Nocturia and nocturnal polyuria in men with lower urinary tract symptoms: oral desmopressin

Evidence summary
Published: 9 April 2013
nice.org.uk/guidance/esuom10

Key points from the evidence

The content of this evidence summary was up-to-date in April 2013. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

Desmopressin acetate is a synthetic analogue of antidiuretic hormone (vasopressin) that produces a decrease in urine output. It does not have a UK marketing authorisation for treating nocturia (needing to wake at least once in the night to void urine) or nocturnal polyuria in men with lower urinary tract symptoms (LUTS), and therefore this use is off-label.

Lower urinary tract symptoms: the management of lower urinary tract symptoms in men (NICE clinical guideline 97) advises that oral desmopressin should be considered for men with nocturnal polyuria if other medical causes have been excluded and they have not benefited from other treatments. This recommendation was based on expert opinion because no studies were located which met the criteria for consideration and which provided reliable evidence.

Two placebo-controlled randomised controlled trials (RCTs) have been published since the NICE clinical guideline. The larger and longer of the 2 RCTs was reported by Wang et al. (2011). This 12-month RCT included 115 men similar to the population group for whom desmopressin is recommended as an option for consideration in the NICE clinical guideline on LUTS. Men taking desmopressin 100 micrograms orally at bedtime needed to void at night at least 2 times less than men taking placebo, a statistically significant difference (61.4% compared with 13.8%, a number

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needed to treat of 2). There were also statistically significant improvements in the duration of sleep until first void and quality of life.

The second, 2-month RCT (Rezakhaniha et al. 2011) included 60 men. It also found a reduction in number of nightly voids and increased duration of sleep until first void with desmopressin 100 micrograms orally at bedtime compared with placebo.

The decrease in urine output produced by desmopressin can result in hyponatraemia and water intoxication in the presence of inappropriate fluid intake. Most cases of hyponatraemia associated with oral desmopressin have been reported in older people being treated for nocturia; the Medicines and Healthcare products Regulatory Agency (MHRA) advises that healthcare professionals and patients should follow closely the advice on fluid intake in the summary of product characteristics and the patient information leaflet to avoid hyponatraemia.

**About this evidence summary**

‘Evidence summaries: unlicensed or off-label medicines’ summarise the published evidence for selected unlicensed or off-label medicines that are considered to be of significance to the NHS, where there are no clinically appropriate licensed alternatives. The summaries provide information for clinicians and patients to inform their decision-making and support the construction and updating of local formularies.

The summaries support decision-making on the use of an unlicensed or off-label medicine for an individual patient, where there are good clinical reasons for its use, usually when there is no licensed medicine for the condition requiring treatment, or the licensed medicine is not appropriate for that individual.

The strengths and weaknesses of the relevant evidence are critically reviewed within this summary, but this summary is not NICE guidance.

**Overview for healthcare professionals**

**Regulatory status of desmopressin**

Desmopressin is available in several formulations and (depending on the formulation) it is licensed in the UK for treating primary nocturnal enuresis, treating nocturia associated with multiple sclerosis when other treatments have failed, and diagnosing and treating vasopressin-sensitive cranial diabetes insipidus. It is also indicated for establishing renal concentration capacity (Medicines and Healthcare products Regulatory Agency [MHRA] 2007). Desmopressin is not
licensed in the UK for treating nocturia or nocturnal polyuria in men with lower urinary tract symptoms (LUTS), and therefore this use is off-label.

In line with the guidance from the General Medical Council (GMC), it is the responsibility of the prescriber to determine the clinical need of the patient and the suitability of using desmopressin outside its authorised indications.

**Evidence statements**

- **Lower urinary tract symptoms: the management of lower urinary tract symptoms in men** (NICE clinical guideline 97, 2010) advises that oral desmopressin should be considered for men with nocturnal polyuria if other medical causes have been excluded and they have not benefited from other treatments. This recommendation was based on expert opinion because no studies were located which met the criteria for consideration and provided reliable evidence.

- Two placebo-controlled randomised controlled trials (RCTs) relating to oral desmopressin for treating nocturia or nocturnal polyuria in men were identified for this evidence summary (Wang et al. 2011 and Rezakhaniha et al. 2011).

- In both trials the dose used was 100 micrograms at bedtime. One trial (Wang et al. 2011) assessed the effects of desmopressin over 1 year; the other trial lasted 8 weeks (Rezakhaniha et al. 2011).

