

**FLOMAX RELIEF MR (PL 00015/0280)**

**UKPAR**

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**FLOMAX RELIEF MR (PL 00015/0280)****LAY SUMMARY**

On 3<sup>rd</sup> December 2009, the MHRA granted Boehringer Ingelheim Limited a Marketing Authorisation (licence) for the medicinal product Flomax Relief MR (PL 00015/0280). This is a pharmacy medicine (P) to treat lower urinary tract symptoms (LUTS) of a common condition called benign prostatic hyperplasia (BPH). This is when the prostate gland gets bigger, which can:

- Make it difficult for you to start urinating (peeing)
- Mean you take longer or have to urinate more often
- Lead to the feeling that you still need to urinate again, even though you have just done so
- Cause you to get up several times in the night to urinate.

Flomax Relief MR relieves these problems by:

- Relaxing the muscles in the prostate gland
- Relaxing the muscles in the urethra (the tube from the bladder to the outside of the body).

This lets urine pass more freely through the urethra, making it easier to urinate.

This product contains the active substance tamsulosin, which belongs to a group of medicines called 'alpha blockers' (or  $\alpha_{1A}$ -adrenoceptor antagonists).

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Flomax Relief MR outweigh the risks. Hence a Marketing Authorisation has been granted.

## **FLOMAX RELIEF MR (PL 00015/0280)**

### **SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Flomax Relief MR (PL 00015/0280) on 3<sup>rd</sup> December 2009. The product is for the treatment of functional symptoms of benign prostatic hyperplasia (BPH).

The application was submitted as a simple abridged application according to Article 10.1(c) of Directive 2001/83/EC, cross-referring to Flomax MR (PL 00166/0171) granted to Astellas Pharma Limited on 16<sup>th</sup> April 1996.

No new data were submitted nor was it necessary for this simple application, as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated.

The product contains the active substance tamsulosin hydrochloride, which is an  $\alpha_{1A}$ -adrenoceptor antagonist.

This submission combined the application for a new product licence with a reclassification application to change the legal status of the product from a prescription-only medicine (POM) to a pharmacy product (P) in patients aged 45 to 75 years with symptoms of benign prostatic hyperplasia. The reclassification was discussed by the Commission on Human Medicines (CHM) on 21<sup>st</sup> May 2009, who advised in favour of the reclassification following earlier advice in July 2007 and June 2008, as well as a period of public consultation. This is supported by study data showing that the in-pharmacy assessment, including a suitable questionnaire, ensures that the supply of product is consistent with current guidelines. The final assessment and CHM advice from 2009 are presented in Appendix 1.

## **PHARMACEUTICAL ASSESSMENT**

**LICENCE NO:** PL 00015/0280

**PROPRIETARY NAME:** Flomax Relief MR

**ACTIVE(S):** Tamsulosin hydrochloride

**COMPANY NAME:** Boehringer Ingelheim Limited

**E.C. ARTICLE:** Article 10c (formerly 10.1(a)(i)) of Directive 2001/83/EC

**LEGAL STATUS:** P

### **1. INTRODUCTION**

This is a simple, piggy back application for Flomax Relief MR (PL 00015/0280) submitted under Article 10c (formerly 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Boehringer Ingelheim Limited, Consumer Healthcare, Ellesfield Avenue, Bracknell, Berkshire RG12 8YS, United Kingdom.

This application cross refers to Marketing Authorisation application for Flomax MR (PL 00166/0171) granted to Astellas Pharma Limited on 16<sup>th</sup> April 1996. This application is considered valid.

### **2. MARKETING AUTHORISATION APPLICATION FORM**

#### **2.1 Name(s)**

The proposed name of the product is Flomax Relief MR. The product has been named in line with current requirements.

#### **2.2 Strength, pharmaceutical form, route of administration, container and pack sizes**

The product contains tamsulosin hydrochloride, equivalent to 400micrograms. The capsules are to be stored in polypropylene-aluminium blister packs containing 7 capsules per strip; which are then placed in cardboard boxes containing 14 and 28 capsules.

The proposed shelf-life of 4 years, with no specific storage instructions is consistent with the cross-reference product.

#### **2.3 Legal status**

On approval, the product will be subject to sale in a pharmacy only (P).

#### **2.4 Marketing authorisation holder/Contact Persons/Company**

Boehringer Ingelheim Limited, Consumer Healthcare, Ellesfield Avenue, Bracknell, Berkshire, RG12 8YS, United Kingdom.

The QP responsible for pharmacovigilance is stated and their CV is included.

#### **2.5 Manufacturers**

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

#### **2.6 Qualitative and quantitative composition**

The proposed composition is consistent with the details registered for the cross-reference product.

**2.7 Manufacturing process**

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

**2.8 Finished product/shelf-life specification**

The proposed finished product specification is in line with the details registered for the cross-reference product.

**2.9 Drug substance specification**

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

**2.10 TSE Compliance**

With the exception of gelatin and calcium stearate, none of the excipients are sourced from animal or human origins. Satisfactory European Directorate for the Quality of Medicines Certificates of Suitability have been provided for gelatin and calcium stearate, showing that they comply with current regulations concerning the reduction of risk of transmission of TSE.

**3. EXPERT REPORTS**

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

**4. PRODUCT NAME & APPEARANCE**

See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product, with the exception of the printing on the capsule.

**5. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)**

The proposed SPC is consistent with the details registered for the cross-reference product.

**6. PATIENT INFORMATION LEAFLET/CARTON****PIL**

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

**Carton and blister**

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included sufficient space for a standard UK pharmacy dispensing label.

## **7. CONCLUSIONS**

The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.

## **PRECLINICAL ASSESSMENT**

No new preclinical data have been supplied with this application and none are required for an application of this type.



## **CLINICAL ASSESSMENT**

No new clinical data have been supplied with this application and none are required for an application of this type.

## **OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT**

### **QUALITY**

The data for this application are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for an application of this type.

### **EFFICACY**

Tamsulosin hydrochloride is a well-known drug and has been used for many years. This application is identical to a previously granted application for Flomax MR (PL 00166/0171) granted to Astellas Pharma Limited on 16<sup>th</sup> April 1996.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with tamsulosin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The risk-benefit is, therefore, considered to be positive.

**FLOMAX RELIEF MR (PL 00015/0280)****STEPS TAKEN FOR ASSESMENT**

|   |   |
|---|---|
| 1 | The MHRA received the marketing authorisation applications on 28 <sup>th</sup> October 2005   |
| 2 | Following standard checks and communication with the applicant the MHRA considered the applications valid on 11 <sup>th</sup> November 2005 |
| 3 | Following assessment of the applications the MHRA requested further information on 18 <sup>th</sup> September 2006                          |
| 4 | The applicant responded to a series of MHRA's requests, providing final information on 2 <sup>nd</sup> December 2009                        |
| 5 | The applications were determined on 3 <sup>rd</sup> December 2009   |

**FLOMAX RELIEF MR (PL 00015/0280)****STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

| <b>Date submitted</b> | <b>Application type</b> | <b>Scope</b> | <b>Outcome</b> |
|-----------------------|-------------------------|--------------|----------------|
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |

**1 NAME OF THE MEDICINAL PRODUCT**

Flomax Relief® MR

**2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each capsule contains as active ingredient tamsulosin hydrochloride 400 microgram, equivalent to 367 microgram tamsulosin.

For excipients, see 6.1

**3 PHARMACEUTICAL FORM**

Capsule modified release, hard (capsule). Orange/olive green coded with T0.4 and the company logo.

**4 CLINICAL PARTICULARS****4.1 Therapeutic indications**

Treatment of functional symptoms of benign prostatic hyperplasia (BPH).

**4.2 Posology and method of administration**

Male 45 to 75 years.

One capsule daily, to be taken after the same meal each day.

The capsule should be swallowed whole and should not be crunched or chewed as this will interfere with the modified release of the active ingredient.

**4.3 Contraindications**

Hypersensitivity to tamsulosin hydrochloride or any other component of the product; a history of orthostatic hypotension; severe hepatic insufficiency.

**4.4 Special warnings and precautions for use**

As with other alpha1 blockers, a reduction in blood pressure can occur in individual cases during treatment with Flomax Relief, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness) the patient should sit or lie down until the symptoms have disappeared.

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients for whom cataract surgery is scheduled is not recommended.

Discontinuing tamsulosin 1 – 2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of stopping therapy prior to cataract surgery has not yet been established.

During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

**Additional warnings when supplied as a non-prescription medicine:**

Flomax Relief should not be given to patients receiving antihypertensive medicines with significant alpha1-adrenoceptor antagonist activity (e.g. doxazosin, indoramin, prazosin, terazosin, verapamil) without first consulting a doctor.

Flomax Relief should not be given to a man who experiences postural hypotension.

Flomax Relief should not be supplied to any man with heart, renal, or liver disease, uncontrolled diabetes, urinary incontinence, or to a man who has had prostate surgery.

Flomax Relief should not be supplied to a man whose symptoms are of less than 3 months' duration.

Flomax Relief should not be given to any man who reports dysuria, haematuria, or cloudy urine, in the past 3 months, or who is suffering from a fever that might be related to a urinary tract infection.

Flomax Relief should not be used in those planning to have eye surgery for cataract, or who have recently experienced blurred or cloudy vision that has not been examined by a GP or Optician.

If urinary symptoms have not improved within 14 days of starting treatment with Flomax Relief, or are getting worse, the patient should stop taking Flomax Relief and be referred to the doctor.

Medical review is required for the diagnosis of BPH. Patients must see their doctor within 6 weeks of starting treatment, for assessment of their symptoms and confirmation that they can continue to take Flomax Relief from their Pharmacist.

