Overactive bladder / Hyperactivité vésicale

Astellas satellite symposium

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The 9th Congress of the Lebanese Urology Society
Sept. 29 - Oct. 1, 2016
Hilton Hotel, Beirut - Lebanon
Disclosure statement

- AMS/Boston Scientific: Speaker
- Allergan: Consultant, investigator, speaker
- Astellas: Consultant, investigator, speaker
- Coloplast: Consultant, investigator
- Medtronic: Speaker
- Ipsen Biotech: Investigator
- Lilly: Consultant
- Pfizer: Consultant
- Promedon: Speaker
- Uromedica: Speaker
- Wellspect: Consultant, investigator
Objectifs

• HAV et HAV réfractaire

• Nouveautés de la prise en charge : place du mirabegron

• Cas cliniques

• Discussion
What is OAB?

International Continence Society
Updated 2016
Standardised terminology report, Abrams et al., Neurourol Urodyn 2002

The Standardisation of Terminology of Lower Urinary Tract Function: Report from the Standardisation Sub-committee of the International Continence Society

Paul Abrams, Linda Cardozo, Magnus Fall, Derek Griffiths, Peter Rosier, Ulf Ulmsten, Philip van Kerrebroeck, Arne Victor, and Alan Wein
Definition of OAB

- Urgency, with or without urgency incontinence, usually with frequency and nocturia

> Urgency: a sudden compelling desire to pass urine which is difficult to defer
> Frequency: the complaint by a patient who considers that he/she voids too often by day
> Nocturia: the complaint that the individual has to wake at night 1 or more times to void
> UUI: involuntary leakage accompanied by or immediately preceded by urgency
LUTS = lower urinary tract symptoms

- STORAGE symptoms
  - Frequency
  - Urgency
  - ...

- VOIDING symptoms
  - Dysuria
  - Dribbling
  - ...

LUTS = lower urinary tract symptoms
OAB Syndrome: Idiopathic and neuropathic

Adapted from Chapple CR, et al. BJU Int. 2005; 95: 335–40
Spectrum of OAB

- OAB defined as “urgency, with or without urgency incontinence, usually with frequency and nocturia”

Urgency: “a sudden compelling desire to pass urine, which is difficult to defer”

Urgency: “the only symptom a patient must have to be described as having OAB”

References:
- Wein AJ, Rackley RR. J Urol 2006; 175:s5-10
- Abrams P. BJU Int 2005; 96 (Suppl 1);1-3
OAB: idiopathic vs. neurogenic

- Neurogenic
  OAB where there is a relevant neurological condition
  - Sensation may be impaired, so urgency is unreliable
- Detrusor overactivity
  - Bladder contractions during the storage phase which may be spontaneous and/or provoked
OAB may originate from...

1. Comorbidities
2. Ageing
3. Myogenic origin
4. Afferent urothelium function
5. Bladder afferents
6. Efferent function
7. Obstruction

Non neurogenic OAB

Nervous system

Bladder

Urothelium

Neurogenic OAB...
OAB in Europe

- 16.6% of the population over 40 years in 6 European countries have OAB symptoms

- OAB prevalence increases with age

Milsom I et al. *BJU Int.* 2001;87:760-766
OAB in US

- 16.5% of the population over 18 years (~33 million) have OAB symptoms

Stewart W et al. World J Urol. 2002
OAB prevalence (standardised definition); EPIC

Table 1. Prevalence of OAB by Sex and Country

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence (%)*</th>
<th>Estimated Population With OAB (millions)</th>
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*Weighted data for individuals ≥18 years.

Figure 2. Prevalence* of OAB by Sex and Age Group

Figure 3. OAB Prevalence* Comparison Between Milsom 1997 Weighted Estimates and EPIC 2005 Weighted Estimates
Assessment : LUTS

- LUTS, severity and bother
  - Exclude malignancy, neurological and UTI
  - Fluid intake
  - Use a symptom assessment tool e.g ICIQ
- Frequency volume chart
- Dipstick urinalysis / MSU
- Flow rate and residual

**Uncomplicated OAB can be treated without further investigation**

LUTS = Lower urinary Tract Symptoms
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* instructions on other side *

**AVERAGE DAILY FLUID INTAKE (in cups) = 14**

With permission of M. Drake
Primary management

• Only if patient wants treatment
  • Bother, QoL, ...