- Both trials found that desmopressin reduced the number of voids per night and increased the duration of sleep until first void, to a statistically significant extent. The trials also found improvement in all other secondary outcomes assessed, including quality of life (Wang et al. 2011) and sleep quality (Rezakhaniha et al. 2011).

- The decrease in urine output produced by desmopressin can result in hyponatraemia and water intoxication in the presence of inappropriate fluid intake. Most cases of hyponatraemia associated with oral desmopressin have been reported in elderly patients being treated for nocturia, and the MHRA advises that healthcare professionals and patients should follow closely the advice on fluid intake in the summary of product characteristics and the patient information leaflet to avoid hyponatraemia.

- The RCT by Wang et al. (2011) reported recognised adverse effects of desmopressin including headache, nausea, dizziness, diarrhoea and asymptomatic hyponatraemia, although the number of adverse events was similar in the placebo group. Rezakhaniha et al. (2011) reported no serious adverse effects.
Summary of the evidence

This section gives a brief summary of the main evidence. A more thorough analysis is given in the Evidence review section.

Efficacy

Two published placebo-controlled RCTs were identified that evaluated oral desmopressin for treating nocturia or nocturnal polyuria in men. The results are summarised in tables 1 and 2.

The RCT by Wang et al. (2011) included 126 men aged 65 years or over (mean age 74 years, range 65 to 88 years) who had benign prostatic hypertrophy (BPH), nocturia (defined by an average of 2 or more nightly voids) and nocturnal polyuria. Only results from the 115 men who completed the study and complied with the protocol were reported. All study participants were receiving treatment with alpha blockers and 29% were taking antimuscarinics; a similar population to that for whom desmopressin is recommended as an option for consideration in the NICE clinical guideline on LUTS. The study was adequately powered for the primary end point but it is unclear whether allocation was concealed.

Participants were randomised to receive 100 micrograms of desmopressin or placebo orally at bedtime for 12 months. Compared with placebo, desmopressin statistically significantly improved the primary outcome of clinical response (reduction by at least 2 in the mean number of nocturnal voids), in addition to secondary outcomes of duration of sleep until first void and quality of life.

Rezakhaniha et al. (2011) included 60 men aged over 50 years who had nocturia, defined as 2 or more nightly voids. The number of men with nocturnal polyuria, BPH or taking medical treatment for LUTS was not reported. Participants were randomised to receive 100 micrograms desmopressin (n=30) or placebo (n=30) for 8 weeks. No power calculation was reported and it is unclear whether allocation was concealed. Desmopressin statistically significantly improved the outcomes of number of voids per night and duration of sleep until first void and a significantly greater number of men reported improvements in sleep quality. The primary outcome of this study was not specified.

Table 1 Summary of Wang et al. (2011)

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy⁹</td>
<td>n=57</td>
<td>n=58</td>
<td></td>
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Primary outcome: reduction by ≥2 in mean number nocturnal voids

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
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<tbody>
<tr>
<td>Randomised</td>
<td>n=30</td>
<td>n=30</td>
<td></td>
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</table>

Selected secondary outcomes:

Duration of first sleep period

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>120.0±17.7 minutes</td>
<td>101.6±19.5 minutes</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Increase in quality of life index >2

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
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<tbody>
<tr>
<td></td>
<td>97.7% (54/57)</td>
<td>13.8% (8/58)</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Safety

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<thead>
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<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
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<tbody>
<tr>
<td></td>
<td>n=57</td>
<td>n=58</td>
<td></td>
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</table>

Any adverse events

<table>
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<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
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<tr>
<td></td>
<td>28.1% (16/57) or 29.8% (17/57)</td>
<td>32.8% (19/58)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NNT, number needed to treat; OR, odds ratio.

a 126 men were initially randomised to treatment groups but results are only presented for the 115 who followed protocol.

b The scale of the quality of life index was not stated.

c Discrepancy between results text and table data.

d 2 men in the placebo group were not included in the analyses because of adverse events; in 1 man this was consciousness disturbance due to hyponatraemia.