Every 12 months, patients should be advised to consult a doctor for a clinical review.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

No interactions have been seen when Flomax Relief was given concomitantly with either atenolol, enalapril, nifedipine or theophylline. Concomitant cimetidine brings about a rise in plasma levels of tamsulosin, and furosemide a fall, but as levels remain within the normal range posology need not be changed.

In vitro neither diazepam nor propranolol, trichlormethiazide, chlormadinon, amitriptyline, diclofenac, glibenclamide, simvastatin and warfarin change the free fraction of tamsulosin in human plasma. Neither does tamsulosin change the free fractions of diazepam, propranolol, trichlormethiazide, and chlormadinon.

No interactions at the level of hepatic metabolism have been seen during in vitro studies with liver microsomal fractions (representative of the cytochrome P450-linked drug metabolising enzyme system), involving amitriptyline, salbutamol, glibenclamide and finasteride. Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin.

There is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure including anaesthetic agents, other alpha1-adrenoceptor antagonists.

#### **4.6 Pregnancy and lactation**

Not applicable as Flomax Relief is intended for male patients only.

#### **4.7 Effects on ability to drive and use machines**

No data is available on whether Flomax Relief adversely affects the ability to drive or operate machines. However, in this respect patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

**4.8 Undesirable effects**

|   | <b>Common</b><br>(>1/100, <1/10) | <b>Uncommon</b><br>(>1/1 000, <1/100)     | <b>Rare</b><br>(>1/10 000, <1/1 000) | <b>Very rare</b><br>(<1/10 000) |
|---|----------------------------------|---|--------------------------------------|---------------------------------|
| Nervous system disorders                            | dizziness (1.3%)                 | headache                                  | syncope                              |                                 |
| Cardiac disorders                                   |                                  | palpitations                              |                                      |                                 |
| Vascular disorders                                  |                                  | postural hypotension                      |                                      |                                 |
| Respiratory, thoracic and mediastinal disorders     |                                  | rhinitis                                  |                                      |                                 |
| Gastrointestinal disorders                          |                                  | constipation, diarrhoea, nausea, vomiting |                                      |                                 |
| Skin and subcutaneous tissue disorders              |                                  | rash, pruritus, urticaria                 | angioedema                           |                                 |
| Reproductive systems and breast disorders           |                                  | abnormal ejaculation                      |                                      | priapism                        |
| General disorders and administration site disorders |                                  | asthenia                                  |                                      |                                 |

As with other alpha-blockers, drowsiness, blurred vision, dry mouth or oedema can occur.

During cataract surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been associated with therapy of tamsulosin during post-marketing surveillance (see also section 4.4).

**4.9 Overdose**

Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed which were treated with fluid replacement and the patient could be discharged the same day. In case of acute hypotension occurring after overdosage cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this does not help then volume expanders, and when necessary, vasopressors could be employed. Renal function should be monitored and general supportive measures applied. Dialysis is unlikely to be of help as tamsulosin is very highly bound to plasma proteins.

Measures, such as emesis, can be taken to impede absorption. When large quantities are involved, gastric lavage can be applied and activated charcoal and an osmotic laxative, such as sodium sulphate, can be administered.

**5 PHARMACOLOGICAL PROPERTIES****5.1 Pharmacodynamic properties**

Alpha<sub>1</sub>-adrenoceptor antagonist.

Preparations for the exclusive treatment of prostatic disease.

**Mechanism of action:**

Tamsulosin binds selectively and competitively to postsynaptic alpha<sub>1</sub>-receptors, in particular to the subtype alpha<sub>1A</sub>, which bring about relaxation of the smooth muscle of the prostate, whereby tension is reduced.

**Pharmacodynamic effects:**

Flomax Relief increases maximum urinary flow rate by reducing smooth muscle tension in prostate and urethra and thereby relieving obstruction.

It also improves the complex of irritative and obstructive symptoms in which bladder instability and tension of the smooth muscles of the lower urinary tract play an important role. Alpha<sub>1</sub>-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with Flomax Relief.

## 5.2 Pharmacokinetic properties

### **Absorption:**

Tamsulosin is absorbed from the intestine and is almost completely bioavailable.

Absorption of tamsulosin is reduced by a recent meal.

Uniformity of absorption can be promoted by the patient always taking Flomax Relief after the same meal each day.

Tamsulosin shows linear kinetics.

After a single dose of Flomax Relief in the fed state, plasma levels of tamsulosin peak at around 6 hours and, in the steady state, which is reached by day 5 of multiple dosing, C<sub>max</sub> in patients is about two thirds higher than that reached after a single dose. Although this was seen in elderly patients, the same finding would also be expected in young ones.

There is a considerable inter-patient variation in plasma levels both after single and multiple dosing.

### **Distribution:**

In man, tamsulosin is about 99% bound to plasma proteins and volume of distribution is small (about 0.2 l/kg).

### **Biotransformation:**

Tamsulosin has a low first pass effect, being metabolised slowly. Most tamsulosin is present in plasma in the form of unchanged drug. It is metabolised in the liver.

In rats, hardly any induction of microsomal liver enzymes was seen to be caused by tamsulosin.

No dose adjustment is warranted in hepatic insufficiency.

None of the metabolites are more active than the original compound.

### **Elimination:**

Tamsulosin and its metabolites are mainly excreted in the urine with about 9% of a dose being present in the form of unchanged drug.

After a single dose of Flomax Relief in the fed state, and in the steady state in patients, elimination half-lives of about 10 and 13 hours respectively have been measured.

The presence of renal impairment does not warrant lowering the dose.

## 5.3 Preclinical safety data

Single and repeat dose toxicity studies were performed in mice, rats and dogs. In addition reproduction toxicity studies were performed in rats, carcinogenicity in mice and rats and in vivo and in vitro genotoxicity were examined. The general toxicity profile as seen with high doses of tamsulosin is consistent with the known pharmacological actions of the alpha-adrenergic blocking agents. At very high dose levels the ECG was altered in dogs. This response is considered to be not clinically relevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings which are probably mediated by hyperprolactinaemia and only occurred at high dose levels are regarded as irrelevant.



**6 PHARMACEUTICAL PARTICULARS****6.1 List of excipients**

Flomax Relief modified release capsules contain the following excipients:

Content of capsule:

microcrystalline cellulose  
methacrylic acid-ethyl acrylate copolymer  
polysorbate 80  
sodium laurilsulfate  
triacetin  
calcium stearate  
talc

Capsule shell:

hard gelatin  
indigotine E132  
titanium dioxide E171  
yellow iron oxide E172  
red iron oxide E172

Printing ink:

shellac  
propylene glycol  
black iron oxide E172

**6.2 Incompatibilities**

None known.

**6.3 Shelf life**

Shelf life as packaged for sale:

Flomax Relief modified release capsules can be used up to four years after manufacture. The expiry date is printed on the package.

**6.4 Special precautions for storage**

None.

**6.5 Nature and contents of container**

Polypropylene-aluminium blister packs containing 7 capsules per strip; cardboard boxes containing 14 and 28 capsules.

**6.6 Special precautions for disposal**

No special instructions.

**7 MARKETING AUTHORISATION HOLDER**

Boehringer Ingelheim Limited  
Consumer Healthcare  
Ellesfield Avenue  
Bracknell  
Berkshire RG12 8YS  
United Kingdom

**8 MARKETING AUTHORISATION NUMBER(S)**

PL 00015/0280

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

03/12/2009

**10 DATE OF REVISION OF THE TEXT**

03/12/2009

Package Leaflet: Information for the User

117023

# FLOMAX<sup>®</sup>

## relief<sup>®</sup> MR


**Boehringer  
Ingelheim**

**Read all of this leaflet carefully because it contains important information for you.** This medicine is available from your pharmacist without prescription. You will need to see your doctor within 6 weeks of starting treatment, in order to confirm that you can take FLOMAX RELIEF long-term from your pharmacist. You need to take FLOMAX RELIEF as instructed in this leaflet to get the best results from it.

- Keep this leaflet. You may need to read it again
- Ask your pharmacist if you need more information or advice, or you do not understand the instructions
- You must contact your pharmacist or doctor if your symptoms worsen or do not improve after 2 weeks of treatment
- If a side effect occurs and gets troublesome, or seems serious, or if you experience any side effect not listed in this leaflet, tell your doctor or pharmacist

### In this leaflet

1. What FLOMAX RELIEF is and what it is used for
2. Before you take FLOMAX RELIEF
3. How to take FLOMAX RELIEF
4. Possible side effects
5. How to store FLOMAX RELIEF
6. Further information

### 1. What FLOMAX RELIEF is and what it is used for

The name of your medicine is FLOMAX RELIEF MR. FLOMAX RELIEF is a modified release capsule which contains a medicine called tamsulosin. This belongs to a group of medicines called 'alpha blockers' (or alpha1A-adrenoceptor antagonists).

FLOMAX RELIEF is used to treat the lower urinary tract symptoms (LUTS) of a common condition called benign prostatic hyperplasia (BPH). This is when the prostate gland gets bigger. The prostate gland is found just below a man's bladder. When your prostate gland gets bigger, it can:

- Make it difficult for you to start urinating (peeing)
- Mean you take longer or have to urinate more often
- Lead to the feeling that you still need to urinate again, even though you have just done so
- Cause you to get up several times in the night to urinate

FLOMAX RELIEF relieves these problems by:

- Relaxing the muscles in the prostate gland
- Relaxing the muscles in the urethra (the tube from the bladder to the outside of the body)

This lets urine pass more freely through the urethra, making it easier to urinate.

### 2. Before you take FLOMAX RELIEF

FLOMAX RELIEF should be used only by men who are 45 to 75 years of age.

