

# Desmopressin ในกรณี Nocturnal polyuria และ primary nocturnal enuresis

## **Desmopressin acetate (DDAVP)**

**รูปแบบ** Tab, nasal spray, nasal sol, sterile sol

**ปรากฏอยู่ในหมวดยา**กลุ่มที่ 6 กลุ่มยา Endocrine system

6.5 Hypothalamic and pituitary hormones

6.5.2 Posterior pituitary hormones and antagonists

**บัญชี**

**เงื่อนไข**

1. ใช้สำหรับ diabetes insipidus
2. ชนิดเม็ดใช้กับผู้ป่วยที่ไม่สามารถให้ยาทางจมูกได้เท่านั้น

## ส่วนที่ 1 ข้อมูลโดยสรุป

ข้อมูลโดยวิชาการโดยสรุป แบ่งข้อมูลเป็น 4 ด้าน คือ ข้อมูลทั่วไป ข้อมูลด้านประสิทธิภาพและความปลอดภัย ข้อมูลด้านรายการยาและการเบิกจ่ายในต่างประเทศ และข้อมูลด้านราคา (รายละเอียดข้อมูล อ่านเพิ่มเติมได้ในส่วนที่ 3 ของเอกสาร)

ด้านข้อมูลทั่วไป เป็นข้อมูลเกี่ยวกับแนวทางการรักษา primary nocturnal enuresis หรือ nocturnal polyuria จากแหล่งอ้างอิงดังต่างๆ ทั้ง NICE clinical guideline, European Association of Urology 2012 guideline, และอื่นๆ<sup>1-6</sup> โดยสรุปพบว่า การรักษาจะเน้นการปรับเปลี่ยนพฤติกรรมเป็นแนวทางการรักษาแนวทางแรก หากต้องให้ยาในการรักษาแล้ว พบว่ามียาอยู่เพียงไม่กี่กลุ่ม ในที่นี้รวมถึง desmopressin ที่เป็นยารายการหนึ่งในยาทางเลือก แต่ต้องคำนึงถึงความปลอดภัยในผลข้างเคียงที่อาจเกิดขึ้นได้

ข้อมูลด้านประสิทธิภาพและความปลอดภัยนั้นพบว่า ยา desmopressin มีการรับรองจาก USFDA ให้ใช้ในข้อบ่งใช้ Primary nocturnal enuresis ทั้งเด็กและผู้ใหญ่ ในขณะที่มีการสืบค้นข้อมูลจาก PUBMED<sup>6-16</sup> พบว่า desmopressin มีประสิทธิภาพมากกว่ายาหลอก ในขณะที่ประสิทธิภาพระหว่าง desmopressin กับการปรับเปลี่ยนพฤติกรรม (alarm therapy) นั้นไม่มีความแตกต่างกัน แต่ผลการศึกษาเปรียบเทียบประสิทธิภาพในแง่ของการกลับมาเป็นซ้ำเมื่อมีการหยุดการรักษาระหว่าง desmopressin กับการปรับเปลี่ยนพฤติกรรม พบว่า desmopressin มีโอกาสกลับมาเป็นซ้ำมากกว่า และผลการศึกษาความปลอดภัยระหว่าง desmopressin กับยาหลอก และการปรับเปลี่ยนพฤติกรรม (alarm therapy) พบว่าไม่มีความแตกต่างกัน โดยผลข้างเคียงที่สำคัญที่เกิดขึ้นคือ fluid retention และ hyponatremia

ข้อมูลด้านรายการยาและการเบิกจ่ายในต่างประเทศ พบว่า ประเทศ Australia<sup>18</sup> อนุมัติให้มีการเบิกจ่ายยา Desmopressin ในผู้ป่วยที่คือ enuresis alarm เท่านั้น และมีหมายเหตุว่ารูปแบบยาพ่นจมูกเพิ่มความเสี่ยงต่อการเกิดภาวะโซเดียมในเลือดต่ำเมื่อเทียบกับยาอื่น ในขณะที่ประเทศ Scotland<sup>19</sup> ไม่ได้อนุมัติการเบิกจ่าย Desmopressin ทั้งรูปแบบกินและพ่นจมูก ในข้อบ่งใช้ nocturnal polyuria ส่วนในบัญชียาของ WHO model list 2011<sup>17</sup> และ India - National List of Essential Medicine 2011<sup>20</sup> นั้นไม่พบข้อมูลรายการยาและการเบิกจ่าย

ข้อมูลด้านราคายา ซึ่งเป็นข้อมูลราคายาในรูปแบบยาที่เกี่ยวข้องกับข้อบ่งใช้คือรูปแบบ Tablets ขนาด 0.1 และ 0.2 mg โดยคิดราคายาต่อวันในขนาดยาที่ต่ำที่สุดและสูงที่สุดดังตาราง

ตัวยาสําคัญ	รูปแบบ/ความแรง	ราคา สธ. ต.ค.-ธ.ค. 54 ม.ค.-มี.ค. 55	ราคาบริษัทฯ เสนอ/1 หน่วย	ราคา/วัน เมื่อคิดขนาด ยาที่ต่ำที่สุด (0.2 mg/day) <sup>5</sup>	ราคา/วัน เมื่อคิดขนาด ยาที่สูงที่สุด (0.6 mg/day) <sup>5</sup>
Desmopressin (MINIRIN®)	tab 0.1 mg	64.20	64.20	128.4	385.2
	tab 0.2 mg	-	124.83	124.83	374.5

มติคณะกรรมการฯ ครั้งที่ 9/2555 วันที่ 7 กันยายน 2555

คงยา desmopressin รูปแบบ tab ไว้ในบัญชีฯ ตามเดิม โดยไม่เพิ่มเงื่อนไขในข้อบ่งใช้ primary nocturnal enuresis ในเด็กที่อายุ 6 ปีขึ้นไป และ nocturnal polyuria ในผู้ใหญ่ ที่หาสาเหตุอื่นไม่พบ **เหตุผล** แม้ว่ายาามีประสิทธิภาพ แต่เสี่ยงต่อการกลับเป็นซ้ำหลังหยุดยา และมีความเสี่ยงต่อการเกิด hyponatremia ควรหาสาเหตุและใช้วิธีการอื่นในการรักษาแทน เช่น alarm therapy อีกทั้งค่าใช้จ่ายในการรักษาหากเริ่มใช้ยา desmopressin ยังสูงอยู่