• Reassurance

• Bladder training

• Suitable fluid intake
PFMT: Pelvic Floor Muscle Training and OAB

• Has to be prescribed
• 10 sessions:
  • To reinforce bladder sensation control
  • To prevent any malfunction of abdominoperineal reflexes
• Caregiver has to be trained
  • Physiotherapist

• To discuss: Tibial nerve stimulation (TENS)
Anticholinergics over years

- Oxybutynin
- Oxybutynin ER
- Tolterodine ER
- Oxybutynin CR
  - Trospium
  - Solifenacin
  - Darifenacin
- Tolterodine
- Oxybutynin patch
- Topical Oxybutynin
- Fesoterodine

ER = extended release; CR = controlled release
Adapted from respective product monographs.
### 4th International Consultation in Incontinence  Antimuscarinics/ Mixed Action Drugs

Fourth International Consultation On Incontinence (ICI) Paris 2012 - Drug Treatment Committee Highlights,

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Comparative studies between Antimuscarinics

• Very limited
  • STAR; solifenacin vs tolterodine
  • ACET; oxybutynin vs tolterodine
  • Fesoterodine vs tolterodine
• Reviews and “meta-analysis”
• No clear winner
• Oxybutynin probably is a clear looser
The Effects of Antimuscarinic Treatments in Overactive Bladder: A Systematic Review and Meta-Analysis

The anti-muscarinics were found to be safe AND efficacious
There were significant differences between the anti-muscarinics in terms of withdrawal and rates and range of adverse events and efficacy outcomes

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How to Define a Refractory Idiopathic Overactive Bladder?

Véronique Phé,1* Stefan de Wachter,2 Morgan Roupret,1 and Emmanuel Chartier-Kastler1

1Department of Urology, Pitie-Salpetriere Academic Hospital, Assistance Publique-Hopitaux de Paris, Pierre et Marie Curie Medical School, Paris 6 University, Paris, France
2Department of Urology, University Hospital Antwerpen, Antwerpen, Belgium

Figure 1. Elements defining success of a treatment by antimuscarinics
Antimuscarinic failure

• A second antimuscarinic can achieve success if the first does not
  • Crucial to engage the patient

• Options;
  • Increase dose (may be exceed licensed dose)
  • Combine drugs (e.g. transdermal + low dose oral)
  • Manage adverse effects e.g. artificial saliva (salivart)

• Glaucoma, GORD
Reasons for failure

- Drug did not work (persistent urgency)
- Adverse effects
- Unrealistic expectations
- Failure to perceive benefit
- Compliance
- Other LUTS
- Other symptoms:
  - Fecal incontinence, pelvic pain, psychological disorders
- Wrong diagnosis
  - UTI
  - Post void residual urine
  - Pelvic inflammation attributed to the bladder
  - Spinal
Polyuria

Components of nocturia

- Urine output exceeds 40 ml/Kg/24 hours
- Nocturnal polyuria
  - Urine output between 11pm and 7 am is < 20% in young and < 33% in elderly
- Low nocturnal bladder capacity

Suprapontine

CVA
post head injury
encephalitis
tumour
dementia
parkinsonism (IPD/MSA)

Subpontine supraspinal

Spinal Cord Lesions
Multiple Sclerosis
Myelodysplasia

Subsacral

cauda equina
nerve injury in pelvis
peripheral neuropathy
Which basic evaluation

• Voiding diary
• Bacterial analysis of urine

• Ultrasound:
  • Kidneys: bladder (post void residual urine)
• Urine cytology
• Cystoscopy (optionnal as a first line management of OAB except unusual symptoms and smokers)
Which antimuscarinic?

• All of them work
• Extended release preferred to immediate
• For the immediate release agents, dose escalation can yield benefits
• No clear first line agent

• Transdermal agents
• Beta-3 agonist

Persistence with prescribed antimuscarinic therapy for overactive bladder over 12 months: a UK experience
Mirabegron is a novel treatment for OAB that works differently to antimuscarinics$^{1,2}$

Mode of action of OAB treatments$^{1,3}$

Adapted from Betmiga Summary of Product Characteristics, December 2012 and Chu et al., 2006.