Table 2 Summary of Rezakhanliha et al. (2011)

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin 100 micrograms</th>
<th>Placebo</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomised n=30</td>
<td>n=30</td>
<td></td>
</tr>
<tr>
<td>Outcomes (primary and secondary not specified)</td>
<td>Men with &lt;2 voids per night</td>
<td>80% (24/30)</td>
<td>50% (15/30)</td>
</tr>
<tr>
<td></td>
<td>Mean number of voids per night</td>
<td>1.6</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Increase in mean duration first sleep period

<table>
<thead>
<tr>
<th></th>
<th>120 minutes (increased from 2 hours to 4 hours)</th>
<th>30 minutes (increased from 2.5 hours to 3 hours)</th>
<th>p&lt;0.01</th>
</tr>
</thead>
</table>
Proportion reporting improvement in sleep quality

<table>
<thead>
<tr>
<th></th>
<th>80% (24/30)</th>
<th>57% (17/30)</th>
<th>p&lt;0.05</th>
</tr>
</thead>
</table>
Safety

<table>
<thead>
<tr>
<th></th>
<th>n=30</th>
<th>n=30</th>
<th></th>
</tr>
</thead>
</table>
Adverse events

<table>
<thead>
<tr>
<th></th>
<th>Not reported</th>
<th>Not reported</th>
<th>No serious adverse events reported; no further information provided</th>
</tr>
</thead>
</table>
Abbreviation: NNT, number needed to treat.

Safety

The sustained decrease in urine output and decrease in plasma osmolality produced by desmopressin can result in hyponatraemia and water intoxication in the presence of inappropriate fluid intake (MHRA 2007). Most cases of hyponatraemia associated with oral desmopressin have been reported in elderly patients being treated for nocturia, and the MHRA advises that healthcare professionals and patients should follow closely the advice on fluid intake in the summary of product characteristics and the patient information leaflet to avoid hyponatraemia.

The summary of product characteristics advises caution when using oral desmopressin in people with reduced renal function or cardiovascular disease. Precautions to prevent fluid overload are recommended in people with conditions characterised by fluid or electrolyte imbalance, and those at risk of increased intracranial pressure. An additive antidiuretic effect may also result from using desmopressin concomitantly with certain medications that may induce water retention or hyponatraemia (including non-steroidal anti-inflammatory drugs [NSAIDs], tricyclic antidepressants, selective serotonin re-uptake inhibitors [SSRIs], chlorpromazine, carbamazepine, and loperamide). Treatment with desmopressin without concomitant reduction of fluid intake may lead to water retention or hyponatraemia with accompanying symptoms of headache, nausea, vomiting, weight gain, decreased serum sodium and in serious cases, convulsions. The summary of product characteristics also states that isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.
The NICE clinical guideline on LUTS advises that if desmopressin is used for LUTS in men, serum sodium should be measured 3 days after the first dose and treatment should be stopped if serum sodium is reduced to below the normal range.

In the RCT by Wang et al. (2011), headache, nausea, dizziness, diarrhoea and asymptomatic hyponatraemia were reported, but the frequency of adverse events was similar in men receiving desmopressin and placebo. One man in the placebo group did not complete the study protocol and was not included in the analyses because of conscious disturbance from hyponatraemia. Rezakhaniha et al. (2011) reported that no serious drug adverse effects were observed in the study, but provided no further information.

Cost effectiveness and cost

No studies of the cost effectiveness of desmopressin for treating nocturia or nocturnal polyuria in men with LUTS were identified.

Desmopressin 100 microgram tablets are available in a 90-tablet pack at a cost of £49.87 (Drug Tariff March 2013, excluding VAT).

Relevance to NICE guidance programmes

NICE has issued a clinical guideline on lower urinary tract symptoms (LUTS) that covers the diagnosis, monitoring and treatment of LUTS in men. The guideline recommends that oral desmopressin may be considered for men with nocturnal polyuria if other medical causes\textsuperscript{[1]} of LUTS have been excluded and they have not benefited from other treatments.

The Guideline Development Group based this recommendation on expert opinion because it found only 1 study that met its inclusion criteria. This was a crossover study of the intranasal formulation of desmopressin that was too small to provide reliable evidence. The Guideline Development Group was also concerned about the greater risk of hyponatraemia associated with the intranasal formulation compared with oral administration of desmopressin.