## ส่วนที่ 2 แนวทางการจัดทำข้อมูล

หาข้อมูลเกี่ยวกับยา Desmopressin เกี่ยวกับข้อบ่งใช้ดังต่อไปนี้

- 1) primary nocturnal enuresis ในเด็กที่อายุ 6 ปีขึ้นไป ที่หาสาเหตุอื่นไม่พบ
- 2) ใช้ในผู้ใหญ่ที่มีปัสสาวะมากผิดปกติในเวลากลางคืน (nocturnal polyuria) ที่หาสาเหตุอื่นไม่พบ

## ส่วนที่ 3 รายละเอียดข้อมูลเชิงวิชาการ

### ข้อมูลทั่วไป

ข้อมูลแนวทางการรักษา primary nocturnal enuresis หรือ nocturnal polyuria จากแหล่งอ้างอิงดังต่างๆ โดยรวมพบว่า การรักษาจะเน้นการปรับเปลี่ยนพฤติกรรมเป็นแนวทางการรักษาแนวทางแรก หากต้องใช้ยาในการรักษาแล้ว พบว่ามีอายุอยู่เพียงไม่กี่กลุ่ม ในที่นี้รวมถึง desmopressin ที่เป็นยารายการหนึ่งในยาทางเลือก แต่ต้องคำนึงถึงความปลอดภัยในผลข้างเคียงที่อาจเกิดขึ้นได้ รายละเอียดดังตารางที่ 1 และ 2

**ตารางที่ 1** แนวทางการรักษา primary nocturnal enuresis หรือ nocturnal polyuria ในเด็ก

แนวทางการรักษา	ข้อความอ้างอิง
Management of nocturnal enuresis in children (UpToDate) <sup>3</sup>	<b>Desmopressin (a synthetic vasopressin analog) is a first-line treatment for enuresis in children older than five years whose bedwetting has not responded to advice about fluid intake, toileting, or an appropriate reward system.</b> It is an alternative to enuresis alarms for children and families who seek rapid or short-term improvement of enuresis; have failed, refused, or are unlikely to adhere to enuresis alarm treatment; and for whom an enuresis alarm is unsuitable. Indications/contraindications — <b>Desmopressin works best for children with nocturnal polyuria and normal functional bladder capacity</b>
NICE clinical guideline 111: Nocturnal enuresis : The management of bedwetting in children and young people	<b>1.10 Initial treatment – desmopressin</b> 1.10.1 Offer desmopressin to children and young people over 7 years, if: • rapid-onset and/or short-term improvement in bedwetting is the priority of treatment <b>or</b> • an alarm is inappropriate or undesirable 1.10.2 <b>Consider desmopressin for children aged 5–7 years if treatment is required and:</b> • rapid-onset and/or short-term improvement in bedwetting is the priority of treatment <b>or</b> • an alarm is inappropriate or undesirable

แนวทางการรักษา	ข้อความอ้างอิง
<p>NOCTURIA: A GUIDELINE For the evaluation and management of a troublesome symptom: A Guideline for assessing and treating patients with nocturia, in a Primary Care setting in New Zealand. Prepared by the Nocturia guidelines group<sup>4</sup></p>	<p><b>To reduce nocturnal polyuria</b> <b>Desmopressin</b> <b>Desmopressin</b> is an analogue of vasopressin with effects like anti-diuretic hormone (ADH) but without any vasopressor effects. <b>Its use has been recommended for <i>persistent primary enuresis in children</i>, and <i>for healthy younger adults with nocturnal polyuria</i>, where no treatable cause is found.</b> <b>Efficacy</b>-Antidiuretics given at night to reduce nocturnal urine production have proved useful. <b>In a placebo controlled RCT of desmopressin in 151 men over 15 years of age with troublesome nocturia, and a nocturnal urine volume exceeding the functional bladder capacity, 34% of the men had fewer than half the number of nocturnal voids than the placebo group which had 3 % reduction. Significant reductions were noted in nocturnal urine volume and duration of the first sleep period before having to get up.</b><sup>50</sup> <b>Another carefully conducted double blind RCT in 20 elderly men with known nocturnal polyuria, showed a significant reduction in nocturnal voiding frequency and nocturnal urine production, but only when the 40 microgram dose was used, not at a dose of 20micrograms.</b><sup>51</sup> <b>There was also a significant reduction in the mean serum osmolality.</b> Its use in the elderly requires specially caution and monitoring by body weight and serum sodium. The marketers of DDAVP do not recommend its use in those over 65. (Level of Evidence 1)</p>

ตารางที่ 2 แนวทางการรักษา primary nocturnal enuresis หรือ nocturnal polyuria ในผู้ใหญ่

แนวทางการรักษา	ข้อความอ้างอิง
<p>NICE clinical guideline 97: Developed by the National Clinical Guideline Centre: Acute and Chronic Conditions<sup>1</sup></p>	<p><i>Lower urinary tract symptoms: The management of lower urinary tract symptoms in men</i> <i>Issue date: May 2010</i> <b>1.4 Drug treatment</b> <b>1.4.9 Consider offering oral desmopressin<sup>2</sup> to men with nocturnal polyuria if other medical causes<sup>3</sup> have been excluded and they have not benefited from other treatments.</b> Measure serum sodium 3 days after the first dose. If serum sodium is reduced to below the normal range, stop desmopressin treatment.</p>
<p>Guidelines on the Management of Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO) European Association of Urology 2012 (Update February 2012)<sup>2</sup></p>	<p><b>Desmopressin has been used for over 30 years in the treatment of diabetes insipidus or primary nocturnal enuresis and <i>has recently been approved in most European countries for the treatment of nocturia polyuria for adult male and female patients.</i></b></p>
<p>NOCTURIA: A GUIDELINE For the evaluation and management of a troublesome symptom: A Guideline for assessing and treating patients with nocturia, in a Primary Care setting in New Zealand. Prepared by the Nocturia guidelines group<sup>4</sup></p>	<p><b>To reduce nocturnal polyuria</b> <b>Desmopressin</b> <b>Desmopressin</b> is an analogue of vasopressin with effects like anti-diuretic hormone (ADH) but without any vasopressor effects. <b>Its use has been recommended for <i>persistent primary enuresis in children</i>, and <i>for healthy younger adults with nocturnal polyuria</i>, where no treatable cause is found.</b> <b>Efficacy</b>-Antidiuretics given at night to reduce nocturnal urine production have proved useful. <b>In a placebo controlled RCT of desmopressin in 151 men over 15 years of age with troublesome nocturia, and a nocturnal urine volume exceeding the functional bladder capacity, 34% of the men had fewer than half the number of nocturnal voids than the placebo group which had 3 % reduction. Significant reductions were noted in nocturnal urine volume and duration of the first sleep period before having to get up.</b><sup>50</sup> <b>Another carefully conducted double blind RCT in 20 elderly men with known nocturnal polyuria, showed a significant reduction in nocturnal voiding frequency and nocturnal urine production, but only when the 40 microgram dose was used, not at a dose of 20micrograms.</b><sup>51</sup> <b>There was also a significant reduction in the mean serum osmolality.</b> Its use in the elderly requires specially caution and monitoring by body weight and serum sodium. The marketers of DDAVP do not recommend its use in those over 65. (Level of Evidence 1)</p>