**SCORPIO: A key European-Australian, 12-week, Phase III trial in patients with OAB**

**SCORPIO trial design**

A randomised, double-blind, placebo- and active-controlled, 12-week Phase III trial of 1978 patients with OAB

**Screening**
- Men and women aged ≥18 years
- OAB symptoms for ≥3 months

**Randomisation**
- Placebo (n=494)
- Tolterodine ER 4mg (n=495) active control
- Mirabegron 50mg (n=493)

**Treatment phase**
- 12 weeks

**End of treatment**
- Follow up*

**Co-primary efficacy endpoints**
- Incontinence episodes/24h (change from baseline to final visit)
- Micturitions/24h

**Key secondary efficacy endpoints**
- Volume voided/micturition (change from baseline to final visit)
- Incontinence episodes/24h (change from baseline to week 4)
- Micturitions/24h (change from baseline to week 4)

*Evaluation of adverse events and concomitant medication by telephone or visit for a period of 30 days.

Tolterodine ER (extended-release) 4mg was included as an active control in this study.


Date of preparation: February 2013. BET13018UK
Patients demographics

MEDICAL DETAILS (FAS)

50.4% Treatment-naive (n=960)
49.6% Treatment-experienced (n=946)

TREATMENT HISTORY

OAB TYPE

39.7% Urgency incontinence only (wet OAB)
37.7% Frequency/urgency (dry OAB)
22.6% Mixed incontinence

PATIENT DEMOGRAPHICS (AII)

AGE

37% ≥65 years (n=734)
63% <65 years (n=1,244)

GENDER

28% Male (n=549)
72% Female (n=1,429)

Khullar V, et al. Efficacy and Tolerability of Mirabegron, a β3-Adrenoceptor Agonist, in Patients with Overactive Bladder: Results from a Randomised European-Australian Phase 3 Trial; Eur Urol (2013) 283-295
SCORPIO: Improvements in incontinence episodes/24h (co-primary endpoint)¹

Incontinence episodes/24h (FAS-I)

<table>
<thead>
<tr>
<th>Adjusted mean change from baseline to final visit (episodes)</th>
<th>Baseline</th>
<th>2.67</th>
<th>2.63</th>
<th>2.83</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=291</td>
<td>-1.17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=300</td>
<td>-1.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=293</td>
<td>-1.57</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Tolterodine ER (extended-release) 4mg was included as an active control in this study.
- FAS-I = all full analysis set patients who had ≥1 incontinence episode at baseline.
- ns = no statistically significant difference vs. placebo.
- *Statistically significant improvement vs. placebo (p<0.05).
- †Mean difference vs. placebo (95% two-sided CI: -0.72, -0.09).

Adapted from Khullar et al., 2013.¹

Date of preparation: February 2013. BET13018UK

**SCORPIO: Improvements in micturitions/24h (co-primary endpoint)**


Tolterodine ER (extended-release) 4mg was included as an active control in this study.

FAS = full analysis set

ns = no statistically significant difference vs. placebo.

*Statistically significant improvement vs. placebo (p<0.05).

‡Mean difference vs. placebo (95% two-sided CI: -0.90, -0.29).
SCORPIO: Most common TEAEs (≥2% in any treatment group)¹

- In the three, 12-week Phase III studies, the most common adverse reactions reported for mirabegron 50mg were tachycardia and urinary tract infections (1.2% and 2.9% respectively). Serious adverse reactions included atrial fibrillation (0.2%)²
- In SCORPIO, rates of drug discontinuation due to TEAEs were low and comparable in the active groups (<5%)¹

### Incidence of most common (≥2%) TEAEs¹

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Placebo (n=494)</th>
<th>Mirabegron 50mg (n=493)</th>
<th>Tolterodine ER 4mg active control (n=495)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>2.6%</td>
<td>2.8%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.4%</td>
<td>1.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7.7%</td>
<td>5.9%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1.6%</td>
<td>2.8%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Headache</td>
<td>2.8%</td>
<td>3.7%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1.4%</td>
<td>1.4%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

For the full list of adverse events refer to the SmPC.²
Tolterodine ER 4mg was included as an active control therefore direct statistical comparisons cannot be made between mirabegron and tolterodine ER 4mg.
Table adapted from Khullar et al., 2013.¹

Data not shown for the unlicensed 100mg dose of Mirabegron.
TEAEs, treatment-emergent adverse events.


Date of preparation: February 2013. BET13018UK
**SCORPIO post hoc analysis:**
Patients who discontinued previous OAB therapy due to lack of effect\(^1,2\)

---

### Micturitions/24h (FAS)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Adjusted mean change from baseline to final visit</th>
<th>Improvement vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.89</td>
<td>-1.03</td>
<td>-1.03</td>
</tr>
<tr>
<td>11.99</td>
<td>-1.11</td>
<td>-1.11</td>
</tr>
<tr>
<td>11.49</td>
<td>-1.62</td>
<td>-1.62</td>
</tr>
</tbody>
</table>

FAS = full analysis set.