\textsuperscript{[1]} The guidance states that medical conditions that can cause nocturnal polyuria symptoms include diabetes mellitus, diabetes insipidus, adrenal insufficiency, hypercalcaemia, liver failure, polyuric renal failure, chronic heart failure, obstructive apnoea, dependent oedema, pyelonephritis, chronic venous stasis, sickle cell anaemia. Medications that can cause nocturnal polyuria symptoms include calcium channel blockers, diuretics, selective serotonin reuptake inhibitors (SSRI) antidepressants
Intervention and alternatives

Desmopressin acetate is a synthetic analogue of antidiuretic hormone (vasopressin) that produces a decrease in urine output.

Condition

The NICE clinical guideline on LUTS explains that these comprise storage symptoms (urgency, frequency, urgency incontinence and nocturia, the need to wake at least once in the night to void urine); voiding symptoms (weak or intermittent urinary stream, straining, hesitancy, terminal dribbling and incomplete emptying) and post-micturition symptoms (post-micturition dribbling) affecting the lower urinary tract.

There are many possible causes of LUTS such as abnormalities or abnormal function of the prostate, urethra, bladder or sphincters. In men, the most common cause is benign prostate enlargement (BPE), which obstructs the bladder outlet. Other conditions that can cause LUTS include detrusor muscle weakness or overactivity, prostatitis, urinary tract infection, prostate cancer and neurological disease. The prevalence of LUTS increases as men get older.

Although LUTS do not usually cause severe illness, they can considerably reduce a man’s quality of life. Bothersome LUTS can occur in up to 30% of men over 65 years.

Alternative treatment options

Initial management of LUTS is often conservative, including the use of containment products for men with storage problems, and lifestyle advice including advice on fluid intake. The NICE clinical guideline on LUTS recommends that drug treatment for bothersome LUTS is offered only if conservative management options have been unsuccessful or are not appropriate.

The guideline recommends the following drug treatment options:

- An alpha blocker (alfuzosin, doxazosin, tamsulosin or terazosin) for men with moderate to severe LUTS.
- An anticholinergic to manage the symptoms of overactive bladder.
- A 5-alpha reductase inhibitor for men with LUTS who have prostates estimated to be larger than 30 g or a prostate specific antigen (PSA) level greater than 1.4 ng/ml, and who are considered to be at high risk of progression (for example, older men).
Combination therapy with an alpha blocker and a 5-alpha reductase inhibitor can be considered in men with bothersome moderate to severe LUTS and enlarged prostates or elevated PSA levels (as above). Combination therapy with an anticholinergic as well as an alpha blocker can be considered in men who still have storage symptoms after treatment with an alpha blocker alone.

Specifically for treating nocturnal polyuria, the guideline recommends considering:

- A late afternoon loop diuretic.
- Oral desmopressin, if other medical causes have been excluded and the man has not benefited from other treatments.

Loop diuretics and desmopressin do not have UK marketing authorisations for this indication.

The Guideline Development Group based its recommendation regarding desmopressin on expert opinion because it found only 1 study that met its inclusion criteria. This was a crossover study of the intranasal formulation of desmopressin that was too small to provide reliable evidence. The Guideline Development Group was also concerned about the greater risk of hyponatraemia associated with the intranasal formulation compared with oral administration of desmopressin.

If LUTS are severe or if conservative management and drug treatment has been unsuccessful or is not appropriate, surgical treatment may be considered.

**Evidence review: efficacy**

Two published placebo-controlled randomised controlled trials (RCTs) were identified that evaluated oral desmopressin for treating nocturia or nocturnal polyuria in men, and that were published since the NICE clinical guideline on lower urinary tract symptoms (Wang et al. 2011 and Rezakhaniha et al. 2011).

**Wang et al. (2011)**

The double-blind RCT by Wang et al. (2011) compared desmopressin with placebo in 126 men aged 65 years or over (mean age 74 years, range 65 to 88 years) who had benign prostatic hypertrophy (BPH), nocturia (defined as an average of 2 or more nightly voids), and nocturnal polyuria (defined as nocturnal volume more than 30% of total daily volume). Screening assessments included digital rectal examination and a review of BPH symptoms, with detailed examinations including transrectal prostate ultrasonography, uroflowmetry and post-void residual urine volume. Exclusion criteria were urge incontinence, other voiding dysfunction or urinary tract infection, receipt of
drugs that may interact with desmopressin, uncontrolled hypertension and diabetes mellitus, or clinically relevant heart failure. Results were reported for only 115 men: the authors state that 2 men in the desmopressin group and 1 in the placebo group withdrew consent; 1 man in the desmopressin group and 2 in the placebo group did not comply with follow-up protocol; and 2 men in the placebo group could not complete follow-up, 1 because of a stroke and 1 because of consciousness disturbance due to hyponatraemia. The reason for excluding the other 3 men was not given. The study was adequately powered for the primary end point but it is unclear whether allocation was concealed.