#### Do not take these capsules if:

- You are allergic (hypersensitive) to tamsulosin or any of the other ingredients of this medicine (listed in Section 6 below)
- You have problems with your heart, liver, or kidneys
- You faint or get dizzy or weak when you sit or stand up suddenly
- You have had your symptoms for less than three months
- You have pain when you urinate, or your urine was cloudy or bloody, at sometime in the last three months
- You have a fever due to an infection of your kidneys or bladder (urinary tract infection)
- You have leaking of your urine which you are unable to control (incontinence)
- You think you have diabetes and it is not properly controlled
- You have had prostate surgery

- You have recently had blurred or cloudy vision and have not been examined by your doctor or optician
- You are about to undergo cataract eye surgery (see Eye surgery below)

Do not take FLOMAX RELIEF if any of the above apply to you, without first consulting your doctor. If you are not sure, talk to your doctor or pharmacist before taking these capsules.

#### Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines that you can buy without a prescription, including herbal medicines.

In particular tell your doctor or pharmacist if you are taking:

- A type of medicine for lowering your blood pressure called an 'alpha blocker' (or alpha,-adrenoceptor antagonist), such as doxazosin, indoramin, prazosin, terazosin, or verapamil. Any of these medicines cause lowering of blood pressure and added to FLOMAX RELIEF can result in dizziness and weakness.

- Tell your doctor or dentist before any operation or dental procedure as there is a potential that your medicine may interfere with the effects of the anaesthetic.

#### Driving and using machines

If you feel weak or dizzy or have blurred vision while taking this medicine, do not drive or use machines.

#### Eye surgery

- Do not start taking FLOMAX RELIEF now if you are about to have an operation on your eye for cloudiness of the lens (cataract)
- Please tell your eye specialist if you have ever taken tamsulosin. The operation may need to be performed differently
- If you are currently taking FLOMAX RELIEF, ask your doctor if you should stop taking it for a short time

### 3. How to take FLOMAX RELIEF

#### Taking this medicine

- Take one capsule each day
- Take it at the same time each day, after a meal
- Swallow the capsule whole with water
- Do not crush, chew, or open the capsules

Make a note of the date you start taking FLOMAX RELIEF.

#### After 2 weeks

If you are using FLOMAX RELIEF for the first time and you have not got any better after 2 weeks, or if you get worse, you must stop taking this medicine and ask your pharmacist or doctor for further advice.

#### Within 6 weeks

You should see your doctor within 6 weeks of starting treatment to confirm that your symptoms are due to BPH.

#### Every 12 months

You should see your doctor every 12 months to check your prostate. See the doctor sooner if your symptoms change or get worse.

#### If you forget to take this medicine

- Take your capsule later the same day after food
- If you have missed a dose, just take your daily capsule on the next day at the usual time
- Do not take two capsules to make up for a forgotten capsule

**If you take more of this medicine than you should, talk to a doctor or pharmacist straight away.**

#### 4. Possible side effects

Like all medicines, FLOMAX RELIEF can cause side effects, although not everybody gets them.

**Serious side effects are rare or very rare. Stop taking this medicine and see a doctor straight away if you experience any of the following symptoms - you may need medical treatment:**

- Allergic reaction - (affects less than 1 in 1,000 people). The signs may include finding it difficult to breathe, having an itchy rash, having a swollen face, throat, or tongue
- Long-lasting and painful erection (usually not during sexual activity) - affects less than 1 in 10,000 people

The following side effects have also been reported:

**Especially when you sit or stand up**

- Feeling dizzy (common - affects less than 1 in 10 people)
- Feeling weak (uncommon - affects less than 1 in 100 people)

If this happens, sit or lie down straight away until you feel better.

**Uncommon** (affects less than 1 in 100 people)

- Headache
- Fast or uneven heart beat (palpitations)
- Runny or blocked nose
- Little or no semen during ejaculation
- Feeling sick or being sick
- Diarrhoea or constipation
- Itching or lumpy rash (urticaria)

**Rare** (affects less than 1 in 1,000 people)

- Feeling faint

**Very rare** (affects less than 1 in 10,000 people)

- During an operation on the eye for cloudiness of the lens (cataract), the pupil (the black circle in the middle of your eye) may not increase in size as needed. Also, the iris (the coloured part of the eye) may become floppy during surgery.

**Other side effects**

As with other medicines of this type, the following side effects may occur:

- Drowsiness
- Blurred vision
- Dry mouth
- Swollen hands or feet

If a side effect occurs and gets troublesome or seems serious, or if you experience any side effect not listed in this leaflet, tell your doctor or pharmacist.

You can also report any side effect you get to the Medicines and Healthcare products Regulatory Agency (MHRA), through the Yellow Card Scheme; you can make a report by filling in a Yellow Card (available from pharmacies), by phoning freephone 0800 100 3352, or on the web at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)

Alternatively, you can also report any side effect you get to the marketing authorisation holder Boehringer Ingelheim Limited, Consumer Safety, Ellesfield Avenue, Bracknell, Berkshire, RG12 8YS, UK, or by phoning free-of-charge on 0800 328 1627.

#### 5. How to store FLOMAX RELIEF

- Keep out of the reach and sight of children
- Do not use the capsules after the expiry date which is stated on the base of the pack
- Do not store above 30°C

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.

#### 6. Further information

**What FLOMAX RELIEF contains**

- The active substance is tamsulosin hydrochloride. Each capsule contains 0.4 mg
- The other ingredients are microcrystalline cellulose, methacrylic acid-ethyl acrylate copolymer, polysorbate, sodium laurilsulfate, triacetin, calcium stearate, and talc. These all help to make the granules which are in the capsule
- The capsule shell contains gelatin, and is coloured with indigotin (E132), titanium dioxide (E171), and yellow and red iron oxide (E172); printing ink is shellac, propylene glycol, and black iron oxide (E172)

**What FLOMAX RELIEF looks like and contents of the pack**

FLOMAX RELIEF capsules have an orange body and an olive-green cap. The capsules come in packs of 14 and 28 capsules, suitable for 14 and 28 days treatment, respectively.

The marketing authorisation for

FLOMAX RELIEF is held by:  
Boehringer Ingelheim Limited,  
Consumer Healthcare,  
Ellesfield Avenue,  
Bracknell,  
Berkshire,  
RG12 8YS,  
UK.

The capsules are manufactured by:

Astellas Pharma Europe B.V.,  
Elisabethhof 19, 2353 EW Leiderdorp,  
The Netherlands, at their site at  
Hogemaat 2, 7942 JG Meppel, The Netherlands.

This leaflet was last revised in **September 2009**.

**Assessing your symptoms**

Your urinary symptoms can be assessed using a questionnaire which you will be asked to complete when you first purchase FLOMAX RELIEF.

**To learn more about BPH** visit

[www.1in4men.com](http://www.1in4men.com) and call the helpline  
free-of-charge on 0800 731 9070

**To request this leaflet free-of-charge** in formats such as audio, Braille or large print, please call the Royal National Institute of the Blind (RNIB) freephone on 0800 198 5000. When prompted, please provide the following information:

Product code number 00015/0280

and be ready to confirm the name of this medicine (FLOMAX RELIEF).

© Boehringer Ingelheim Limited 2009

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Under licence from Astellas Pharma Europe Ltd.

### Registration Card

**Name:** \_\_\_\_\_

is taking Flomax Relief (tamsulosin hydrochloride 0.4 mg)

**Date treatment started:** \_\_\_\_\_


**Other medicines being taken:** \_\_\_\_\_

\_\_\_\_\_

**Any known allergies:** \_\_\_\_\_

\_\_\_\_\_

Please keep this card and show it to your pharmacist when you next buy Flomax Relief.



## Join the Flomax Relief Support Programme for *free access* to:


• lifestyle tools • educational updates • symptoms checks

Join today at: [www.1in4men.com](http://www.1in4men.com) or freephone 0800 731 9070

## Men's Health Booklet

Please refer to the Patient Information Leaflet contained inside the Flomax Relief pack

Date of revision 10.2009

126735 

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### LUTS tips

#### Your top 5 lower urinary tract symptoms (LUTS) tips:

1. Drink plenty of water to prevent dehydration.
2. Try to minimise your alcohol and caffeine intake.
3. Limit drinking too much an hour or two before bed or a long journey.
4. Keep track of your symptoms and talk to your pharmacist if you have any questions.
5. Have a regular (at least once a year) men's health check with your doctor.

#### For more useful information, try these links:

- NHS Direct – [www.nhsdirect.nhs.uk](http://www.nhsdirect.nhs.uk). NHS-provided online information.
- 1in4 men – [www.1in4men.com](http://www.1in4men.com). Website designed specifically for men with LUTS due to BPH.

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## Welcome

Taking a positive step forward to managing your lower urinary tract symptoms (LUTS) can help you enjoy life with greater confidence and more freedom. You are not alone, approximately one in four men over the age of 40 suffer from LUTS due to a common condition known as Benign Prostatic Hyperplasia (BPH).

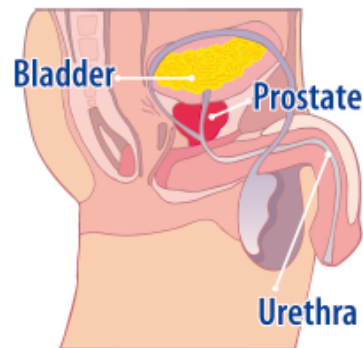
Along with the information contained in this booklet, please read the Patient Information Leaflet. By registering your details and joining the Flomax Relief Support Programme you'll be provided with further information, guidance and support to help you stay on track.

Please register at [www.1in4men.com](http://www.1in4men.com)

3

## Your prostate

The prostate gland is slightly larger in size than a walnut. It is found just underneath your bladder and produces a milky fluid which, together with sperm, makes up semen. The urethra is the tube that carries urine from the bladder out through the penis and runs through the middle of your prostate gland.