### ด้านประสิทธิภาพและความปลอดภัย

จาก Micromedex 2012<sup>5</sup> พบข้อมูลว่า ยา desmopressin มีการรับรองจาก USFDA ให้ใช้ในข้อบ่งใช้ Primary nocturnal enuresis ทั้งเด็กและผู้ใหญ่ โดยมีประสิทธิภาพในระดับ effective ความหนักแน่นของข้อมูลระดับ A รายละเอียด ดังตารางที่ 3

ตารางที่ 3 แสดง US FDA Approval Data ของยา desmopressin ในข้อบ่งใช้ที่เกี่ยวข้อง จาก Micromedex 2012<sup>5</sup>

disease	FDA approval		Recommendation		Strength of Evidence		Efficacy	
	adult	children	adult	children	adult	children	adult	children
Primary nocturnal enuresis	Yes (Tablets)	Yes (6 years and older - tablets)	IIa	IIa	A	A	Effective	Effective

Summary: Desmopressin acetate oral) is indicated for the management of primary nocturnal enuresis (Prod Info DDAVP(R) oral tablets, 2007)

#### PUBMED search

จากการสืบค้นข้อมูลจาก PUBMED, Search term : ("Deamino Arginine Vasopressin"[Mesh]) AND ("Nocturnal Enuresis"[Mesh] OR "Polyuria"[Mesh]) เมื่อวันที่ 9 สิงหาคม พ.ศ. 2555 พบ 180 การศึกษา โดยการศึกษาที่เป็นการศึกษาแบบการทดลองแบบ Randomized control trial นั้นมีทั้งหมด 18 การศึกษา พบว่า มีการศึกษาที่เกี่ยวข้องและนำมาอ้างอิงได้ทั้งหมด 11 การศึกษา โดยมีผลสรุปของการศึกษาโดยรวมเป็น ดังนี้<sup>6-16</sup>

1. ผลการศึกษาเปรียบเทียบประสิทธิภาพระหว่าง desmopressin กับยาหลอก พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ โดย desmopressin มีประสิทธิภาพมากกว่า (การศึกษาที่ 2, 6 และ 15)
  2. ผลการศึกษาเปรียบเทียบประสิทธิภาพระหว่าง desmopressin กับการปรับเปลี่ยนพฤติกรรม (alarm therapy) พบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (การศึกษาที่ 1, 3, 4, 10, 13 และ 14)
  3. ผลการศึกษาเปรียบเทียบประสิทธิภาพในแง่ของการกลับมาเป็นซ้ำเมื่อมีการหยุดการรักษาระหว่าง desmopressin กับการปรับเปลี่ยนพฤติกรรม (alarm therapy) พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ โดย desmopressin มีโอกาสกลับมาเป็นซ้ำมากกว่า (การศึกษาที่ 3 และ 13)
  4. ผลการศึกษาเปรียบเทียบความปลอดภัยระหว่าง desmopressin กับยาหลอก และการปรับเปลี่ยนพฤติกรรม (alarm therapy) พบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ โดยผลข้างเคียงที่สำคัญที่เกิดขึ้นคือ fluid retention และ hyponatremia (การศึกษาที่ 2 และ 17)
- โดยมีรายละเอียดบางส่วนของการศึกษาตามตารางด้านล่างนี้

**("Deamino Arginine Vasopressin"[Mesh]) AND ("Nocturnal Enuresis"[Mesh] OR "Polyuria"[Mesh])  
Results: 18 Filters activated: Randomized Controlled Trial**

1. Urol Nurs. 2011 Sep-Oct;31(5):286-9.

Desmopressin versus behavioral modifications as initial treatment of primary nocturnal enuresis.  
Fera P, Lelis MA, Glashan Rde Q, Pereira SG, Bruschini H.

The purpose of this study was to compare the effectiveness of desmopressin to behavioral modifications as the initial treatment of primary monosymptomatic nocturnal enuresis (PMNE). Study results determined that either intervention led to a significant reduction in PMNE episodes. These results suggest that either method is equally effective for treatment of PMNE.

2. J Urol. 2011 Jan;185(1):219-23. Epub 2010 Nov 13.

Low dose oral desmopressin for nocturnal polyuria in patients with benign prostatic hyperplasia: a double-blind, placebo controlled, randomized study.

Wang CJ, Lin YN, Huang SW, Chang CH.

**PURPOSE:** We evaluated the long-term efficacy and safety of low dose oral desmopressin in elderly patients with benign prostatic hyperplasia with more than nocturnal voids and nocturnal polyuria more than 30% of total daily urine volume.  
**MATERIALS AND METHODS:** Eligible patients with benign prostatic hyperplasia older than 65 years with nocturia, nocturnal polyuria and International Prostate Symptom Score 14 or greater were included in the study. All patients received placebo or 0.1 mg desmopressin orally at bedtime. Patients were required to visit the outpatient clinic from the first visit, and after 1, 3, 6 and 12 months of treatment. Patients maintained flow volume charts and used diaries to record voiding data throughout the study. During followup urinalysis, urine sodium, urine osmolality, serum electrolytes, prostate specific antigen, International Prostate Symptom Score, quality of life, transrectal ultrasonography of prostate, uroflowmetry and post-void residual urine volume were performed at each visit.  
**RESULTS:** A total of 115 patients were enrolled in the study and randomized as 58 in the placebo group and 57 in the desmopressin group. Desmopressin significantly decreased nocturnal urine output and the number of nocturia episodes, and prolonged the first sleep period ( $p < 0.01$ ). Compared to before treatment desmopressin gradually decreased serum sodium and induced statistically but not clinically significant hyponatremia after 12 months of treatment. No serious systemic complications were found during medication. **CONCLUSIONS:** Low dose oral desmopressin is an effective and well tolerated treatment for nocturnal polyuria in the lower urinary tract symptoms of patients with benign prostatic hyperplasia. Long-term desmopressin therapy gradually decreases serum sodium and it might induce hyponatremia even in patients without initial hyponatremia. For long-term desmopressin administration serum sodium should be assessed carefully, at least at 1 week after treatment.