Participants were randomised to receive 100 micrograms desmopressin (n=57) or placebo (n=58) orally at bedtime. Advice was given to urinate just before bed, not to drink more than sufficient to satisfy thirst from 1 hour before bed to 8 hours after taking the drug, and to avoid drinking caffeinated and alcoholic drinks at night.

Assessments were taken at 1, 3, 6 and 12 months after randomisation. The primary outcome was the proportion of men with clinical response as defined by a reduction of at least 2 in the mean number of nocturnal voids at 12 months. Secondary outcomes included the number of nightly voids, duration of sleep until first void, quality of life (scale not stated), and safety (especially related to serum sodium levels). There were no significant differences in baseline age, body mass index (BMI), comorbidity, history of BPH, and treatment with an alpha blocker (taken by all participants) or antimuscarinics (taken by 21 [36%] men in the placebo group and 12 [21%] men in the desmopressin group).

A statistically significant improvement in clinical response was seen in 61.4% of the desmopressin group (35 out of 57) compared with 13.8% of the placebo group (8 out of 58) (p<0.001, odds ratio [OR] 4.5, 95% confidence interval [CI] 4.0 to 105.2, number needed to treat [NNT]=2).

Desmopressin was also reported to produce statistically significant improvements in all secondary outcomes including duration of first sleep (120.0±17.7 minutes in the desmopressin group compared with 101.6±19.5 minutes in the placebo group) and quality of life index.

Rezakhaniha et al. (2011)

The double-blind RCT by Rezakhaniha et al. (2011) included 60 men aged over 50 years (mean age 63 years) who had symptoms of voiding 2 or more times per night. No requirement for nocturnal polyuria was specified. Exclusion criteria were uncontrolled diabetes or heart disease, use of diuretics, hypertension, diabetes insipidus, diseases which influence the renal medulla such as cystic disease, multiple sclerosis, urge incontinence, recent surgical treatment for BPH, neurogenic bladder or other functional disease of the urinary system. No power calculation was reported and it
is unclear whether allocation was concealed; the authors report taking care to match each group in terms of age and clinical criteria.

Participants were randomly assigned to 100 micrograms of desmopressin (n=30) or placebo (n=30) 1 hour before bedtime, with instructions not to drink more than to satisfy their thirst and to avoid drinks with a diuretic effect. There were no significant baseline differences between groups in terms of comorbidity. The numbers of men with BPH or taking medical treatment for LUTS were not reported.

Assessments were performed at baseline, 4 weeks and 8 weeks. The outcomes assessed were number of voids per night (less than 2, 2, and more than 2), mean number of voids, mean duration of the first sleep period before voiding and safety. Sleep quality was also assessed but details of the scale used were not reported. Primary and secondary outcomes were not specified.

At baseline, 26 of the 30 men in the desmopressin group voided twice per night and 4 men had more than 2 voids per night. In the placebo group, 23 of the 30 men voided twice per night and 7 men had more than 2 voids per night. After 8 weeks of treatment, 24 men (80%) in the desmopressin group had fewer than 2 voids per night compared with 15 men (50%) in the placebo group (p for change from baseline 0.004 for desmopressin and >0.05 for placebo; no p value given for the comparison of desmopressin and placebo groups).

After 8 weeks, desmopressin also decreased the mean number of voids per night (from 2.6 at baseline to 1.6, p<0.001) whereas in the placebo group there was no statistically significant decrease (from 2.5 to 2.3, p=0.344). The mean number of nightly voids was statistically significantly lower in the desmopressin group than in the placebo group at the end of the study (p<0.05). Desmopressin also improved the mean duration of first sleep period (from 2 hours to 4 hours compared with an increase from 2.5 hours to 3 hours in the placebo group, p for inter-group difference <0.01). A greater proportion of men receiving desmopressin also reported an improvement in sleep quality (80% compared with 56.7%, p<0.05).