**Adapted from:** Khullar et al., 2012\(^1\) and Betmiga Summary of Product Characteristics, December 2012\(^2\).

Tolterodine ER (extended-release) 4mg was included as an active control in this study.

\(^1\)Mean difference vs. placebo (95% two-sided CI: -1.15, -0.04).

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SCORPIO: Conclusions

- Mirabegron 50mg, over 12 weeks, demonstrated superior efficacy compared with placebo for co-primary endpoints of micturitions and incontinence episodes/24 hours\(^1\)
- Mirabegron 50mg is an effective treatment for OAB in treatment-naïve patients and previously treated patients\(^1\)
- Mirabegron 50mg is effective in patients who discontinued antimuscarinic therapy due to lack of effect\(^2\)
- Mirabegron 50mg was generally well tolerated\(^1\)


Date of preparation: February 2013. BET13018UK
TAURUS trial design: long-term safety and efficacy of mirabegron

A multi-centre, 12-month, double-blind study of 2444 patients with OAB

Tolterodine ER 4mg was an active control

Screening
- Men and women aged ≥18 years
- OAB symptoms for ≥3 months

Placebo run-in
2 weeks

Visits
VISIT 1 Week -2
VISIT 2 Week 0
VISIT 3 Month 1
VISIT 4 Month 3
VISIT 5 Month 6
VISIT 6 Month 9
VISIT 7 Month 12

Randomisation
- Tolterodine ER 4mg (n=812)
  active control
- Mirabegron 50mg (n=812)

End of treatment

Primary endpoints
- Frequency and severity of TEAEs

Secondary endpoints
- Incontinence episodes/24h
- Micturitions/24h
- Volume voided/micturitions
- Plus additional measures

Adapted from Chapple et al., 2013. Eligible patients who completed Phase III, 12-week mirabegron studies could be enrolled, but required a minimum 30-day drug washout. The study was not designed to demonstrate a statistically significant difference in efficacy between treatment groups. Tolterodine ER 4mg was an active control. No direct statistical comparisons can be made between tolterodine ER 4mg and mirabegron 50mg.

TAURUS: Efficacy variables over 52 weeks (secondary endpoint)

Mean number of micturitions/24h (FAS)\(^1\)

Adapted from Chapple CR et al., 2013.\(^1\)
Tolterodine ER (extended-release) 4mg was included as an active control in this study.
FAS = full analysis set.

TAURUS: 12-month extension study

- In the three, 12-week Phase III studies, the most common adverse reactions reported for mirabegron 50mg were tachycardia and urinary tract infections (1.2% and 2.9% respectively). Serious adverse reactions included atrial fibrillation (0.2%)

- The long-term safety and tolerability profile of mirabegron 50mg was demonstrated in a multi-centre, 12-month, double-blind study (n=2444)
  - The incidence and severity of TEAEs (primary endpoint) was similar across the active treatments in this study
  - Most TEAEs were mild to moderate in severity

TEAE, treatment-emergent adverse event.

**TAURUS:**
**Most frequent (≥2% in any group) TEAEs**¹

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Mirabegron 50mg (n=812) n (%)</th>
<th>Tolterodine ER 4mg active control (n=812) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>75 (9.2%)</td>
<td>78 (9.6%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>48 (5.9%)</td>
<td>52 (6.4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>33 (4.1%)</td>
<td>20 (2.5%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>32 (3.9%)</td>
<td>25 (3.1%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>23 (2.8%)</td>
<td>13 (1.6%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>23 (2.8%)</td>
<td>22 (2.7%)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>23 (2.8%)</td>
<td>70 (8.6%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>22 (2.7%)</td>
<td>12 (1.5%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>22 (2.7%)</td>
<td>21 (2.6%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>21 (2.6%)</td>
<td>28 (3.4%)</td>
</tr>
<tr>
<td>Cystitis</td>
<td>17 (2.1%)</td>
<td>19 (2.3%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>17 (2.1%)</td>
<td>16 (2.0%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>15 (1.8%)</td>
<td>16 (2.0%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>8 (1.0%)</td>
<td>25 (3.1%)</td>
</tr>
</tbody>
</table>

*For full list of side effects, please consult the SmPC²*

Safety Analysis Set (SAF) - all randomised patients who took ≥1 dose of double-blind study drug; TEAE, treatment-emergent adverse event.