3. J Urol. 2010 Dec;184(6):2521-6. Epub 2010 Oct 18.

Efficacy of desmopressin and enuresis alarm as first and second line treatment for primary monosymptomatic nocturnal enuresis: prospective randomized crossover study.  
Kwak KW, Lee YS, Park KH, Baek M.

**PURPOSE:** We compared the efficacy of desmopressin and enuresis alarm as first and second line treatment options for monosymptomatic nocturnal enuresis.  
**MATERIALS AND METHODS:** A total of 104 children with monosymptomatic nocturnal enuresis were randomly assigned to either desmopressin (54) or enuresis alarm (50) as first line treatment. Following 12 weeks of first line treatment children with a full response were evaluated for relapse 12 weeks after withdrawal of treatment. Children with partial or no response were switched to the alternative treatment and then evaluated after 12 weeks of crossover treatment. Relapse was defined as more than 1 episode of bedwetting monthly. **RESULTS:** Following first line treatment 77.8% of the desmopressin group and 82% of the enuresis alarm group achieved a successful result, including full response in 37% and 50% of the groups, respectively ( $p=0.433$ ). Of the children with a full response 50% in the desmopressin group and 12% in the enuresis alarm group experienced a relapse when treatment stopped ( $p=0.005$ ). Following second line crossover treatment 71.4% of the enuresis alarm-desmopressin group and 67.8% of the desmopressin-enuresis alarm group achieved a successful result, including full response in 47.6% and 45.2% of the groups, respectively ( $p=0.961$ ). **CONCLUSIONS:** There was no difference between desmopressin and enuresis alarm during treatment for achieving dryness, but the chance of relapse after treatment stopped was higher following desmopressin. Switching to the alternative treatment following partial or no response provided an additional benefit.

4. J Pediatr Urol. 2011 Feb;7(1):21-9. Epub 2010 Jun 25.

Randomized comparison of long-term desmopressin and alarm treatment for bedwetting.  
Evans J, Malmsten B, Maddocks A, Popli HS, Lottmann H, et.al.

**OBJECTIVE:** To compare the efficacy of long-term primary nocturnal enuresis (PNE) treatment using desmopressin versus enuresis alarm.  
**MATERIALS AND METHODS:** A 6-month randomized trial was performed with patients from 29 enuresis clinics: 251 patients  $\geq 5$  years in age with severe PNE (mean 5.5-5.6 wet nights/week) were randomized to desmopressin (0.2-0.4 mg daily) or alarm. Efficacy was assessed by percentage reduction in mean number of wet nights/week; patients achieving dryness, mean initial duration of sleep and compliance were evaluated. Efficacy analyses were performed using the intent-to-treat population (all patients) and excluding patients who withdrew; 12-month follow-up data were collected.  
**RESULTS:** Data could not be evaluated for the 32% of alarm patients and 7% of desmopressin patients who withdrew early. In intent-to-treat analyses, a similar proportion of patients across groups showed a  $\geq 50\%$  reduction in wet nights/week (desmopressin: 37.5%, alarm: 32.2%) and achieved dryness (desmopressin: 32%, alarm: 37%). Compliance was higher with desmopressin: 95-98% of patients took  $>75\%$  of tablets; 50-78% used alarm  $>75\%$  of nights. Initial sleep duration was 1.02 h longer at the end of treatment with desmopressin (95% CI: 0.045, 1.99). **CONCLUSION:** Desmopressin and alarm demonstrated comparable efficacy in the treatment of PNE. Withdrawal from the alarm group was high, indicating the importance of considering family motivation before selecting treatment, for optimal outcome.

5. Zhongguo Dang Dai Er Ke Za Zhi. 2010 Mar;12(3):198-200. → คัดออก เนื่องจากเป็นการศึกษาในแง่ของการถอนยาแบบมีขั้นล้าดับกับการถอนยาแบบทันที [Comparison of therapeutic effects in severe nocturia: gradual versus immediate drug withdrawal].

Tang FZ, Liu YL, Wen FQ, Zhang ZX.

**OBJECTIVE:** To investigate possible differences in the prognosis in children with severe nocturia who received different drug withdrawal schedules.  
**METHODS:** Ninety-seven children with severe nocturia were randomly assigned to two groups: control (n=47) and observed (n=50). The control group accepted drug withdrawal immediately, while the observed group accepted dose tapering gradually after a 12-week treatment course. The frequency of enuresis was observed three months after complete drug withdrawal.  
**RESULTS:** During the treatment, the frequency of enuresis in all of children from both the control and the observed groups was reduced by over 90%. Forty-six children (92%) from the observed group showed the frequency of enuresis was reduced by over 90%, but 28 children (60%) from the control group ( $p<0.01$ ) three months after the complete drug withdrawal. There were no significant differences in the adverse effect and the medication compliance between the two groups.  
**CONCLUSIONS:** The different schedules of drug withdrawal may lead to different prognosis, and the schedule of gradual drug withdrawal may be superior to the immediate one in children with nocturnal enuresis.

6. Acta Paediatr. 2010 Jul;99(7):1037-41. Epub 2010 Mar 2.

Effects of desmopressin on the sleep of children suffering from enuresis.

Rahm C, Schulz-Juergensen S, Eggert P.

AIM: To evaluate the effect of 1-desamino-8-D-Arginine Vasopressin (DDAVP) on sleep architecture and arousal reactions in children with primary monosymptomatic nocturnal enuresis (PME).

METHODS: A prospective, placebo-controlled, randomized, double-blind, cross-over study was performed on children suffering from bed-wetting. Placebo and DDAVP were given for 7 days each after which an unattended home polysomnography (PSG) was recorded. After lifting the blinding, the PSGs were compared.

RESULTS: A total of 20 children with PME, aged 6-15 years, were enrolled in the study. The number of wet nights decreased significantly with DDAVP treatment. Delta power, distribution of sleep stages, number of arousals, arousal index and the effect of arousals on sleep stages did not differ significantly. Bed-wetting occurred within each sleep stage and did not follow any particular pattern. In most cases, it was preceded by an arousal reaction, but no awakening occurred.

CONCLUSION: DDAVP has no effect on the sleep architecture of children with PME when analysed by classical PSG, which is determined by collecting the electric activity of cortical neurons. Taking recent research findings into account, this supports the thesis that the disturbances causing PME occur at brain stem level and do not reach consciousness.