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## Joining the Flomax Relief Support Programme

Please go to [www.1in4men.com](http://www.1in4men.com) or call freephone 0800 731 9070 and register to sign up for our support programme.

Following registration you will receive regular educational updates and handy tips to help you stay on track with your treatment. Your Registration Card can be found on the back cover.

You will need to see your doctor within 6 weeks of starting treatment, in order to confirm that you can take Flomax Relief long-term from your pharmacist.

It is important that you monitor your symptoms, keep your pharmacist updated and have an annual consultation with your doctor.

4

## Do I have BPH?

You may have BPH if you experience LUTS such as:

- The need to pee often ('frequency')
- The need to pee urgently ('urgency')
- The need to pee at night, sometimes many times ('nocturia')
- Not being able to hold on when you need a pee ('urge incontinence')
- Finding it difficult to start peeing ('hesitancy')
- Stopping and starting during a pee ('intermittent stream')
- Having to push to get the pee out ('straining')
- Having a weak, dribbly flow of pee ('weak stream')
- Dribbling once you've finished a pee ('terminal dribbling')
- Never feeling that you've completely emptied your bladder ('incomplete voiding')

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### What is BPH?

LUTS are often caused by the prostate enlarging and obstructing the urethral tube, impeding the flow of urine. The bladder wall muscle may also start to thicken, causing it to become less stretchy, so the bladder can't hold as much pee.

BPH (benign prostatic hyperplasia) describes an enlarged prostate. Benign means that it's not malignant, in other words it's not cancer. BPH commonly occurs in men as they get older and one in four men (25%) over the age of 40 can expect to suffer from LUTS caused by BPH.

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### Flomax Relief: *the role of your pharmacist*

In addition to supplying you with Flomax Relief, your pharmacist has an important role in advising you over time on your symptoms, checking that your treatment is working and helping to answer any questions you may have. When you return to your pharmacy for your next supply, the pharmacist will ask you about your symptoms to see if you've had any change since your last visit, so it is important to keep a record. See pages 16–18 for useful tools.

It is best for you to return to the same pharmacy, but should you visit a different one, you will be asked for your Registration Card or to complete the symptom-check questionnaire again, just to confirm the treatment is still right for you. It is important to tell the pharmacist when you first started taking Flomax Relief.

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### Your treatment

Flomax Relief contains tamsulosin, a medicine used to relieve the urinary symptoms caused from an enlarged prostate. It works by relaxing the muscles in your bladder and around the prostate, allowing pee to flow out more freely. Few men get side-effects and they are generally mild. For more information on side-effects please refer to the Patient Information Leaflet contained inside the Flomax Relief pack or speak to your pharmacist.

It is important that you make a note of the date that you first start taking Flomax Relief (see page 18 for your Treatment Calendar) so you can check that your symptoms are improving. Keeping a record of the date will help you at your next pharmacy visit.

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### Flomax Relief: *the role of your pharmacist (cont)*

**Your pharmacist will advise you to visit your doctor within 6 weeks of starting treatment with Flomax Relief.**

A referral letter has been provided in this booklet (see page 19) to show your doctor. It may also help if you take your Treatment Calendar – showing your treatment start date and your symptom-check questionnaire scores.

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### Flomax Relief: *the role of your doctor*

You will need to see your doctor within 6 weeks of starting treatment with Flomax Relief in order to confirm that you can take Flomax Relief long term from your pharmacist. Your doctor will want to speak to you about your symptoms and how you are finding your treatment so far. There is no single test to confirm a diagnosis of BPH; your doctor will want to rule out other conditions by asking you questions about your symptoms and may do a physical examination.

You should see your doctor for an annual check up to check your prostate and your general health.

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### What else to expect at your doctor's appointment

Like many men, you may not visit your doctor regularly. If this sounds like you, it is possible that your doctor may want to take this opportunity to review your general health too. This shouldn't take long and may help to catch any other health problems early.

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### Are LUTS affecting your daily life?

Your lower urinary tract symptoms (LUTS) may be affecting your quality of life. For example, you may feel tired because of the need to keep getting up at night to pee or you may feel embarrassed at social gatherings when you have to keep disappearing to the loo.

Many men like you may not realise how much they modify their lives around their urinary symptoms. Taking positive steps to overcome your urinary symptoms could help you to live life with more confidence and freedom.

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### Monitoring your symptoms

Regularly tracking your urinary symptoms, using a symptom-check questionnaire, can help to evaluate how Flomax Relief is working for you, and give you a useful tool that will help you to describe your urinary symptoms to your pharmacist or doctor.

To help with this there is a symptom-check questionnaire on page 16 which you should fill out before you start treatment, and also at regular intervals during treatment. You can record all your scores on the Treatment Calendar on page 18.

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### Monitoring your symptoms

After the first 2 weeks of taking Flomax Relief you may notice an improvement in your urinary symptoms, and over a period of time you may continue to experience improvements. If your symptoms have not improved or if they are getting worse, you should stop taking Flomax Relief and make an appointment to see your doctor.

To help the pharmacist advise on your progress it may be helpful to complete a new symptom-check questionnaire every time you visit your pharmacist - so it's a good idea to record your score each month.

More copies of the symptom-check questionnaire can be downloaded from the website [www.1in4men.com](http://www.1in4men.com), or by contacting us on freephone 0800 731 9070.

Please see overleaf for your symptom-check questionnaire.

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### Symptom-check questionnaire

Urinary Symptoms (score each from 0-5)

Your Score

Over the past month, how often have you typically...

**Incomplete emptying:** had a sensation of not emptying your bladder completely after you finish urinating (peeing)?

**Frequency:** had to urinate again less than 2 hours after you have last urinated?

**Intermittency:** found you stopped and started again several times when you urinated?

**Urgency:** found it difficult to postpone urination?

**Weak stream:** had a weak urinary stream?

**Straining:** had to push or strain to begin urination?

**Nocturia:** had to get up to urinate from the time you went to bed until the time you got up in the morning?

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Score your response to each of the following questions using the keys below. Then total your Urinary Symptoms and Quality of Life scores.

Symptom-check questionnaire key:

Key for Urinary Symptoms questions on page 17:

Never (Score 0)  
Less than 1 in 5 times (Score 1)  
Less than half the time (Score 2)  
About half the time (Score 3)  
More than half the time (Score 4)  
Almost always (Score 5)

Key for Quality of Life question below:

Delighted (Score 0)  
Pleased (Score 1)  
Mostly satisfied (Score 2)  
Half satisfied & half dissatisfied (Score 3)  
Mostly dissatisfied (Score 4)  
Unhappy (Score 5)  
Terrible (Score 6)

**Total Symptom-Check Score (Urinary Symptoms + Quality of Life)**

Quality of Life (score 0 to 6)

QOL Score

If you were to spend the rest of your life with your urinary (peeing) condition the way it is now, how would you feel about that?

16

### Your Treatment Calendar

The table below shows what to do and when. At each of the weeks you should use the symptom-check questionnaire to check your progress and complete the relevant action alongside. **Date treatment first started:**

| Week  | Your Score | Action Checklist  | Tick when complete       |
|---|------------|---|--------------------------|
| Week 0  |            | Register for the Flomax Relief Support Programme.                                       | <input type="checkbox"/> |
| Week 2  |            | After you have started taking Flomax Relief discuss your progress with your pharmacist. | <input type="checkbox"/> |
| Week 4-5                                      |            | Book an appointment to see your doctor.   | <input type="checkbox"/> |
| Week 6  |            | See your doctor to discuss taking Flomax Relief longer term.                            | <input type="checkbox"/> |
| After 6 weeks<br>(enter results from page 16) |            | Visit your pharmacist to discuss the outcome of your doctor's appointment.              | <input type="checkbox"/> |

18 Don't forget to keep track of your symptoms over time on the [www.1in4men.co.uk](http://www.1in4men.co.uk) site.



### A letter for you to take to your doctor

Doctor's name:

My Flomax Relief treatment start date:

My pharmacist's name:

My pharmacy's name and address:

I have started taking Flomax Relief (tamsulosin 0.4mg) for Lower Urinary Tract Symptoms. My pharmacist has asked me to visit you to confirm that I am suffering from BPH and suitable to continue purchasing Flomax Relief from my pharmacy.

Thank you.

My name:

My date of birth:

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### Frequently asked questions

#### Will BPH affect my sex drive?

BPH does not directly affect your sex drive, but bothersome urinary symptoms can often put men off from having sex.

#### Should I drink less fluid?

You should in fact drink more to keep urine flowing through the bladder and help prevent infection. However, restricting fluid intake at specific times of the day can help, like just before going to bed.

#### Can urinary symptoms be caused by anything else?

A number of conditions can cause similar symptoms, including urinary tract infections, inflammation of the prostate, and prostate cancer. Men suffering from BPH are no more likely than men without BPH to develop prostate cancer.

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### Lifestyle advice

There are a number of lifestyle measures you can adopt to help minimise your symptoms, including:

- Minimise alcohol consumption. Alcohol can irritate the bladder resulting in an urge to pee.
- Steer clear of coffee, tea and other caffeinated drinks. These act as diuretics, making your body produce more urine.
- Try what doctors call 'double voiding': when you think you're finished, try going again. This helps to make sure your bladder is empty.
- Try to relax when you pee, this will help it to flow better.
- Try to hold on a bit longer each time you need to go. This way your bladder gets used to holding more urine (this is called bladder retraining).

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### Men's health conditions

Other men's health conditions to be aware of include:

**Epididymitis** – an inflammation of the tube that transports sperm to the penis causing pain and swelling in the testicles.

**Testicular cancer** – generally quite rare, with about 1 in 400 men affected, but the most common type of cancer in men aged 20-34.