**Evidence review: safety**

**Precautions for use**

The sustained decrease in urine output and decrease in plasma osmolality produced by desmopressin can result in hyponatraemia and water intoxication in the presence of inappropriate fluid intake ([Medicines and Healthcare products Regulatory Agency (MHRA) 2007](https://www.mhra.gov.uk/)). Most cases of hyponatraemia associated with oral desmopressin have been reported in elderly patients being
treated for nocturia, and the MHRA advises that healthcare professionals and patients should follow closely the advice on fluid intake in the summary of product characteristics and the patient information leaflet to avoid hyponatraemia.

The summary of product characteristics advises caution when using oral desmopressin in people with reduced renal function or cardiovascular disease. Precautions to prevent fluid overload are recommended in people with conditions characterised by fluid or electrolyte imbalance, and those at risk of increased intracranial pressure. An additive antidiuretic effect may also result from using desmopressin concomitantly with medications that may induce water retention or hyponatraemia. Treatment with desmopressin without concomitant reduction of fluid intake may lead to water retention or hyponatraemia with accompanying symptoms of headache, nausea, vomiting, weight gain, decreased serum sodium and in serious cases, convulsions. The summary of product characteristics also states that isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

The NICE clinical guideline on lower urinary tract symptoms (LUTS) advises that if desmopressin is used for LUTS in men, serum sodium should be measured 3 days after the first dose and treatment should be stopped if serum sodium is reduced to below the normal range.

**Adverse events reported in randomised controlled trials**

Wang et al. (2011) reported that, among those who completed the study, adverse events were experienced by 16 (28.1%) or 17 (29.8%) men in the desmopressin group (discrepancy between results text and table) and 19 in the placebo group (32.8%), which comprised headache (3 in the desmopressin group and 4 in the placebo group), dizziness (4 in each group), nausea (1 in the placebo group) and hyponatraemia without clinical symptoms (9 in the desmopressin group and 10 in the placebo group). In addition, 1 man in the placebo group did not complete the study protocol and was not included in the analyses because of consciousness disturbance due to hyponatraemia (116 mmol/l), and 1 man had a stroke. The authors state that there were no differences between groups in serum chloride or potassium, urine sodium or urine osmolarity, peak flow rate, International Prostate Symptom Score (I-PSS), peak flow rate, prostate volume and prostate specific antigen (PSA).

Rezakhaniha et al. (2011) reported that no serious drug adverse effects were observed in the study, but provided no further information.
Evidence review: economic issues

Cost effectiveness

No studies of the cost effectiveness of desmopressin for treating nocturia or nocturnal polyuria in men with lower urinary tract symptoms (LUTS) were identified.

Cost

Desmopressin 100 microgram tablets are available in a 90-tablet pack at a cost of £49.87 (Drug Tariff March 2013, excluding VAT).

Current drug usage

It is not possible to determine the indications for which desmopressin is prescribed, therefore no information on prescribing rates of desmopressin for nocturia or polyuria in men with LUTS is available.

Evidence strengths and limitations

The 2 identified randomised controlled trials (RCTs) provide moderate but consistent evidence that desmopressin can reduce the number of voids per night and prolong the duration of sleep before first void compared with placebo. This improvement was demonstrated both in the 12-month trial by Wang et al. (2011) and the 8-week trial by Rezakhaniha et al. (2011). The body of evidence relates to a dose of desmopressin of 100 micrograms orally at bedtime.

The trials were small, with population sizes of 115 (Wang et al. 2011) and 60 (Rezakhaniha et al. 2011); they also differed in their inclusion and exclusion criteria. It was unclear whether allocation had been concealed in either study and Rezakhaniha et al. (2011) did not include a power calculation. A limitation of this study is that results from only the 115 men (of 126 randomised) who completed the study and complied with the protocol were reported.

Wang et al. (2011) considered the effect of desmopressin on quality of life, and Rezakhaniha et al. (2011) considered its effect on sleep quality. Improvements in these outcomes were reported but neither study provided information on how these outcomes were assessed.

All participants in the RCT by Wang et al. (2011) were taking an alpha blocker, and 29% were taking an antimuscarinic, therefore they were similar to the population group for whom desmopressin is
recommended as an option for consideration in NICE clinical guideline on LUTS. The number of men in the RCT by Rezakhaniha et al. (2011) with benign prostatic hypertrophy (BPH) or taking medical treatment for LUTS was not reported.