7. BJU Int. 2010 May;105(10):1456-9. Epub 2009 Sep 17. → คัดลอก เนื่องจากเป็น combined therapy

Evaluation of different modes of combined therapy in children with monosymptomatic nocturnal enuresis.

Vogt M, Lehnert T, Till H, Rolle U.

OBJECTIVE: To evaluate the efficacy of different modes of combined therapy in children with monosymptomatic nocturnal enuresis (MNE).

PATIENTS AND METHODS: A randomized prospective study was performed to compare the order of two types of combined therapy in children with MNE. Group A was treated with primary desmopressin treatment that was combined with alarm treatment after 3 months, while group B was treated with primary alarm treatment that was combined with desmopressin after 3 months.

RESULTS: Within a period of 18 months, 43 previously untreated children fulfilled the inclusion criteria. Thirteen children achieved dryness after initial monotherapy or discontinued the study. Group A consisted of 16 children and group B of 14 children. After the standardized treatment course of 6 months, 11/16 children in group A and 11/14 children in group B became dry (<3 wet nights/month). Altogether, 22/30 (73%) children were dry after combined treatment, consisting of 12/18 boys and 10/12 girls. Of the children with a normal maximum voided volume, 79% (19/24) achieved dryness, whereas only three of six children with small maximum voided volumes became dry. In all, 13/19 (68%) children with nocturnal polyuria and nine of 11 without nocturnal polyuria became dry. Only one child relapsed (group A).

CONCLUSIONS: Combined therapy proved effective in children with MNE after 6 months, with no statistically significant differences between the two different orders of treatment.

8. Prog Urol. 2009 Feb;19(2):132-8. Epub 2009 Jan 8. → คัดลอก เนื่องจากเป็น sublingual dosage form

[Comparison of two sublingual types of desmopressin in 6-year-old and more children with primary nocturnal enuresis. About an international randomized cross-over study].

Lottmann H.

OBJECTIVE: Desmopressin (a structural analogue of hormone arginine-vasopressine) is an effective treatment of primary nocturnal enuresis (PNE). A new oral formulation (oral lyophilisate; Minirinmelt has recently been developed. The principal objective of this study was to compare the preference of patients for the oral lyophilisate versus tablet.

METHODS: This open-label, randomized, cross-over study was undertaken at 26 centres across Europe and included patients with PNE. All were already receiving a stable dose of desmopressin tablets 0,2 or 0,4 mg. Two hundred and fourteen patients aged 6 to 15 years were randomised (1:1) to receive the treatment in the order lyophilisate/tablet (n=108) or tablet/lyophilisate (n=106). Each formulation was taken during 3 weeks. RESULTS: Of the patients (intention to treat), 55,2% preferred the oral lyophilisate (p=0,16). Patients less than 12 years (n=153) had a preference for the lyophilisate compared to tablets (60,1%; p=0,015). Efficacy was the same for both formulations in terms of mean incidence of bedwetting episodes per week (treatment difference: -0,08; p=0,33). No serious adverse event was reported. The use was considered to be easy for the two forms (p=0,85). Of patients on the lyophilisate, 94,3% had compliance levels of greater or equal to 80%.

CONCLUSIONS: The majority of patients preferred the sublingual lyophilisate. This preference was marked in patients less than 12 years on exploratory analysis. The new formulation of desmopressin requires no water intake and retains similar levels of efficacy and safety than the tablet.

9. Pediatrics. 2008 Nov;122(5):1027-32. → คัดลอก เนื่องจากเป็น combined therapy เมื่อใช้ desmopressin แล้วไม่ได้ผล

Combination therapy with desmopressin and an anticholinergic medication for nonresponders to desmopressin for monosymptomatic nocturnal enuresis: a randomized, double-blind, placebo-controlled trial.

Austin PF, Ferguson G, Yan Y, Campigotto MJ, Royer ME, Coplen DE.

OBJECTIVE: Desmopressin is an approved medical therapy for the treatment of monosymptomatic primary nocturnal enuresis. In cases of limited response to desmopressin, we have added anticholinergic therapy to desmopressin (combination therapy). To evaluate this treatment strategy, we examined the efficacy of combination therapy for primary nocturnal enuresis in desmopressin-nonresponders.

METHODS: Only patients with primary nocturnal enuresis refractory to the maximal dosage of desmopressin were enrolled. Children with lower urinary tract symptoms or bowel dysfunction were excluded, on the basis of a 3-day, 24-hour, frequency-volume chart and elimination record. Children continued to take desmopressin and were assigned randomly, in a double-blind manner, to receive either extended-release anticholinergic medication or placebo. Patients were reassessed after 1 month of therapy, with a 1-week nocturnal record.

RESULTS: Forty-one desmopressin-nonresponders were enrolled, and 7 patients were excluded because of noncompliance. The treatment groups were equally matched with respect to age, gender, functional bladder capacity, and number of wet nights per week. After 1 month of treatment, there was a significant reduction in the mean number of wet nights in the combination therapy group, compared with the placebo group. With a generalized estimating equation approach, there was a significant 66% decrease in the risk of a wet episode, compared with the placebo group.

CONCLUSIONS: This study represents the first prospective, placebo-controlled trial examining the effect of desmopressin in combination with long-acting, anticholinergic, bladder-relaxing therapy for monosymptomatic primary nocturnal enuresis.

10. Int Urol Nephrol. 2008;40(3):583-6. Epub 2008 Mar 5.

The efficacy of the addition of short-term desmopressin to alarm therapy in the treatment of primary nocturnal enuresis.  
Ozden C, Ozdal OL, Aktas BK, Ozelci A, Altinova S, Memis A.

**OBJECTIVE:** The purpose was to evaluate the efficacy of the addition of short-term desmopressin to enuretic alarm in patients with primary monosymptomatic nocturnal enuresis (PMNE).