**Balanitis** – an inflammation of the head of the penis (the glans) and the foreskin, often caused by a bacterial or fungal infection.

**Erectile dysfunction (ED)** – a very common condition that means you can't get a full erection, or you can't keep an erection for long enough to ejaculate.

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**Prostate cancer** – early stages generally have no symptoms but, as it develops you can have difficulty and pain urinating or blood in the urine.

**Prostatitis** – an inflammation or infection of the prostate causing pain when passing urine, needing to go often, blood in the urine or a fever.

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**High blood pressure** - as the blood flows it pushes on the artery walls exerting pressure (blood pressure). The higher your blood pressure, the more damage to your veins and greater your risk of getting heart disease or a stroke. High blood pressure doesn't usually have any symptoms so you probably won't know if you have it without getting checked.

**Diabetes** - a condition where the body can't regulate the amount of sugar in the blood effectively. This can make you urinate often, make you feel tired and very thirsty. In the long term, poorly controlled blood sugar can damage small blood vessels leading to problems with your eyes, kidneys and/or nerves.

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### General health conditions

**Heart disease** - is the most common cause of death in the UK and occurs when the arteries supplying blood to the heart become narrowed. You may have no symptoms at first, but as it progresses you'll begin to feel chest pain. When a coronary artery becomes completely blocked it causes a heart attack and will need to be treated in hospital. The pain can be severe and ongoing, and you may also feel sick, breathless and sweaty.

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### Healthy living tips

**Healthy eating** - try to eat at least five servings of fruit and vegetables every day and choose wholegrains and low fat proteins. High-sugar and high-fat foods like cakes, crisps and chocolate are only OK as an occasional treat.

**Exercise** - try to do at least half an hour of exercise, five days a week. Being physically active is linked with many health benefits, including reducing the risk of heart disease.

**Smoking** - we all know that smoking kills, it's linked to almost every life-threatening condition going, from cancer to heart disease.

**Alcohol** - too much alcohol is linked with cancer of the mouth, throat and liver, and it can also contribute to high blood pressure, depression, and liver disease.

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|  |   |
|--|---|
| Lot:   |   |
| MON  | TUE   |
| WED  | <b>FLOMAX</b><br>relief <sup>®</sup> MR<br>tamsulosin           |
| Boehringer<br>Ingelheim<br>under licence from<br>Astellas Pharma Europe Ltd. |   |
| FRI  | <b>FLOMAX</b><br>relief <sup>®</sup> MR<br>tamsulosin<br>116896 |
| SAT  | SUN   |
| Exp:   |   |

## **Appendix 1: Final assessment of the reclassification from POM to P and CHM advice (2009)**

**Product:** Flomax Relief  
**Product No:** PL 00015/0280  
**Company:** Boehringer Ingelheim  
**Active Ingredient:** Tamsulosin 400mcg  
**Legal Status:** POM to P

### **1. INTRODUCTION**

CHM advice is sought following consultation on a proposal for pharmacy availability of Flomax Relief tablets containing tamsulosin for the treatment of the functional symptoms of Benign Prostatic Hyperplasia (BPH). The proposed lower age limit for pharmacy supply is 45 years. There is no such restriction on the current POM licence.

### **2. BACKGROUND**

Tamsulosin is an alpha blocker which binds selectively and competitively to postsynaptic alpha1-receptors in particular to the subtype alpha 1A, which brings about relaxation of the smooth muscle in the prostate, and the urethra, thereby relieving obstruction and improving the urinary flow rate. This effect has been shown after the first dose, and symptomatic relief is usually obtained within 7-14 days of starting treatment. It also improves the complex of irritative and obstructive symptoms in which bladder instability and tension of the smooth muscles of the lower urinary tract play an important role.

This is the first reclassification request for an alpha blocker. The applicant proposes that urinary symptoms be assessed and treated in the pharmacy, while the diagnosis of BPH is confirmed at subsequent GP review.

The applicant has developed a pharmacy questionnaire, which will be used to screen for lower urinary tract symptoms (LUTS) in symptomatic men. Flomax will be supplied to eligible patients, who will then be reviewed by the pharmacist following a 2-week therapeutic trial. In the event of an improvement in urinary symptoms, a further supply of 4 weeks will take place, which will be followed by an additional 4-week supply if the symptomatic

improvement is maintained. At each pharmacy visit patients will be referred to their general practitioners if symptoms are not relieved or if exclusion criteria are found. After 10 weeks Flomax will only be supplied if the doctor has confirmed the diagnosis of BPH. The applicant also proposes a clinical review by the General Practitioner (GP) at 12-monthly intervals.

### 3. CHM ADVICE

CHM gave preliminary consideration to the proposal at its meeting in July 2007 and advised that a group of experts should be consulted on the proposal with particular regard to the issue of any delay in establishing the medical diagnosis of BPH in patients with LUTS treated with tamsulosin in the pharmacy setting. The Commission was concerned that in the proposed pharmacy protocol, clinical investigation would not be carried out at the same time when treatment commenced and expressed concerns that the proposed questionnaire did not adequately address a differential diagnosis of other possible causes of LUTS. The Commission noted that there had not been evidence provided to show that the proposal would have drawn more patients with LUTS into healthcare. Therefore, the CHM was not reassured about the positive risk/benefit balance of the proposal.

The applicant provided further data to address the above concerns and the application was reconsidered by CHM in June 2008 following advice from a specially constituted EAG.

CHM advised that consultation could take place under the following circumstances:

- Treatment of functional symptoms of benign prostatic hyperplasia (BPH) in men over the age of 45 years.
- Strength and pharmaceutical form: 0.4mg tablets
- Pack size: max. 28 tablets.

The Commission also reviewed the proposed pharmacy model and made the following recommendations:

- Assessment of IPSS (International Prostate Symptom Score) is suggested at each pharmacy visit to help pharmacist to decide if patient's symptoms have improved and tamsulosin supply can be continued
- Patients should be encouraged to sign up with one pharmacy with the aim of continuity of care. To allow suitable follow up of supply patients should also be prepared to share the record with their GP and feedback to the pharmacist on the results of any tests conducted.

#### **4. CONSULTATION**

ARM 56 proposing pharmacy availability of tamsulosin 400mcg tablets was issued on 27 November 2008, with a deadline for comments of 15 January 2009.

No new issues were raised during public consultation. A total of 31 responses were received, of which 7 organisations were in favour (total 8 favourable responses) whilst 7 organisations were not (total 18 non-favourable responses), 2 raised issues but expressed no definitive views, whilst 3 had no comment.

##### **4.1 Responses in favour**

Those in favour included 'The Royal College of Physicians of Edinburgh', 'The Royal Pharmaceutical Society of Great Britain' (RPSGB), 'The National Pharmacy Association' (NPA), 'The Nursing and Midwifery Council' (NMC) and 'The Company Chemists Association', the 'Association of Independent Multiple Pharmacies' (CCA and AIMp) and the British Association of Urology Nurses (BAUN).

Those in favour considered wider availability of tamsulosin represents a considerable public benefit for the vast majority of the men who suffer from BPH but do not currently receive any positive treatment. Availability of Flomax Relief will enable more men to benefit from treatment and access from a pharmacist is generally considered to be less threatening than a visit to a GP. A limitation to 10 weeks treatment will ensure that men will be referred to their doctor for the appropriate diagnosis and will encourage men to take greater involvement in their own health care.

In relation to patient safety, the pharmacy protocol will help avoid inappropriate sale to any one who does not meet the treatment criteria and those with red flag symptoms will be referred to their GP for earlier investigation. Limiting the length of treatment to 10 weeks will ensure that patients receive the benefit of GP scrutiny within a short period of starting treatment. Any concerns about missed or delayed diagnosis of prostate cancers are addressed by the likelihood that the sufferer may visit a pharmacy and be screened by a pharmacist long before they would have otherwise visited their GP.

##### **4.2 Responses not in favour**

Organisations not in favour included 'The Royal College of General Practitioners' (RCGP), 'The British Medical Association' (BMA), 'The British Association of Urological Surgeons' (BAUS), 'The British Pharmacological Society' and various individual Medical practitioners.



#### 4.3 Issues raised

A number of responders raised concern in relation to the following:

- The need for a diagnosis of BPH before commencing treatment with tamsulosin
- Mis-diagnosis and delay for cancer of the prostate
- A missed opportunity for 'watchful waiting' and the risks of unnecessary medication
- The risks for those having cataract surgery
- Concern about the safety of tamsulosin especially if it is taken with anti-hypertensive drugs
- Concern that men will visit numerous pharmacies in order to extend the 10 week period between first receiving treatment and eventually visiting their GP for a diagnosis.

Many responders commented on the diagnosis of BPH pointing out that, even with the use of a protocol and questionnaire, an accurate diagnosis was difficult. Treatment prior to doctor diagnosis would also rule out the option of 'watchful waiting' for those with mild symptoms which could resolve without the need for drug intervention. Other concerns were raised about the delay in examination and assessment of those who may have prostate cancer.

The question of intraoperative floppy iris syndrome (IFIS) was also raised with a claim that this condition occurs in the majority of patients receiving tamsulosin. Clinical experience of ophthalmologists suggests that the effect of tamsulosin on the iris is long-lasting or possibly permanent and the advice that stopping tamsulosin for a short time prior to surgery can reverse the effect on the iris is questioned. There is concern that a pharmacy medicine may not appear on GP records of prescribed medicines and this will not be declared by the patient at the pre-operative assessment for cataract surgery.

Issues have been raised in relation to the safety measures for supply of the medicine, specifically in relation to the steps to be put in place to ensure that the patient does not attend many different pharmacies to obtain the drug numerous times, thus not seeing a doctor by the 10 week cut off.

