ASHFORD & ST PETER'S HOSPITALS NHS TRUST

DRUGS & THERAPEUTICS COMMITTEE EVALUATION FOR:

Noqdirna

Requested by: *Dr Nimalan Arumainayagam, Consultant Urologist*

Approved Name	Desmopressin
Brand Name (Manufacturer)	Noqdirna Ferrin Pharmaceutical Ltd
Therapeutic Comment	Noqdirna contains desmopressin a synthetic analogue of naturally occurring anti-diuretic hormone arginine vasopressin (AVP). Desmopressin mimics vasopressin's anti-diuretic effect, binding to the V2 receptors in the renal collecting tubules of the kidneys, causing reabsorption of water into the body. This reabsorption in turn decreases night-time urine production. Due to the proposed low gender-specific doses (25 microgram for females and 50 microgram for males), and the limited duration of action of Noqdirna, the antidiuretic activity is limited to the night-time sleep period
Presentation	Oral lyophilisate sublingual tablets
BNF Category	Pituitary and hypothalamic hormones and analogues. Chapter 6
Formulary	None
Licensed use	Symptomatic treatment of nocturia due to idiopathic polyuria in adults
Intended use	Symptomatic treatment of nocturia due to idiopathic polyuria in adults
Sector of use	Initial prescribing by secondary care and all further prescribing passed to primary care
Formulary status in regional Trusts	
Course details	Women: 25 microgram daily, one hour before bedtime, administered sublingually without water. • Men: 50 microgram daily, one hour before bedtime, administered sublingually without water.
Estimated usage	Maximum 3472 patients across primary and secondary care

Hospital Cost
(Including VAT) *Multiply cost by 1.2 (current VAT rate 20%)*

Formulation	Dose	Cost for 28 days treatment £	Cost per annum (28 days x 13) £	Cost per annum per x No. of patients £
Requested drug		*£17.46*		
Similar drugs on the formulary		-		

Community Cost
(Excluding VAT)
(Prices from eMIMs/eBNF)

Formulation	Dose	Cost for 28 days treatment £	Cost per annum (28 days x 13) £	Cost per annum per x No. of patients £
Requested drug		£15.16		
Similar drugs on the formulary				

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Clinical benefits or disadvantages compared to current treatment

Noqdirna is licensed for the treatment of Idiopathic nocturnal polyuria in male and female. Existing higher-dose formulations of desmopressin are indicated for use only in patients up to 65 years, because of the increased risk of hyponatraemia in the elderly. However, with the recommended monitoring of serum sodium, Noqdirna can be used in patients over 65 years.
Current practice may also include off license usage of diuretics (which require longer term serum electrolyte monitoring) or treatment with anticholinergics or alpha blockers which are used to treat overactive bladder (OAB) or benign prostatic hyperplasia (BPH) respectively. This will result in only a limited response if the patient has a component of nocturnal polyuria causing the nocturia symptoms. Noqdirna could therefore be beneficial inpatients with OAB and BPH who have a component of nocturnal polyuria and who remain sub-optimally treated in clinical studies.
The once-daily sublingual tablets are available in gender-specific doses of 50 microgram for men and 25 microgram for women, both taken one hour before bedtime. To reduce the risk of fluid overload, fluid intake should be limited to a minimum from one hour before and until eight hours after administration.
The effect of Noqdirna on nocturia was evaluated in separate randomised, placebo –controlled double-blind trials in men (Weiss JP et al 2013 n=385) and women (Sand PK et al 2013 n=261).
Over 3 months of treatment, desmopressin reduced the average number of night-time urinations from baseline compared with placebo by 0.22 in women (p=0.028) and 0.37 in men (p=0.0003).
The number of patients with at least a 33% decrease in the mean number of nocturnal voids nearly doubled with desmopressin treatment, with odds ratios of 1.98 in men (p=0.0009) and 1.85 in women (p=0.006) compared with placebo.
Nocturnal urine volume, a secondary endpoint, decreased by 209ml in men treated with desmopressin and 235ml in women treated with desmopressin, compared with 131ml and 151ml, respectively, in men and women receiving placebo (p=0.009 and p=0.003, respectively).
Desmopressin was well tolerated by both men and women, according to the investigators. The most commonly reported adverse reactions were dry mouth (13%), headache (3%), hyponatraemia (3%), and dizziness (2%).
Desmopressin is analogue of endogenous vasopressin. It binds to specific receptors in the kidneys, concentrating urine and leading to reduced night-time urine production.