Date of preparation: February 2013. BET13018UK
Patients remaining on OAB treatments over 8 months

Patients starting a new course of OAB therapy in the 8 months to July 2013 who are then tracked for 8 months to measure how many have remained on treatment

Source: CSD Patient Data, Cegedim Strategic Data UK Ltd, March 2014
Urinary retention

Rates of urinary retention in mirabegron-treated patients

Chapple, C.R.¹, Nitti, V.W.², Herschorn, S.³, Blauwet, M.B.⁴, Traudtner, K.⁵, Walters, C.⁶, Siddiqui, E.⁶

◆ 3 large 12-week RCTs and a 1-year, active-controlled trial for efficacy and safety of mirabegron (25, 50, 100 mg)
  ◆ Tolterodine 4 mg ER as an active control in two studies
  ◆ Women and men

◆ Incidence of retention 0.1%; placebo 0.2% / tolterodine 0.6% (189 events in 253430 patients)

◆ Almost all patients had ≥1 confounding factor, e.g. age >70 yrs, BOO, neurologic disorders, infections, or concomitant medications such as antimuscarinics
SYMPHONY: mirabegron & solifenacin

Change from baseline to end of treatment in mean number of micturitions/24 hours: difference vs placebo

SYMPHONY Study: safety summary

◆ All six combinations were well tolerated
◆ No additive/ synergistic effect on pulse rate, hypertension, bladder pressure, QTc interval
◆ Appear to be no major safety concerns
◆ Constipation is the only event which showed increased frequency in combination arms; a dose-related trend could not be excluded
BESIDE study

◆ A Trial Comparing Combination Treatment (Solifenacin Plus Mirabegron) With One Treatment Alone (Solifenacin)

◆ Primary Outcome Measure: Change from Baseline in mean number of incontinence episodes per 24 hours

https://clinicaltrials.gov/ct2/show/NCT01908829
Conclusions

- OAB; definitions
- Assessment; symptom score and diary
  - Nocturia may be unrelated to OAB
- Conservative treatment before drugs
- Antimuscarinic problems are not seen with Mirabegron
  - Efficacy for incontinence episodes and micturition frequency
  - Well tolerated
  - In the future; combination therapy
## Mirabegron

<table>
<thead>
<tr>
<th>Evidence summary</th>
<th>LE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirabegron is better than placebo for improvement of UUI symptoms</td>
<td>1a</td>
</tr>
<tr>
<td>There is no evidence that mirabegron is better than placebo for curing incontinence.</td>
<td>1b</td>
</tr>
<tr>
<td>Mirabegron is no more effective than tolterodine.</td>
<td>1b</td>
</tr>
<tr>
<td>Adrenergic-mediated side effects of mirabegron appear mild and not clinically significant in a trial setting.</td>
<td>1a</td>
</tr>
<tr>
<td>Discontinuation rates from mirabegron are similar to tolterodine in a trial setting.</td>
<td>1b</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offer mirabegron to people with urgency urinary incontinence, but warn patients receiving mirabegron that the possible long-term side effects remain uncertain.</td>
<td>B</td>
</tr>
</tbody>
</table>

Lucas MG et al. EAU Guidelines on Urinary Incontinence (update 2015)
http://www.uroweb.org/gls/pdf/16052013Urinary_Incontinence_LR.pdf
Women vs. men

Discuss management

Individualised behavioural and physical therapies including pelvic floor muscle training

Stress incontinence
- Advise on bowels, drugs, co-morbidity, fluid intake (C)
- Advise on weight loss (A)
- Offer pads or other containment device if needed (A*)
- Consider topical vaginal oestrogen for post-menopausal women (A)
- Offer desmopressin for short term symptom relief (B)
- Offer timed or prompted voiding in elderly/care-dependent people (A)

Mixed incontinence

Urgency incontinence

Discuss management options

Individualised behavioural and physical therapies including pelvic floor muscle training

Stress incontinence

Mixed incontinence

Urgency incontinence

Anti-muscarinics (A) or mirabegron (B)

Consider P-PTNS (B)

Failed conservative or drug therapy - discuss surgical options

Anti-muscarinics (A) or mirabegron (B)

Consider P-PTNS (B)