#### 5. PHARMACY MODEL

The applicant has developed a range of materials to support the correct delivery of tamsulosin by pharmacists and use by patients, including a draft Pharmacy Training Guide with an appendix on how to interpret the Symptoms Check Questionnaire and a Men's Health Booklet for inclusion in the product packaging.

### 5.1 Pharmacy Training Guide

The aim of the guide is to enable the pharmacist to appropriately manage the supply of Flomax Relief. It includes:

- A discussion on the value of treating BPH in the pharmacy with Flomax.
- Background on BPH, the symptoms and its impact on quality of life.
- Details of the pharmacy model for Flomax Relief and advice on how to operate the scheme.
- Information on how to use the validated Questionnaire to assess customer symptoms of BPH.
- Advice on when to refer individuals to the GP straight away.
- Support tools for the pharmacy consultation - symptom questionnaire, men's health booklet and medication card.
- Information on Flomax Relief
- A section on Pharmacy's role in improving men's health
- Case studies and points to consider for additional advice.

### 5.2 Symptoms-check (Pharmacy) Questionnaire and Guide

The questionnaire includes important questions to help identify individuals who are suitable for supply of Flomax Relief and those who should be referred to their GP directly. The Guide for pharmacists assists them in assessing the suitability (or otherwise) of a particular man for treatment with tamsulosin.

### 5.3 Men's Health Booklet

The applicant is proposing to include this in the product packaging, in addition to the Patient Information Leaflet. It gives information about how the pharmacy supply scheme works; it includes a copy of the IPSS to allow for self assessment of urinary symptoms, together with advice on managing BPH such as lifestyle measures and other men's health educational information. It also includes tear off sections, one as a letter to send to the GP, the other to record purchases of Flomax Relief.

#### Assessor's comments

*The draft guide and other materials are generally well designed and include the necessary information to help ensure safe supply of tamsulosin. The materials are under consideration with relevant professional pharmacy organisations and have been well received; presentational and other improvements are planned before they are finalised,*

*Based on the symptoms reported in the questionnaire, the pharmacist will assess a patient's suitability for tamsulosin. Lifestyle measures are recognised as a possible first step in the treatment of LUTS. Where the score on the Symptoms questionnaire reflects mild symptoms, the pharmacist will not supply tamsulosin and the patient will be advised to see their GP for a health check. The questionnaire also highlights "red flag" symptoms for immediate referral and other circumstances where the product should not be supplied, e.g. acute conditions such as urinary tract infection. The guide for pharmacists to assess the questionnaire responses is helpful and the training material provides more detailed information on supply of tamsulosin and the circumstances where it is not suitable.*

*The method of supply of tamsulosin encourages men to return to the same pharmacy, for example by counselling and to avoid the need to complete the questionnaire again. Also the Men's Health booklet advises men to be consistent and a registration card is provided as a link to the pharmacy.*

*The pharmacy training includes suitable information on the maximum 10 week period of supply of tamsulosin before GP diagnosis is necessary. Provision is also included for yearly check-up thereafter. This is mirrored in the Men's health booklet.*

*Although the pharmacy training material is generally acceptable the following elements should be discussed in more detail to enable pharmacists to provide suitable advice to patients:*

- *The option of watchful waiting for men with mild symptoms should be emphasised*
- *The section about differential diagnosis should be expanded to include suitable detailed information on other conditions such as prostate cancer, urinary tract infection, chronic urinary retention and diabetes*
- *The discussion on the safety of tamsulosin should include information on hypotension and intraoperative floppy iris syndrome*

## **6. DISCUSSION**

### **6.1 Diagnosis of BPH, mis-diagnosis or delaying the diagnosis of prostate cancer**

The CCA, the NPA, the RPSGB and BAUN - who are in favour of the reclassification - provided comments on the above issues.

Comments were also received from BAUS, the BMA, the RCGP, NHS Central Lancashire Medicines Management Committee, Great Western Hospital Foundation Trust, individuals (including pharmacists, GPs and a consultant urological surgeon) and a group of independent prescribers, who expressed concerns over the above issues and are against the proposal.

The NPA commented that the pharmacy availability of tamsulosin for LUTS due to BPH not only will improve the quality of life of men seeking treatment, but also will enable them to seek advice for other conditions. *"Pharmacists when screening for BPH, may well identify other conditions for which referral to the GP is necessary, which would have otherwise gone untreated."* The NPA considers that *"men will receive a higher standard of care by speaking to the pharmacist about their LUTS rather than either ignoring them or buying herbal products ... without advice from a healthcare professional."*

The NPA considered that encouraging men to visit a community pharmacy for advice on BPH will be, for many, the first step to accessing the healthcare they need for other conditions which they may have. The Heart of Birmingham PCT 'Improving Male Life Expectancy' scheme offered cardiovascular risk assessments through community pharmacy particularly. 57% of those who

accessed the service were men, demonstrating that men will visit pharmacies for services which they haven't accessed from their GP, providing they know the service exists. However, the NHS Central Lancashire Medicines Management Committee and an individual pharmacist considered that men who are unwilling to discuss their symptoms and seek treatment from a GP would be equally unlikely to do so from a community pharmacy.

The NPA acknowledged that there may be concerns around missed or delayed diagnosis of prostate cancers. However, it considered that in reality diagnosis might be made earlier as the sufferer may be screened by the pharmacist long before they would have otherwise visited their GP. Men with red flag symptoms will be referred to their GP and all sufferers will see a GP within ten weeks if they wish to continue purchasing Flomax Relief from a pharmacy. The NPA recognises that Digital Rectal Examination (DRE) will only take place when the sufferer visits their GP, however as early prostate cancer rarely presents with LUTS, and DRE is only one of a number of tests which would be carried out to confirm a diagnosis of cancer of the prostate.

The CCA provided similar comments and added that pharmacy availability would increase men's contact with healthcare professionals, which will allow other healthcare messages to be conveyed.

The BAUN commented that the gold standard for a man presenting with bothersome urinary symptoms is to be seen by his GP, Urologist or Specialist Assessment Clinic where a full assessment including physical examination can be undertaken. However, BAUN accepts that some men may decide to seek treatment from a pharmacy where they would receive a full assessment of urinary symptoms by a trained pharmacist. After this assessment, if appropriate they would be given a trial of Flomax. It is important that men with contraindications and symptoms needing medical assessment are excluded. It is imperative that patients are warned of the risk of prostate cancer.

The RPSGB expressed some concerns over the issue of missing or delaying the diagnosis of other serious conditions and commented that some patients may not seek a diagnosis by a doctor after 2 weeks if symptoms do not improve or get worse and continue taking tamsulosin for 10 weeks. The RPSGB also commented that the NHS Clinical Knowledge Summaries advises patient referral in case of microscopic haematuria. The RPSGB seeks clarification how microscopic haematuria will be flagged up by the pharmacist.

BAUS commented that there are many conditions that mimic bladder outflow obstruction and alpha blockers should only be prescribed after a full history and physical examination. This exam must include palpation of the abdomen to exclude chronic retention of urine and possible associated renal failure, examination of the genitalia to exclude phimosis - a possible cause of such symptoms on older men - and a rectal examination, with a flow rate test. In order to exclude potential patients with cancer who often present with LUTS only, it is important to carry out dipstick testing of urine and rectal examination. BAUS recommends that this drug should not be supplied by pharmacists, until NICE issues its guidance on male Lower Urinary Tract

Symptoms and associated medications, which is currently in preparation. The BMA and the RCGP expressed similar views.

The BMA commented that a full clinical assessment by a GP of a patient displaying symptoms of BPH would normally include a digital rectal examination, establishment of the patient's estimated glomerular filtration rate, and a test for prostate specific antigens, which would establish potential differential diagnoses.

The RCGP commented that the area of screening for prostate cancer was unclear, and the Department of Health did not advocate Prostate Specific Antigen (PSA) screening. The RCGP considers that the proposed reclassification would inevitably lead to an increase in the amount of PSA testing requested by worried patients, but whether this is desirable needed to be properly considered.

BAUS also commented that as alpha blockers do not treat BPH and are essentially designed to improve quality of life by improving symptoms, it is essential that the underlying diagnosis of bladder outflow obstruction is established before other conditions are disguised by the symptomatic improvement. BAUS considers that the proposed 10 weeks to establish the diagnosis of BPH by a GP is too long.

A consultant urological surgeon commented that black men have a threefold risk of developing prostate cancer and PSA should be offered them at the first presentation.

The RPSGB seeks clarification on whether there will be an upper age limit for pharmacy supply.

*Assessor's comments:*

*The issue of delaying or missing the diagnosis of serious underlying conditions (including prostate cancer) has been previously considered by CHM. The Commission noted that the NHS Clinical Knowledge Summaries and BAUS guideline recommend undertaking DRE to exclude prostate carcinoma, but a recent article in the BMJ ((BMJ 336:146-149) states that although measurement of PSA and DRE are widely used to try to detect cancer, these approaches are not routinely indicated.*

*The NHS Clinical Knowledge Summaries states that there are no diagnostic tests that can be routinely carried out in primary care. Urinalysis is recommended to check for blood, leucocytes, nitrite, and glucose. Urine culture is recommended to exclude UTI. Serum creatinine is optional, but recommended in men with chronic retention to exclude renal impairment. Routine measurement of PSA, urine flow, and other specialist investigations are not recommended. In the proposed model patients with symptoms suggestive to infection and prostate cancer will either be excluded from pharmacy supply or since their symptoms will not fully respond to treatment, they will be referred to the doctor following a 2-week therapeutic trial period.*

The 'red flag' symptoms included in the pharmacy questionnaire are pain on urination, fever, haematuria and cloudy urine experienced in the past 3 months. A question if the man has been diagnosed with diabetes is also included.