For evaluation of safety, the 2 small studies provide limited evidence regarding the potential adverse effects of desmopressin, in particular the risk of hyponatraemia. Wang et al. (2011) reported a similar rate of adverse effects in both desmopressin and placebo groups. Rezakhaniha et al. (2011) reported that no serious drug adverse effects were observed in the study, but provided no further information.

Summary for patients

A summary written for patients is available on the NICE website.

References

Ferring Pharmaceuticals Ltd (2011) DDAVP Tablets 0.1mg summary of product characteristics [online; accessed 20 February 2013]


Development of this evidence summary

This evidence summary was developed for NICE by Bazian Ltd. The interim process statement sets out the process NICE uses to select topics for the evidence summaries for unlicensed/off-label medicines and how the summaries are developed, quality assured and approved for publication.
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Declarations of interest

No relevant interests declared.

Appendix: Search strategy and evidence selection

Search strategy

General background, guidelines and technology assessments:

- NHS Evidence
- NICE
- Euroscan
- Broad internet search: Google, for example, drug name/condition AND (~guideline OR ~algorithm) filetype:pdf
- Scirus
Nocturia and nocturnal polyuria in men with lower urinary tract symptoms: oral desmopressin (ESUOM10)

MEDLINE (via Ovid)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

1. exp review/ (1740168)
2. (scisearch or psychinfo or psycinfo or medlars or embase or psychlit or psyclit or cinahl or pubmed or medline).ti,ab,sh. (69585)
3. ((hand adj2 search$) or (manual$ adj2 search$)).ti,ab,sh. (6082)
4. ((electronic or bibliographic or computeri?ed or online) adj4 database$).ti,ab. (13533)
5. (pooling or pooled or mantel haenszel).ti,ab,sh. (45210)
6. (peto or dersimonian or der simonian or fixed effect).ti,ab,sh. (2603)
7. or/2-6 (119641)
8. 1 and 7 (53176)
9. Meta Analysis/ (36775)
10. (meta-analys$ or meta analys$ or metaanalys$).ti,ab,sh. (65129)
11. ((systematic$ or quantitativ$ or methodologic$) adj5 (review$ or overview$ or synthesis$)).ti,ab,sh. (52182)
12. (integrative research review$ or research integration).ti,ab,sh. (82)
13. or/9-12 (101389)
14. 8 or 13 (128944)
15. clinical trials, phase iv/ or clinical trials, phase iii/ or randomized controlled trials/ or multicenter studies/ (234207)
Nocturia and nocturnal polyuria in men with lower urinary tract symptoms: oral desmopressin (ESUOM10)

16. (random$ or placebo$ or ((singl$ or double$ or triple$ or treble$) and (blind$ or mask$))).ti,ab,sh. (863927)
17. 15 or 16 (958497)
18. (animal$ not human$).sh. (3662859)
19. 17 not 18 (854873)
20. (cost$ or economic$).tw. (418775)
21. 14 or 19 or 20 (1308988)
22. (Desmopressin or Desmopressin acetate or Desmopressin oral or DDAVP or Apo-Desmopressin or Minirin or Octostim or Stimate).tw. (3596)
23. Prostatic hyperplasia/ (17120)
24. (Benign prostat$ disease or benign prostat$ hyperplasia or benign prostat$ enlargement or enlarged prostate).tw. (10410)
25. lower urinary tract symptom$.tw. (3876)
26. urinary symptom$.tw. (2571)
27. (LUTS or LUTD).tw. (1844)
28. Nocturia/ (313)
29. Urination disorders/ (9994)
30. Polyuria/ (1728)
31. nocturia.tw. (1840)
32. (Polyuria or nocturnal polyuria).tw. (3232)
33. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 (36906)
34. 22 and 33 (358)
35. 21 and 34 (51)
36. limit 35 to english language (50)
Nocturia and nocturnal polyuria in men with lower urinary tract symptoms: oral desmopressin (ESUOM10)

37. from 36 keep 1-50 (50)

**Embase (via Ovid)**

Database: Embase <1988 to 2013 January 23>

Search Strategy:

1. exp review/ (1736313)

2. (scisearch or psychinfo or psycinfo or medlars or embase or psychlit or psyclit or cinahl or pubmed or medline).ti,ab,sh. (88552)