**MATERIALS AND METHODS:** A total of 58 [corrected] children with PMNE were included in this study. The patients were randomized into two groups. In group 1 (n=30), the patients were given 6 weeks of additional oral desmopressin to 12 weeks of enuretic alarm therapy, as a single dose of 0.2 mg at the first 3 weeks and 0.4 mg at the following 3 weeks. In group 2 (n=28), the patients were given 12 weeks of enuretic alarm therapy alone. According to the number of wet nights after 12 weeks of treatment, the patients were defined as complete responders (dry or more than 75% reduction in wet nights), partial responders (50 to 75% reduction) and non-responders (less than 50% reduction). Relapse was defined as the reappearance of >1 wet night per week for complete responders and >50% increase in pre-treatment wetting frequency for partial responders, and all these patients were called relapsers. **RESULTS:** The mean number of wet nights after 3 and 6 weeks treatment was significantly lower in group 1 compared to group 2. However, there was no significant difference between the groups regarding the mean number of wet nights after 12 and 24 weeks of treatment. There was no significant difference between the groups regarding the number of responders, partial responders, non-responders and relapsers. In the group with additional desmopressin therapy given, the number of patients who abandoned therapy was lower than the alarm therapy alone group, but it was not statistically significant.

**CONCLUSION:** Our data showed that the addition of short-term desmopressin to alarm therapy was more effective only in the period when it was given, and it did not change the response to alarm therapy in the long term.

11. J Pediatr. 2007 Dec;151(6):571-4. Epub 2007 Oct 24.

Effect of 1-desamino-8-D-arginine vasopressin on prepulse inhibition of startle supports a central etiology of primary monosymptomatic enuresis.  
Schulz-Juergensen S, Rieger M, Schaefer J, Neuss A, Eggert P.

**OBJECTIVE:** To test the hypothesis that 1-desamino-8-D-arginine vasopressin (dDAVP) has an effect on prepulse inhibition (PPI) of startle in patients with primary monosymptomatic enuresis (PME), thus indicating a central effect.

**STUDY DESIGN:** Patients with PME (n = 21, age 6 to 12 years) were enrolled in a prospective, randomized, double-blinded, cross-over study. Startle reflexes and PPI were measured under dDAVP treatment versus placebo.

**RESULTS:** The data show that dDAVP has a significant effect on PPI, raising it from 38.88% under placebo to the age-related normal level of 62.6% with dDAVP treatment (P = .0127).

**CONCLUSIONS:** Our findings revive the concept of a central pathophysiology of PME and offer a different explanation for the effects of dDAVP, which not only acts on the kidney, but also is (as is AVP) a central neurotransmitter with a signal cascade on relevant reflex mechanisms.

12. Int J Clin Pract. 2007 Sep;61(9):1454-60. Epub 2007 Jul 26. → คัดลอก เนื่องจากเป็น sublingual dosage form

A randomised comparison of oral desmopressin lyophilisate (MELT) and tablet formulations in children and adolescents with primary nocturnal enuresis.

Lottmann H, Froeling F, Alloussi S, El-Radhi AS, Rittig S, Riis A, Persson BE.

**AIMS:** Desmopressin is a useful treatment for primary nocturnal enuresis (PNE), a common childhood condition that can persist into adolescence. This open-label, randomised, cross-over study evaluated the preference of children and adolescents with PNE for sublingual desmopressin oral lyophilisate (MELT) vs. tablet treatment, and the efficacy, safety, compliance and ease of use associated with each formulation. In total, 221 patients aged 5-15 years who were already receiving desmopressin tablets were randomised 1 : 1 to receive desmopressin treatment in the order MELT/tablet (n = 110) or tablet/MELT (n = 111) for 3 weeks each. Each formulation was administered in bioequivalent doses (0.2/0.4 mg tablets identical with 120/240 microg MELT). Following treatment, patients were questioned regarding treatment preference. Diary card data and 100 mm Visual Analogue Scale scores were also recorded.

**RESULTS:** Overall, patients preferred the MELT formulation to the tablet (56% vs. 44%; p = 0.112). This preference was age dependent (p = 0.006); patients aged < 12 years had a statistically significant preference for desmopressin MELT (p = 0.0089). Efficacy was similar for both formulations (MELT: 1.88 +/- 1.94 bedwetting episodes/week; tablet: 1.90 +/- 1.85 episodes/week). Ease of use of both formulations was high. Compliance (> or = 80%) was 94.5% for MELT patients vs. 88.9% for the tablet (p = 0.059). No serious/severe adverse events were reported. **CONCLUSIONS:** There was an overall preference for the MELT, and a statistically significant preference for desmopressin MELT in children aged 5-11 years. Desmopressin MELT had similar levels of efficacy and safety at lower dosing levels than the tablet, and therefore facilitates early initiation of PNE treatment in children aged 5-6 years.

13. Zhonghua Er Ke Za Zhi. 2007 Mar;45(3):167-71.

[A randomized controlled clinical trial for treatment of children with primary nocturnal enuresis].

[Article in Chinese]

Ma J, Zhang YW, Wu H, Jiang F, Jin XM.

**OBJECTIVE:** Applying three treatment methods for enuresis in children with primary nocturnal enuresis (PNE) in a randomized controlled clinical trial (RCT) to compare the curative effects and characteristics of the three methods.

**METHODS:** If the parents and children consented to accept the treatment for 4 months and to keep on follow-up, the children diagnosed as primary nocturnal enuresis in the department of developmental and behavioral pediatrics in Shanghai Children's Medical Center from April 2003 to August 2004 were randomized into three groups: 52 children were in physio-psychological treatment group and were treated by utilizing the conditioning training role of alarm and other psychological and behavioral training programs; 46 children were in drug treatment group and were treated by taking DDAVP tablets orally; 40 children were in combined treatment group who were treated by applying the former two methods simultaneously. If the parents and children did not accept treatment, they were enrolled into the control group and were followed-up. Then, the curative effects of the four groups were compared statistically when the 4-month treatment was over and compared again 3 months later.

**RESULTS:** Applying the physio-psychological treatment for 4 months, the short-term cure rate of children with enuresis was 75.0%. Three months after the end of the treatment, the long-term cure rate was 71.2%. As for drug treatment group, the short-term cure rate of children with enuresis was 47.8%, the long-term cure rate was 28.3%; As for combined treatment group, the short-term cure rate of children with enuresis was 85.0%, the long-term cure rate was 80.0%. The short-term and long-term curative effects of physio-psychological treatment group and combined treatment group were better than that of drug treatment group (P < 0.01). However, the short-term and long-term curative effects were not significantly different between physio-psychological treatment and combined treatment group (P > 0.05). Physio-psychological treatment exerts effects slowly, but showed sustained curative effects. While Drug treatment exerts effects rapidly, but the relapse rate was very high after discontinuation of the medication.

**CONCLUSIONS:** Physio-psychological treatment and drug treatment are currently generally recognized the best ways to treat enuresis, both of them are suitable for Chinese enuresis children, both of them showed good curative effects. Physio-psychological treatment develops children's ability to control nocturnal micturition, its curative effects were better than that of the drug treatment whilst its relapse rate is lower as compared to drug treatment. So, physio-psychological treatment is more suitable for widespread use to treat PNE in China.