The applicant argues that patients with LUTS are no more likely to have prostate cancer than patients without LUTS. In the proposed model, the pharmacist would be screening patients based on symptoms and referring them to the GP as and when appropriate. Pharmacy availability of tamsulosin will bring more men into healthcare. The 10-week timeframe for medical review is not a delay in most instances, because these men would probably not otherwise seek medical advice on their condition. Additionally, the 10-week period should be seen as a guide: men will be referred to their GP much earlier by the pharmacist if their symptoms are not improving or if any 'red flag' symptoms develop. The drug will not normally be supplied after 10 weeks unless an earlier diagnosis has been made by the GP.

The CHM acknowledged that currently men with BPH do not necessarily visit their GP and the proposed clinical review at 12 monthly intervals is a welcome improvement in their management. It was considered that a delay in the diagnosis of prostate cancer of 10 weeks did not present a significant danger as it was accepted that prostate cancer is a slowly progressing disease and patients with LUTS are no more likely to have prostate cancer than patients without LUTS. However, to ensure that men do not take tamsulosin longer than 10 weeks without their GP establishing the diagnosis of BPH, CHM advised that men should be followed up and receive treatment from the same pharmacist (see also section 5.5 of this report).

In its response to the public consultation BAUS referred to a NICE guideline under preparation on male LUTS. The expected consultation period for this new guideline is between August and October 2009 and the expected date of issue is April 2010.

Some of the responders commented on the issue of measuring PSA to exclude prostate cancer. The DOH has developed a Prostate Cancer Risk Management Programme, which aims to help the primary care team to give clear and balanced information to men who ask about testing for prostate cancer. The information booklet provided for GPs states that "prostate cancer is largely a disease of older men and is rare below the age of 50. The median age of both diagnosis and mortality is 75 years. Over 90% of prostate cancer deaths occur in the 65 and over age group. By the age of 80 about 60-70% of men will have some cancer cells in their prostate. However only around 1 in 30 of these men will die of their prostate cancer." The strongest risk factor is age, but ethnicity can play a role with African American men having an incidence of prostate cancer twice as high than white men.

In relation to differential diagnosis the booklet states: "Lower urinary tract symptoms (LUTS) are common in older men. However, early prostate cancer usually will not produce symptoms and LUTS are usually the result of BPH. 70-80% of prostate tumours originate in the peripheral zone of the gland

*distant from the urethra. As a consequence, by the time prostate cancer itself causes LUTS it will usually have reached an advanced and incurable stage. Due to the high incidence of BPH and prostate cancer in the older age group, some men will have a benign pathology and a co-existing early prostate cancer. When a man seeks advice about LUTS this can set in train investigations which diagnose what is a coincidental prostate cancer."*

*As the proposal aims to draw more men into healthcare it is possible that a man with LUTS due to BPH who receives tamsulosin treatment from the pharmacy and following 10-week treatment presents at his GP for a prostate check, his coincidental prostate cancer is diagnosed at a curable stage. On the other hand if a man presents at the pharmacy with LUTS due to advanced prostate cancer he will be referred to the GP either immediately due to 'red flag' symptoms or following a 2-week unsuccessful trial supply with tamsulosin.*

*In the responses it was highlighted that African American men have a higher risk of prostate cancer. The pharmacy model aims to supply the product in response to symptoms; risk factors for prostate cancer, such as ethnicity, would be addressed within the GP consultation*

*BAUS highlighted chronic urinary retention as one of the possible differential diagnoses. Chronic urinary retention can present with enuresis due to outflow. Any form of incontinence should alert a healthcare professional to chronic urinary retention with outflow. The CHM may consider that the pharmacy questionnaire should include a question about incontinence in order to refer these patients to the GP.*

*The RPSGB raised the issue whether an upper age limit should be considered for pharmacy supply. The BAUS guideline states that the prevalence of LUTS in Europe is more than 40% in men 60 years old. BPH is common in older men, being found in 80% of men over 80 years of age. As age is also a risk factor for prostate cancer with 75 years being the median age of diagnosis and mortality, the CHM may consider that an upper age limit of 75 years would provide an additional safeguard in the pharmacy setting.*

*CHM may consider that the product information should be updated to exclude men older than 75 years.*

## **6.2 Missed opportunity for 'watchful waiting' and the risks of unnecessary medication**

Comments were received from the BMA and an individual.

The BMA expressed concerns that the reclassification would lead easier access to this drug and the approach of 'watchful waiting' (which avoids unnecessary use of drugs) with a doctor's supervision would not be applied to men, who were experiencing urinary symptoms, which fall into a fully acceptable range of normality. The individual expressed similar views.

*Assessor's comments:*

*CHM has previously considered the issue of watchful waiting. It was noted that the NHS Clinical Knowledge Summaries recommends a stepwise approach to the management of BPH. Watchful waiting may be appropriate for men who feel their symptoms are tolerable. This strategy avoids the risks of adverse effects from treatment. The goal of treatment would be to improve urinary flow rate and relieve both the common voiding and bothersome storage problems.*

*The applicant considers that the proposed pharmacy model recognises the importance of lifestyle advice and patient monitoring as a possible first step in the management of urinary symptoms. The pharmacy questionnaire includes the IPSS scoring system and a quality of life question to establish the man's suitability for pharmacy supply. A man who has mild symptoms (IPSS score 0 to 7) based on the pharmacy questionnaire or has only minor impact on quality of life (QoL score < 4) is not recommended for supply of tamsulosin, and the pharmacist is advised to give lifestyle advice and suggest that the man visit his GP for a health check. The Pharmacist Training material provides training on lifestyle advice. The PIL refers to the applicant's disease awareness website, which includes information on watchful waiting for the patient. Lifestyle advice can also be incorporated into the PIL. The applicant has developed a Men's Health Pack, which includes lifestyle advice on managing urinary symptoms.*

**6.3 Intraoperative Floppy Iris Syndrome (IFIS)**

Comments were received from the Royal College of Ophthalmologists (RCOphth) and BAUS.

The RCOphth commented that IFIS occurs in the majority of patients receiving tamsulosin and its effect on the iris is long-lasting. The RCOphth considered that it is very important that it is known preoperatively that a patient is taking tamsulosin so that the cataract surgery is assigned to a suitable experienced surgeon. The RCOphth was concerned that if tamsulosin became a pharmacy medicine it would not appear on GP records and may not be considered worth declaring by the patient at pre-operative assessment for cataract surgery. The RCOphth therefore recommended that there is a prominent warning included in the product information that *"the start of tamsulosin treatment is delayed in patients who are awaiting cataract surgery and that patients already taking it must notify their surgeon that they are (or have been) taking it prior to cataract surgery."*

*Assessor's comments:*

*The issue of IFIS has previously been considered by the CHM.*

*The applicant proposes to include the following wording to section 4.4 of the SPC in line with recommendations by the PhVWP:*



*"The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. IFIS may lead to increased procedural complications during the operation.*

*The initiation of therapy with tamsulosin in patients for whom cataract surgery is scheduled is not recommended.*

*Discontinuing tamsulosin 1 – 2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of stopping of therapy prior to cataract surgery has not yet been established.*

*During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery."*

*The applicant was requested to include planned cataract surgery in the 'P' SPC as a contraindication and amend the wording of section 4.4 by replacing the third sentence with the following: 'In the event of cataract eye surgery, use of tamsulosin is not appropriate. See also Section 4.3 Contraindications'*

*The Patient Information Leaflet includes the following warning:*

***"Eye surgery***

*If you are about to have an operation on your eye because of cloudiness of the lens (cataract), do not start taking FLOMAX RELIEF just now and tell the eye specialist if you have ever taken tamsulosin.*

*The specialist can then take appropriate precautions during the surgical procedure. Ask your doctor if you should stop taking FLOMAX RELIEF for a short time."*

*The pharmacy questionnaire includes a question if any eye operation is planned on the man. In case of a 'yes' answer the patient will be referred to his doctor.*

*The CHM considered that experienced ophthalmologists are able to handle IFIS. However, it is important that patients inform the ophthalmologist if they are taking tamsulosin. The CHM considered that the proposed wording in the product information and the proposed question in the questionnaire is acceptable. Additionally, the proposed wording is in line with the recommendations from the RCOphth.*

#### **6.4 Concomitant medication with anti-hypertensive drugs**

Comments were received from the RCOphth and the RCGP on the above issue.

The RCOphth commented that tamsulosin can cause clinically significant postural hypotension when used in combination with hypertensive drugs. The

RCOph is concerned that this is a safety issue in elderly male patients, many of whom are on antihypertensive treatment and are already vulnerable to falls. The RCGP had similar views and added that over dosage of tamsulosin could lead to hypotension, bradycardia and cardiac arrest.

*Assessor's comments:*

*The issue of hypotension and concomitant medication with other hypertensive drugs has been previously considered by CHM.*

*The CHM considered that although tamsulosin can affect blood pressure, its effect on BP and postural hypotension is clinically not relevant even in older patient. However, it was considered that excluding patients with dizziness and those on several hypotensive drugs from the pharmacy supply – as proposed by the applicant – was desirable. In relation to the possible interaction of tamsulosin with anti-hypertensive drugs, the CHM considered that it was preferable for men to be warned about the enhanced anti-hypertensive potential of co-medication rather than to contra-indicate concomitant administration. It was considered that tamsulosin supply was safe for older patients. However, frail elderly (i.e. house-bound) patients should be excluded from pharmacy supply.*

## 6.5 Men visiting numerous pharmacies

Comments were received from the NMC, the RPSGB and the RCP Edinburgh.

