3A4 inhibitors – Moderately increased exposure to alpha-blockers.

Side effects:

Common **(≥1/100 to <1/10)**	**Uncommon** **(≥1/1,000 to <1/100)**	**Very Rare** **<1/10,000)**
Dizziness, drowsiness, dry mouth, dyspnoea, GI discomfort, influenza like illness, skin reaction, peripheral oedema, urinary incontinence	Anxiety, depression, angina pectoris, abnormal appetite, gout, MI, stroke, constipation, impotence	Alopecia, bronchospasm, gynaecomastia, priapism, hepatic disorder, malaise, leukopenia, thrombocytopenia
See SPC/ BNF for full list of potential adverse drug reactions		

Outpatient Prescribing Principles for Specialist:

- Assess need for medication.
- Take a baseline blood pressure to exclude hypotension.
  (normal blood pressure is considered to be between 90/60mmHg and 120/80mmHg)
- A Form C PC- prescribing request to primary care for unlicensed medicine and patient consent form should be completed and sent to the patient's GP alongside baseline blood pressure results.
- Recommend dosing schedule and titration to patient's GP.
- It may be appropriate to check blood pressure if signs of hypotension (eg: dizziness, light headedness) but routine monitoring is not necessary. Patients should be made aware of the symptoms of hypotension.
- Regular reviews should take place. Although a duration of treatment is not well established, discontinuation may be considered after a period of stability.
- Initiating specialist to please ensure appropriate monitoring equipment is available

Inpatient Prescribing Principles for Specialist:

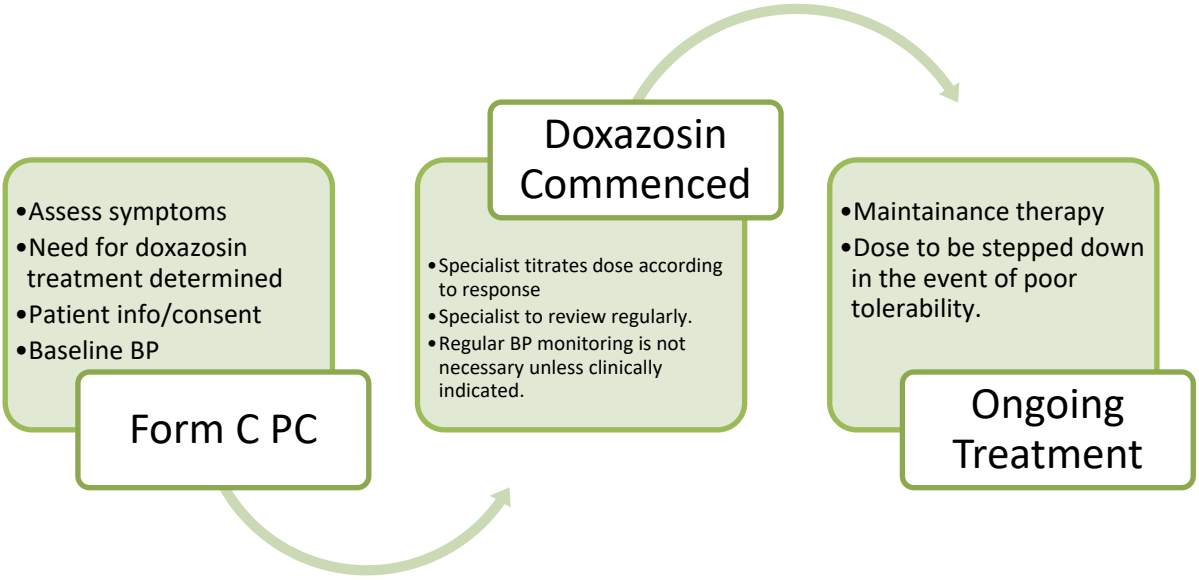
- Assess need for medication.
- Take a baseline blood pressure to exclude hypotension.
- Initiate and titrate as per dosing schedule.
- It may be appropriate to check blood pressure if signs of hypotension (eg: dizziness, light headedness) but routine monitoring is not necessary. Patients should be made aware of the symptoms of hypotension.
- A Form C PC- prescribing request to primary care for unlicensed medicine and patient consent form should be completed and sent to the patient's GP together with discharge letter.
- Regular reviews should take place. Although a duration of treatment is not well established, discontinuation may be considered after a period of stability.