14. Urol Int. 2007;78(3):260-3.

Is second-line enuretic alarm therapy after unsuccessful pharmacotherapy superior to first-line therapy in the treatment of monosymptomatic nocturnal enuresis?

Tuygun C, Eroglu M, Bakirtas H, Gucuk A, Zengin K, Imamoglu A.

**INTRODUCTION:** We aimed at comparing the success rates of primary enuretic alarm therapy with those of secondary alarm therapy after failed pharmacotherapy in the treatment of monosymptomatic nocturnal enuresis (MNE).

**PATIENTS AND METHODS:** We randomly applied enuretic alarm therapy in 35 MNE patients (group 1) and desmopressin therapy in 49 MNE patients (group 2). The success and rebound rates after 3 and 6 months were determined. We also applied enuretic alarm therapy as a secondary treatment in 19 group 2 patients with complete rebound after 6 months (group 3). The success rates of patients who have received primary and secondary enuretic alarm therapy were compared.

**RESULTS:** The success rates for groups 1 and 2 were 82.65 and 81.63%, respectively ( $p = 0.885$ ), at 3 months and 54.28 and 26.53%, respectively ( $p = 0.007$ ), at 6 months. The success rates in group 3 were 84.21 and 52.63%, respectively, at 3 and 6 months. When these success rates were compared between groups 1 and 3, no statistically significant difference was found ( $p = 1.000$ ).

**CONCLUSION:** Prior pharmacotherapy did not increase success rates of alarm therapy in our MNE patients.

15. Pediatr Nephrol. 2008 Feb;23(2):269-74. Epub 2007 Feb 20.

Homotoxicological remedies versus desmopressin versus placebo in the treatment of enuresis: a randomised, double-blind, controlled trial.

Ferrara P, Marrone G, Emmanuele V, Nicoletti A, Mastrangelo A, Tiberi E, Ruggiero A, Fasano A, Paolini Paoletti F.

The aim of this trial was to compare the safety and efficacy of homotoxicological remedies versus placebo and versus desmopressin (dDAVP) in the treatment of monosymptomatic nocturnal enuresis (MNE). We conducted a randomised, double-blind, double-dummy, controlled trial in which 151 children with MNE were randomly assigned to receive oral homotoxicological remedies ( $n = 50$ ), dDAVP ( $n = 50$ ) or placebo ( $n = 51$ ). The primary outcomes were: the reduction of wet nights per week after 3 months of therapy; the evaluation of the numbers and percentages of non-responders and responders; the number of children relapsing after initial response and the number of children attaining 14 consecutive dry nights during the treatment. The secondary outcome was the detection of adverse effects. Baseline clinical characteristics were similar in the three groups of patients. After the 3 months of therapy there was a significant difference between the three groups ( $P < 0.001$ ) in the mean number of wet nights per week. The daily dose of dDAVP produced a statistically significant decrease (62.9%) in wet nights compared to placebo (2.4%) ( $P < 0.001$ ) and compared to homotoxicological remedies (30.0%) ( $P < 0.001$ ). There was a significant decrease in wet nights among the group treated with homotoxicological medications if compared with placebo ( $P < 0.001$ ). The full response achieved with homotoxicological remedies (20%) was superior if compared with placebo (0%) ( $P < 0.001$ ). Homotoxicology was superior to placebo ( $P < 0.001$ ) with regard to the number of children attaining 14 consecutive dry nights during treatment. Our study demonstrates that homotoxicology is safe and effective when compared with placebo, even if it is significantly less effective than dDAVP in this clinical condition.

16. J Clin Pharmacol. 2006 Oct;46(10):1204-11. . → คัดลอก เนื่องจากเป็นการศึกษาเกี่ยวกับ Pharmacokinetics

Pharmacokinetics of desmopressin administered as an oral lyophilisate dosage form in children with primary nocturnal enuresis and healthy adults. Osterberg O, Savic RM, Karlsson MO, Simonsson US, Nørgaard JP, Walle JV, Agersø H.

The population pharmacokinetics of desmopressin in children with nocturnal enuresis and in healthy adults were compared using a 1-compartment model with first-order absorption and first-order elimination. In addition, the model consisted of a number of transit compartments before absorption to describe a lag-time. The model gave an adequate description of adult as well as children data and provided a statistically significant better fit to data than a standard lag-time model. The main difference in the pharmacokinetics between children and adults was the absorption delay. The pharmacokinetic difference was minor and presumably of no clinical relevance.

17. BJU Int. 1999 Jul;84(1):20-4. . → คัดลอก เนื่องจากเป็น sublingual dosage form

Desmopressin in the treatment of nocturnal polyuria in the male.

Cannon A, Carter PG, McConnell AA, Abrams P.

**OBJECTIVES:** To assess whether desmopressin (1-desamino 8-d-arginine vasopressin) is safe and effective in the treatment of nocturnal polyuria in elderly men.

**PATIENTS AND METHODS:** Twenty men (age 52-80 years) complaining of nocturia were found to have nocturnal polyuria, determined from frequency-volume charts and defined as the production of >33% of the 24 h urine volume overnight, averaged over a 1-week period. In a double-blind study of cross-over design, a 1-week placebo run-in period was followed by two 2-week periods of placebo or 20 microg intranasal desmopressin, and ended with an open 2-week treatment period with 40 microg desmopressin.

**RESULTS:** Desmopressin caused a significant reduction in nocturnal urine volume and the percentage of urine passed at night, but the reduction in nocturnal frequency was only significant during treatment with 40 microg desmopressin. Four patients on desmopressin experienced side-effects, three of which were thought to be due to fluid retention.

**CONCLUSION:** Desmopressin is an effective treatment for nocturnal polyuria in some elderly men. However, it can cause fluid retention and should not be given to patients with cardiac failure. Those undergoing treatment must be closely monitored.

18. BJU Int. 1999 Apr;83(6):591-5.

Oral desmopressin for nocturnal polyuria in elderly subjects: a double-blind, placebo-controlled randomized exploratory study.

Asplund R, Sundberg B, Bengtsson P.

**OBJECTIVE:** To evaluate the decrease in nocturnal diuresis, nocturnal polyuria and the safety of oral desmopressin in elderly subjects with nocturia.