Failed conservative or drug therapy - discuss surgical options
1 Guidance

1.1 Mirabegron is recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects.

1.2 People currently receiving mirabegron that is not recommended for them in 1.1 should be able to continue treatment until they and their clinician consider it appropriate to stop.
CAS CLINIQUE 1

◆ Femme de 55 ans
◆ HAV, prise de solifénacine pendant 6 mois et arret pour bouche sèche
◆ Abandon de suivi 6 mois
◆ Catalogue mictionnel
  ◆ 12 mictions par jour, 3 la nuit, 255 cc en moyenne et 3 épisodes d’urgenturie par jour en moyenne
◆ Quelle stratégie de prise en charge?
  ◆ Deuxième ligne d’emblée? (Botox, SNM)
  ◆ Association anticholinergiques
  ◆ Mirabegron?
CAS CLINIQUE 2

- Homme de 66 ans
- HAV avec 2 épisodes de nycturie.
  - inquiet pour la détection d’un cancer de prostate
- ICIQ M-LUTS*; gène et urgenturie. Dysurie ancienne
- Pas de traitements, ni de comorbidités
- TR: 25g HBP, examen neurologique normal,
- Qmax 11ml/s (volume uriné 120mls, Pas de résidu)
- Catalogue mictionel;
  - pollakiurie 12 / jour, 2 nycturies, mictions 100mls.

- Quelle prise en charge?
Mirabegron, prescribing informations

**Presentation:** Betmiga™ (mirabegron) 25 mg and 50 mg prolonged-release tablets. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Posology and Method of Administration:** Posology: Adults, including the elderly patients: The recommended dose is 50 mg once daily with or without food. Paediatric population: The safety and efficacy of mirabegron in children below 18 years of age have not yet been established. No data are available. Betmiga™ has not been studied in patients with end stage renal disease (GFR < 15 ml/min/1.73 m² or patients requiring haemodialysis) or severe hepatic impairment (Child-Pugh Class C) and it is therefore not recommended for use in these patient populations. **Method of administration:** The tablet is to be taken once daily, with liquids, swallowed whole and is not to be chewed, divided, or crushed. **Contraindications:** Mirabegron is contraindicated in patients with: - Hypersensitivity to the active substance or to any of the excipients listed. - Severe uncontrolled hypertension defined as systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥110 mmHg. **Warnings and Precautions:** Renal impairment: Betmiga™ has not been studied in patients with end stage renal disease (GFR < 15 ml/min/1.73 m² or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 ml/min/1.73 m²); based on a pharmacokinetic study a dose reduction to 25 mg is recommended in this population. Betmiga™ is not recommended for use in patients with severe renal impairment (GFR 15 to 29 ml/min/1.73 m²) concomitantly receiving strong CYP3A inhibitors. Hepatic impairment: Betmiga™ has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga™ is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors. Hypertension: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga™, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg). Patients with congenital or acquired QT prolongation: Betmiga™, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies. However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinic medications for OAB: Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with Betmiga™; however, Betmiga™ should be administered with caution to patients with clinically significant BOO. Betmiga™ should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Interactions:** Caution is advised if mirabegron is co-administered with CYP2D6 substrates that are individually dose titrated. Undesirable Effects: Common (≥1/100, <1/10): Urinary tract infection, Tachycardia and Nausea. Uncommon (≥1/1000, <1/100): Vaginal infection, Palpitation, Atrial fibrillation, Dyspepsia, Gastritis, Cystitis, Urticaria, Rash, Rash macular, Rash papular, Pruritus, Joint swelling, Vulvovaginal pruritus, Laboratory elevation in Blood pressure, GGT, AST and ALT. Rare (≥1/10000, <1/1000): Lip oedema, Purpura, Angiodema, Eyelid oedema, Leukocytoclastic vasculitis and Urinary retention. Not known (cannot be estimated from the available data): Insomnia. Legal category: POM. MA Holder: Astellas Pharma Europe B.V., Sylvisweg 62, 2333 BE, Leiden, NL. Further information available upon request from: Astellas Pharma DMCC, P.O. Box 282872, Dubai, UAE Date of issue: October 2015

In case of suspected adverse event(s) or any safety information, please report it immediately to nazira.hamadeh@mersaco.com or contact local Astellas office at Mersaco S.A.I. J. Klbury Blvd, Sami Solh Street P.O. Box 11-9073, Riad El Solh Beirut 1107 2280, Lebanon Tel: +961 1396000 If you have a medical information request, please forward it to Medical Information. MENASSA@astellas.com