Form C PC is available via the following link:
form-c-pc-prescribing-request-to-primary-care-for-unlicensed-medicine.pdf (scot.nhs.uk)

Patient information resources
The Choice and medication website is a useful source of written information for patients on psychotropic medication and includes information on the use of doxazosin for this indication.
https://www.choiceandmedication.org/nhs24/

Need for ongoing monitoring:

- Specialists hold responsibility for BP monitoring
- Regular monitoring of BP is not necessary once therapeutic dose established
- BP only taken, if there are concerns about common doxazosin related side effects, eg: dizziness.



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Appendices

1. Governance information for Guidance document

Lead Author(s):	Mogese Abbas (Clinical Pharmacist)
Endorsing Body:	Mental Health and Learning Disability Drug and Therapeutics Committee (MHLD D&T) Area Drug and Therapeutics Committee (ADTC)
Version Number:	1
Approval date	24/07/2024
Review Date:	24/07/2027
Responsible Person (if different from lead author)	

CONSULTATION AND DISTRIBUTION RECORD	
Contributing Author / Authors	Lorna Templeton (Lead Pharmacist MHLD) David Semple (Consultant Psychiatrist)
Consultation Process / Stakeholders:	MHLD D&T ADTC
Distribution	Dissemination to MHLD services. NHSL Clinical Guidelines website and app.

Appendix 1- Form C PC for Doxazosin

Prescribing Request to Primary Care for Unlicensed Medicine

NHS Lanarkshire

Dear Dr _____ Date _____

Patient		CHI no.

I would be obliged if you would prescribe the following for this patient

Medicine *Doxazosin*	Form *Immediate release tablets*
Dose	Frequency *Once daily*
Indication *Trauma-related nightmares*	

This request falls under the following GMC reason for prescribing an unlicensed medicine *(please tick)*

THERE IS NO SUITABLY LICENSED MEDICINE THAT WILL MEET THE PATIENT'S NEED	
i. Medicine is not licensed for the specific age of the patient but is licensed for the indication in other age groups	
ii. Medicine is not licensed for the specific age and for the specific indication but is licensed for other indications in that age group and for the indication in other age groups	
iii. The licensed dosage would not meet the patient's needs	
iv. The patient requires a formulation that is not available as a licensed product	
v. Other (*specify*) – *Medication is being used for an indication that is not licenced*	x

A SUITABLY LICENSED MEDICINE THAT WOULD MEET THE PATIENT'S NEED IS NOT AVAILABLE	
i. Temporary shortage of licensed medicine	
ii. No licensed formulation available in UK but is available for import from abroad	
iii. Medicine is at pre-marketing authorisation stage or has been discontinued and can be used for a named patient on compassionate grounds	
vi. Other (*specify*) – *Medication is being used for an indication that is not licenced*	x

PRESCRIBING FORMS PART OF A PROPERLY APPROVED RESEARCH PROJECT	

Evidence for use of medicine

The unlicensed / off-label use of this medicine is described as an evidence based treatment option within established guidelines referenced below. *Quote Guideline(s) e.g. SIGN, NICE, BNF, The Maudsley Prescribing Guidelines in Psychiatry, Scottish Palliative Care Guidelines, British Association of Dermatologists.*	☐
Treatment is not described in established guidelines but approval from the relevant body (e.g. clinical director, ADTC) has been obtained in this instance. *NHS Lanarkshire's Doxazosin for Trauma-related nightmares guidance*	☒

I consider this treatment necessary for the following reasons

Distress / functional impairment in an individual experiencing trauma-related nightmares.

Monitoring Arrangements

Requirements	Who will take responsibility for monitoring & where	Frequency
Baseline BP (to rule out hypotension)	*Completed by recommending specialist*	

Initial duration of medication trial	Treatment review date

Special precautions (*if any*): *Further BP monitoring only required if clinically indicated (e.g. in event of dizziness)*

I have explained to the patient/patient representative that this treatment is unlicensed and the reasons for this and have attached a signed copy of consent (*see overleaf*).

Signature _____ Name _____ Job title _____

A copy of this form should be retained in the patient notes, a copy should be sent to the patient's GP and if requested a copy should be given to pharmacy (hospital or community).
ADTC ratified: March 2019