The NMC commented that safety measures should be put in place to ensure that patient does not attend many different pharmacies to obtain the drug repeatedly and not to see a doctor by the 10 week cut off. The RPSGB expressed also concerns that customers may purchase the product from more than one pharmacy, which can lead to delayed diagnosis. The RCP Edinburgh expressed similar views.

*Assessor's comments:*

*The above issue has been considered by CHM. CHM made the following recommendation:*

*"Patients should be encouraged to sign up with one pharmacy with the aim of continuity of care. To allow suitable follow up of supply patients should also be prepared to share the record with their GP and feedback to the pharmacist on the results of any tests conducted."*

*In its response to CHM's recommendation, the applicant has provided data from a survey, which showed that 60-78% of patients return to the same pharmacy and this increases with age (the publication has not been provided). Loyalty schemes have been introduced to encourage return to the same pharmacy. The applicant states that communicating drug information - which is a prominent feature of the proposal - has the potential to increase*

consumer patronage and loyalty to a community pharmacy. Additionally, the pharmacy model will have the following elements, which is intended to encourage men to sign up with one pharmacy:

- In order to obtain a supply of Flomax Relief, every man will have to complete the pharmacy questionnaire. Each time a man goes to a different pharmacy, he will have to complete again the questionnaire.
- Upon commencement of supply, the man will be given a registration card which will be stamped with the name and address of the originating pharmacy and the date of first supply of tamsulosin.
- Men supplied with Flomax Relief will be able to register into a patient support programme (see also section 6.6 of this report). This programme will include advice to return to the same pharmacy.
- Men's Health Pack recommends that a man return to the same pharmacy. (Similar advice can be incorporated into the PIL.)

CHM may consider that with the above elements incorporated in the pharmacy model, the applicant has provided sufficient reassurance that men are encouraged to sign up with one pharmacy. The medication card, which will be provided at the commencement of treatment will encourage men to share records with their GP.

## 6.6 Engaging men in their healthcare

Comments were received from the CCA, the NPA, the RCGP, the HS Central Lancashire Medicines Management Committee, an individual respondent.

The CCA commented that the proposal is an important step in engaging men in their own healthcare and increasing access to effective treatments.

The NPA considered that "any programme that not only raises men's awareness of the treatable nature of LUTs, but encourages them to seek healthcare advice to obtain Flomax Relief has to be of positive benefit to men."

The RCGP commented that "men with lower urinary tract symptoms (LUTS) would be unlikely to speak to a pharmacist at all, and in fact there was evidence to indicate that urinary symptoms were often considered too embarrassing a condition to discuss freely."

The HS Central Lancashire Medicines Management Committee considered that the application did not give any evidence that men who are unwilling to talk to a GP were willing to talk to a pharmacist. An individual expressed similar views.

### Assessor's comments:

The CHM discussed this issue when it gave preliminary consideration to the application and noted that there had not been evidence provided to show that the proposal would have drawn more patients with LUTS into healthcare.

Therefore, the CHM was not reassured about the positive risk/benefit balance of the proposal.

To address CHM's concerns the applicant argued that BPH is a common condition affecting one in four men over the age of 40 years. LUTS reduce the quality of life of many sufferers. The majority of men are not aware that there are treatments available for LUTS. The applicant considers that educational and disease awareness communication about BPH can help to encourage men with LUTS to seek advice from a healthcare professional.

The applicant launched a disease awareness website on the internet to give information and advice about BPH. The site contains specific sections for sufferers, partners and pharmacists and includes interactive features such as email to an urologist expert, opportunity to fill in the IPSS questionnaire and an online symptom diary. The applicant states that as of 1<sup>st</sup> March 2008 there were 10,851 visits detected on the website, which demonstrates the need for such information and the success of the initiative.

The assessor concurs with the applicant's opinion that the high number of visitors indicates that there is an interest in information on BPH/LUTS. However, no further information was provided from the interactive features of the website to indicate whether the initiative is really successful in engaging men in their healthcare.

The applicant also states that men are less willing to visit their GP than women. According to a study 50-75% of men although feel they need help with their urinary symptoms; they actually fail to seek it. The applicant considers that increased access to information on LUTS and BPH and wider availability to tamsulosin will help capturing these men. Additionally, the applicant proposes to launch a post-authorisation compliance programme to follow-up men's adherence to the pharmacy protocol. Within the compliance programme all patients who are supplied with Flomax Relief will receive an application card, which gives the opportunity of registering their details. Patients who are registered on the programme will receive further information and will be involved in an ongoing communication with the applicant to ensure that they have consulted their GP by week 10 of their treatment. Through the programme the applicant will monitor the real life performance of the pharmacy questionnaire and collect information on any adverse events. The applicant plans to run the programme for 2 years initially and report the results to the MHRA.

The NPA referred to a programme in Birmingham (Vascular Checks Case Study: Improving Life Expectancy), which offered opportunistic cardiovascular disease (CVD) risk assessment service (called "Heart MOT") from community pharmacies. The aim was to attract people into the service and measure and communicate their risk of developing CVD. Following assessment the individuals were either given life style advice (and also encouraged to share their results with their GP) or referred to the GP if their CVD risk was high. From April 2007 to June 2008 there were 868 people tested in 14 pharmacies. Those who attended the service 57% were male, which confirms that

*community pharmacy can play a significant role in providing good access to healthcare services for men.*

## **7. PRODUCT INFORMATION**

The applicant has updated the SPC, Patient Information Leaflet and labelling (Annexes 9, 10 and 11 respectively) to reflect CHM advice in June 2008.

The following further revisions should be addressed:

### **7.1. Summary of Product Characteristics**

#### **7.1.1 Section 4.1**

The age range 45 – 75 years should be specified.

### **7.2. Patient Information Leaflet**

This should be updated to reflect the revised SPC.

### **7.3. Labelling**

This should be updated to reflect the revised SPC.

## **8. CONCLUSION**

No new issues have been identified during public consultation. The number of organisations responding was equally balanced, although fewer favourable views were received from individuals responding than from those not in favour. Although contacted by MHRA, no response was received from a major patient organisation, the Men's Health Forum which had contributed positively to the company's application.

Although the majority view was not in favour of the proposal, the issues highlighted had previously been considered by the CHM and addressed by the applicant. In relation to the main issue of missing or delaying the diagnosis of serious underlying conditions, the CHM considered that pharmacy availability of tamsulosin will not necessarily result in missing or delaying the diagnosis of a serious underlying condition, because the aim of the proposal is to reach out for men who otherwise would not have attended healthcare services. The information provided by the NPA on the Birmingham Vascular Checks Case Study provides reassurance that this can be achieved via community pharmacies.

The CHM advised the applicant to encourage men to sign up with one pharmacy. To address this, the applicant proposes to give the man a registration card, which will be stamped with the name and address of the pharmacy who originated tamsulosin supply and the date of first supply of tamsulosin. Additionally, every man will have to complete the pharmacy questionnaire in order to obtain a supply of Flomax Relief. Each time a man goes to a different pharmacy, he will have to complete again the questionnaire. The post-authorisation compliance programme and the

information pack (Men's Health Pack) will include advice to return to the same pharmacy.

CHM may consider that with the above elements incorporated in the pharmacy model, the applicant has provided sufficient reassurance that men are encouraged to sign up with one pharmacy.

The CHM also advised the applicant that patients should be encouraged to share the record with their GP and feedback to the pharmacist on the results of any tests conducted to allow suitable follow up of supply. The registration card, which will be provided at the commencement of treatment, will provide an opportunity for two-way communication between the GP and the pharmacist.

## 9. RECOMMENDATION

The CHM is asked to consider the responses to the public consultation and advise on the following

1. whether the reclassification application may be approved under the following conditions:
  - Treatment of functional symptoms of benign prostatic hyperplasia (BPH) in men aged between 45 and 75 years.
  - Strength and pharmaceutical form: 0.4mg tablets
  - Pack size: max. 28 tablets.
2. the applicant should further tighten the pharmacy protocol by including an upper age limit of 75 years in the pharmacy supply.
3. the applicant should submit the results of the post-authorisation compliance programme at 6 monthly intervals for further consideration by the CHM together with any consequential amendments to the pharmacy protocol, if needed.

|                               |  |
|-------------------------------|--|
| COMMISSION ON HUMAN MEDICINES | : DRAFT ADVICE   |
| DATE OF MEETING               | : 21 May 2009  |
| M.A. No                       | : PL 00015/0280  |
| COMPANY                       | : Boehringer Ingelheim   |
| PRODUCT                       | : Flomax Relief  |
| ACTIVE CONSTITUENT            | Tamsulosin 0.4mg   |
| LEGAL STATUS                  | POM to P   |
| KEY WORDS                     | tamsulosin, benign prostatic hyperplasia, legal reclassification |

#### LEGAL CLASSIFICATION

The Commission considered whether Flomax Relief falls within a description or class specified for the purpose of Section 58 of the Medicines Act 1968 by Order made under Section 58 (1), as being appropriate for supply on a prescription only basis in accordance with Section 58A (2) of that Act and advised in favour of non-prescription availability under the following conditions:

- Treatment of functional symptoms of benign prostatic hyperplasia (BPH) in men aged between 45 and 75 years.
- Strength and pharmaceutical form: 0.4mg tablets
- Pack size: max. 28 tablets.

#### Marketing Authorisation

The following changes to the product information are required to reflect the non-prescription use of the product.

##### 1. Summary of Product Characteristics

###### 1.1 Section 4.1

The age range 45 – 75 years should be specified.

##### 2. Patient Information Leaflet

This should be updated to reflect the revised SPC.

##### 3. Labelling

This should be updated to reflect the revised SPC.

#### Remark to the applicant

The results of the post-authorisation compliance programme should be submitted at 6 monthly intervals for further consideration by the CHM together with any consequential amendments to the pharmacy protocol, if needed.