**SUBJECTS AND METHODS:** After being identified using a population-based questionnaire, subjects were included in the study if they; (i) were healthy and free from medication with possible influence on the diuresis or voiding pattern; (ii) had an increased nocturnal frequency (>=2 nocturnal



voids/night, as reported before screening); (iii) had a nocturnal urinary output of  $\geq 0.9$  mL/min; (iv) completed and responded to an initial dose-titration study. Twelve men and five women (mean age 67.7 years, sd 4.6 years) met these criteria and were treated with oral desmopressin or placebo at bedtime for 2 weeks on each medication in a randomized, double-blind, crossover design.

**RESULTS:** Subjects treated with desmopressin had a significantly reduced nocturnal diuresis of 0.59 mL/min compared with those on placebo (95% confidence interval, CI, 0.33-0.85). The 24-h diuresis was unaffected by desmopressin treatment. Patients treated with desmopressin had fewer micturitions at night than had those on placebo (1.1 and 1.7, respectively;  $P < 0.001$ ; mean difference = 0.59; 95% CI, 0.32-0.85). The reduction in nocturnal diuresis was dependent on the baseline level of night-time diuresis ( $r = 0.886$ ;  $r^2 = 0.785$ ;  $P < 0.0001$ ) and the nocturnal part of the baseline 24 h-diuresis ( $r = 0.708$ ;  $r^2 = 0.502$ ;  $P < 0.001$ ). After desmopressin treatment was withdrawn, diuresis returned to the levels before treatment. The time from falling asleep to first awakening was improved by 1.4 h in patients treated with desmopressin. There was no change in body weight or ankle circumference during desmopressin treatment. Overall, the treatment was well tolerated and no serious adverse events were observed.

**CONCLUSION:** Desmopressin was effective in reducing nocturnal diuresis and nocturnal voids in polyuric elderly subjects, with no significant adverse events or inconvenience to the patient. The length of uninterrupted sleep was also improved.

### ข้อมูลด้านรายการยาและการเบิกจ่ายในต่างประเทศ

1. WHO model list 2011 - ไม่พบข้อมูล<sup>17</sup>
2. Australia<sup>18</sup>

อนุมัติให้เบิกจ่ายยา Desmopressin ในผู้ป่วยที่คือ enuresis alarm เท่านั้น และมีหมายเหตุว่ารูปแบบยาพ่นจมูกเพิ่มความเสี่ยงต่อการเกิดภาวะโซเดียมในเลือดต่ำเมื่อเทียบกับยากิน

#### Posterior pituitary lobe hormones

##### *Vasopressin and analogues*

##### **DESMOPRESSIN ACETATE**

##### **Authority required (STREAMLINED)**

**1678** Cranial diabetes insipidus.

##### **DESMOPRESSIN ACETATE**

##### **Authority required (STREAMLINED)**

**2641** Primary nocturnal enuresis in patients aged 6 years or older who are refractory to an enuresis alarm;

**2642** Primary nocturnal enuresis in patients aged 6 years or older for whom an enuresis alarm is contraindicated. The reason that an alarm is contraindicated must be documented in the patient's medical records when treatment is initiated.

**Note:** Not to be used in preference to enuresis alarms. Desmopressin nasal spray may be associated with an increased risk of hyponatraemia compared to the oral formulations. Only one application per six months with no more than twice the maximum quantity will be authorised for the tablets.

3. Scotland<sup>19</sup>

ไม่ได้อนุมัติการเบิกจ่าย Desmopressin ทั้งรูปแบบกินและพ่นจมูก ในข้อบ่งใช้ nocturnal polyuria

#### Posterior pituitary hormones and antagonists 6.5.2

##### **(a) diabetes insipidus**

First choice: desmopressin nasal spray

Second choice: desmopressin tablets

##### **Dose**

- **Desmopressin nasal spray 10 micrograms/metered spray; intranasal solution 100micrograms/mL:** intranasally, diabetes insipidus, treatment, 10–40 micrograms daily in 1–2 divided doses.

- **Desmopressin tablets 100micrograms, 200micrograms:** diabetes insipidus, treatment, initially 300micrograms daily in 3 divided doses; maintenance 300–600micrograms daily in 3 divided doses; range 0.2–1.2mg daily.

- **Desmopressin sublingual tablets 60 micrograms, 120 micrograms, 240 micrograms:** diabetes insipidus, initially 180 micrograms daily in 3 divided doses; range 120 – 720 micrograms daily.

##### **Prescribing notes**

· A single dose of desmopressin is also used as part of a test following fluid deprivation in the differential diagnosis of thirst and polyuria.

· For nephrogenic diabetes insipidus, the usual treatment is a thiazide diuretic. Caution if due to lithium; refer to endocrinologist.

· Desmopressin injection 4micrograms/mL may be indicated in unconscious patients (dose 1– 4micrograms daily by subcutaneous, intramuscular or intravenous injection).

· Measurement of plasma sodium once or twice a year guards against excessive water intake which would be reflected by a low plasma sodium.

4. India - National List of Essential Medicine 2011 – ไม่พบข้อมูล<sup>20</sup>

ข้อมูลด้านราคาขาย

ตารางที่ 4 แสดงราคาขาย Desmopressin ในรูปแบบต่างๆ

ตัวยาสําคัญ	รูปแบบ/ความแรง	ราคา สธ. ต.ค.-ธ.ค. 54 ม.ค.-มี.ค. 55	ราคาบริษัทฯ เสนอ/1 หน่วย	ราคา/วัน เมื่อคิดขนาด ยาที่ต่ำที่สุด (0.2 mg/day)	ราคา/วัน เมื่อคิดขนาด ยาที่สูงที่สุด (0.6 mg/day)	ปริมาณ นำเข้า/ ผลิต ปี 2554
Desmopressin (MINIRIN®)  [The recommended dose of desmopressin for the treatment of primary nocturnal enuresis is 0.2 mg orally once daily at bedtime, titrated to 0.6 mg to achieve the desired response.] <sup>5</sup>	tab 0.1 mg	64.20	64.20	128.4	385.2	777,630
	tab 0.2 mg	-	124.83	124.83	374.5	5,400
	Nasal spray 0.1 mg/ml (2.5 ml)	1246.37	1326.80	-	-	7,020
	Nasal sol 0.1 mg/ml (2.5 ml)	1255.47	1326.80	-	-	14,931
	sublingual tab60 mcg	ไม่พบข้อมูล	ไม่พบข้อมูล	-	-	6,000
	sol for inj or infusions 4 mcg/1 ml	ไม่พบข้อมูล	ไม่พบข้อมูล	-	-	16,850

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