3. ((hand adj2 search$) or (manual$ adj2 search$)).ti,ab,sh. (7354)

4. ((electronic or bibliographic or computeri?ed or online) adj4 database$).ti,ab. (17876)

5. (pooling or pooled or mantel haenszel).ti,ab,sh. (52388)

6. (peto or dersimonian or der simonian or fixed effect).ti,ab,sh. (3377)

7. or/2-6 (147162)

8. 1 and 7 (56984)

9. Meta Analysis/ (68612)

10. (meta-analys$ or meta analys$ or metaanalys$).ti,ab,sh. (97786)

11. ((systematic$ or quantitativ$ or methodologic$) adj5 (review$ or overview$ or synthesis$)).ti,ab,sh. (91935)

12. (integrative research review$ or research integration).ti,ab,sh. (88)

13. or/9-12 (161696)

14. 8 or 13 (189398)

15. clinical trials, phase iv/ or clinical trials, phase iii/ or randomized controlled trials/ or multicenter studies/ (29698)
Nocturia and nocturnal polyuria in men with lower urinary tract symptoms: oral desmopressin (ESUOM10)

16. (random$ or placebo$ or ((singl$ or double$ or triple$ or treble$) and (blind$ or mask$))).ti,ab,sh. (989382)

17. 15 or 16 (992624)

18. (animal$ not human$).sh. (2468558)

19. 17 not 18 (895629)

20. (cost$ or economic$).tw. (475630)

21. 14 or 19 or 20 (1435057)

22. (Desmopressin or Desmopressin acetate or Desmopressin oral or DDAVP or Apo-Desmopressin or Minirin or Octostim or Stimate).tw. (4369)

23. Prostatic hyperplasia/ (21805)

24. (Benign prostat$ disease or benign prostat$ hyperplasia or benign prostat$ enlargement or enlarged prostate).tw. (13376)

25. lower urinary tract symptom$.tw. (5670)

26. urinary symptom$.tw. (3412)

27. (LUTS or LUTD).tw. (3229)

28. Nocturia/ (3400)

29. Urination disorders/ (5992)

30. Polyuria/ (4492)

31. nocturia.tw. (2645)

32. (Polyuria or nocturnal polyuria).tw. (3174)

33. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 (42212)

34. 22 and 33 (582)

35. 21 and 34 (89)

36. limit 35 to english language (86)
37. from 36 keep 1-50 (50)

38. limit 37 to exclude medline journals (4)

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 Desmopressin ti,ab,kw

#2 polyuria/

#3 nocturia/

#4 lower urinary tract symptom* OR LUTs

#5 #2 OR #3 OR #4

#5 AND #1

CRD HTA, DARE and EED database

(Desmopressin OR DDAVP) AND (Polyuria OR nocturia OR Lower urinary tract symptom* OR LUTs or Benign prostatic hyperplasia or BPH) in any field

Grey literature and ongoing trials

- FDA
- EMA
- MHRA
- Scottish Medicines Consortium
- All Wales Medicine Strategy Group
- metaRegister of Controlled Trials (mRCT)
- ClinicalTrials.gov

Manufacturers' websites

Ferring Pharmaceuticals Ltd
Evidence selection

Studies were included based on predetermined criteria for relevance to the question set at scoping. The highest-quality research was selected as the basis for answering the questions set on efficacy, safety and cost. Only randomised controlled trials that included more than 20 people and were conducted in male-only populations were included. Trials conducted in mixed male/female populations or female-only populations were not included. Trials previously considered and rejected in the production of NICE clinical guidelines were also excluded from this evidence summary.

About 'Evidence summaries: unlicensed or off-label medicines'

NICE evidence summaries for off-label or unlicensed medicines summarise the published evidence for selected unlicensed or off-label medicines that are considered to be of significance to the NHS, where there are no clinically appropriate licensed alternatives. They support decision-making on the use of an unlicensed or off-label medicine for an individual patient, where there are good clinical reasons for its use, usually when there is no licensed medicine for the condition requiring treatment, or the licensed medicine is not appropriate for that individual.

This document provides a summary of the published evidence. The strengths and weaknesses of the identified evidence are critically reviewed within this summary, but this summary is not NICE guidance and does not provide formal practice recommendations.

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