Additional information	<u>Side effects</u> Hyponatraemia (in more serious cases with convulsions) on administration without restricting fluid intake; nausea, dry mouth, headache, dizziness. <u>Monitoring</u> In elderly patients serum sodium must be within the normal range, before initiating treatment, in the first week (4-8 days after initiation) and again at one month. Noqdirna should be discontinued if the serum sodium level falls below the lower limit of normal range.
Advantages over existing therapy as seen by the requesting consultant	There are no other licensed treatments for nocturria due to idiopathic nocturnal polyuria in adults including over 65s.
Is the drug PbR	

excluded?	
Does the drug pose any significant potential for medication error?	No
Points to consider	• Noqdirna is the only drug licensed for the treatment of nocturia due to idiopathic nocturnal polyuria in adults including over 65 • European association of Urology state that desmopressin may be prescribed to decrease nocturia due to nocturnal polyuria in men under the age of 65. **Scottish Medicines Consortium (SMC)** **https://www.scottishmedicines.org.uk/media/1552/desmopressin_nogdirna_resubmission_final_july_2017_for_website.pdf** ***Desmopressin oral lyophilisate (Noqdirna®)*** *is accepted for restricted use within NHS Scotland.* ***Indication under review:*** *Symptomatic treatment of nocturia due to idiopathic nocturnal polyuria in adults.* ***SMC restriction:*** *For use in patients aged 65 years and over.* *Two phase III, placebo-controlled studies demonstrated that desmopressin, at licensed doses over three months, significantly reduced the mean number of nocturnal voids and resulted in higher proportions of responders compared with placebo, in patients with nocturia.* **All Wales Medicines Strategy Group** **http://www.awmsg.org/awmsgonline/app/appraisalinfo/3282** ***Desmopressin acetate (Noqdirna®)*** *for the treatment of nocturia due to idiopathic nocturnal polyuria in adults is recommended for restricted use within NHS Wales.* *Desmopressin acetate (Noqdirna®) should be restricted for use in the following subpopulation within its licensed indication for the treatment of nocturia due to idiopathic nocturnal polyuria in adults:* • *aged over 65, for whom treatment options are currently limited.* **NICE guidance** NICE Clinical guideline 171 Sept 2013 Urinary incontinence in women: management **https://www.nice.org.uk/guidance/cg171** states: • *The use of desmopressin may be considered specifically to reduce nocturia in women with UI or OAB who find it a troublesome symptom. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. [2006, amended 2013]* NICE Clinical guideline 97 (updated 2015) Lower Urinary tract symptoms

	in men: management **https://www.nice.org.uk/guidance/cg97** states: • *Consider offering oral desmopressin to men with nocturnal polyuria if other medical causes have been excluded and they have not benefited from other treatments. Measure serum sodium 3 days after the first dose. If serum sodium is reduced to below the normal range, stop desmopressin treatment. [2010]* **Surrey PAD:** The Area Prescribing Committee (APC – formerly PCN)) considered the updated NICE CG97 (above) in Dec 2017 and made the following recommendation re desmopressin: • *The PCN recommends oral desmopressin as treatment option for the management of nocturnal polyuria in men.* • *Oral desmopressin will be assigned a BLUE (with information sheet) traffic light status and specialists in secondary care, should prescribe at least one month of treatment prior to requesting transfer of care. Note: This is an off-label use* *Post NICE publication - Noqdirna was not available as a licensed preparation when this clinical guideline was published* **www.medicines.org.uk** Noqdirna (desmopressin) – Licensed in May 2016 (after NICE guidance above was published)
Recommendation	Based on evidence should drug be: 1. Accepted?
Prepared by	Adesola Olajitan
Date of Preparation	September 2018