Tamsulosin Prolonged-release Tablets

General Notices

Prolonged-release Tamsulosin Tablets

Details for the public consultation of this monograph are as follows:

<table>
<thead>
<tr>
<th>EAG/Panel/Working Party</th>
<th>Medicinal Chemicals 2</th>
</tr>
</thead>
</table>
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| Deadline for Comment   | 31 March 2020          |
| Target Publication Date (subject to change) | BP 2021 |
| Notes                  | Revised monograph     |
|                        | If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. |
|                        | Related substances Updated related substances test following lab work |
|                        | Impurities section added. New impurity 1. |

Tamsulosin Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Alpha₁-adrenoceptor antagonist.

DEFINITION

Tamsulosin Prolonged-release Tablets contain Tamsulosin Hydrochloride. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Tamsulosin. The dissolution profile reflects the in vivo performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets and with the following requirements.
Content of tamsulosin hydrochloride, \( C_{26}H_{28}N_2O_5S \cdot HCl \)

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. The light absorption, Appendix II B, in the range 210 to 400 nm of the solution prepared in the Assay exhibits a single maximum at 225 nm.

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following freshly prepared solutions protected from light.

Solution A: 1% v/v of 18 M ammonia in methanol.

Solution B: acetonitrile (10%)

(1) Disperse a quantity of the powdered tablets containing 0.8 mg of Tamsulosin Hydrochloride in 20 mL of solution A and stir. Centrifuge a portion of this solution and pass through a filter previously rinsed with solution A (a PVDF 0.45-µm filter is suitable), discarding the first 3 mL of the filtrate. Evaporate 3 mL of the filtrate to dryness under reduced pressure using a water bath maintained at 30 °C. Add 5 mL of solution B immediately to the dried residue, shake, and mix with the aid of ultrasound. Pass through a filter previously rinsed with solution B (a PVDF 0.45-µm filter is suitable), and use the filtrate.

(2) Dilute 1 volume of solution (1) to 100 volumes with solution B.

(3) 0.000024% w/v of tamsulosin for system suitability BPCRS in solution B.

(4) Dilute 1 volume of solution (2) to 10 volumes with solution B.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm \( \times \) 4.6 mm) packed with octadecylsilyl silica gel for chromatography (3.5 µm) (Zorbax Eclipse XDB C18 is suitable).

(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1.2 mL per minute.

(d) Use a column temperature of 40°.

(e) Use an autosampler temperature of 7°.

(f) Use a detection wavelength of 225 nm.

(g) Inject 200 µL of each solution.

MOBILE PHASE

Mobile phase A Dissolve 4 g of sodium hydroxide and 10 mL of perchloric acid in 2 L of water, adjusted to pH 2.0 with perchloric acid.

Mobile phase B acetonitrile
Mobile phase C methanol

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Mobile phase A (% v/v)</th>
<th>Mobile phase B (% v/v)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>95</td>
<td>5</td>
<td>isocratic</td>
</tr>
<tr>
<td>4-10</td>
<td>95→90</td>
<td>5→10</td>
<td>linear gradient</td>
</tr>
<tr>
<td>10-70</td>
<td>90→30</td>
<td>10→5</td>
<td>linear gradient</td>
</tr>
<tr>
<td>70-70.1</td>
<td>30→95</td>
<td>5</td>
<td>linear gradient</td>
</tr>
<tr>
<td>70.1-80</td>
<td>95</td>
<td>5</td>
<td>re-equilibration</td>
</tr>
</tbody>
</table>

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to tamsulosin (retention time of about 36 minutes) are: impurity B, about 0.2; impurity 1, about 0.8; impurity H, about 1.4.

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (3), the resolution between the peaks due to tamsulosin hydrochloride and impurity 1 is at least 5.0.

LIMITS

Identify any peaks corresponding to impurity 1 and impurity H in the chromatogram obtained with solution (1) using the chromatogram obtained with solution (3).

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity H is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of all the secondary peaks is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Tamsulosin Hydrochloride comply with the requirements stated under Tablets using the following method of analysis.

Carry out the method for liquid chromatography, Appendix III D, using the following solutions.

1. Intermittently shake 1 tablet with 10 mL of 1\text{M} methanolic hydrochloric acid for at least 15 minutes with the aid of ultrasound, filter through a 0.7-µm glass fibre filter, dilute 1 volume of the filtrate to 10 volumes with 1\text{M} methanolic hydrochloric acid and filter through a 0.7-µm glass fibre filter.

2. Prepare a 0.04% w/v solution of tamsulosin hydrochloride BPCRS in methanol with the aid of ultrasound, cool and dilute 1 volume to 100 volumes with 1\text{M} methanolic hydrochloric acid.

CHROMATOGRAPHIC CONDITIONS
The chromatographic conditions described under Related substances may be used.

**DETERMINATION OF CONTENT**

Calculate the content of $C_{20}H_{28}N_2O_5S\cdot HCl$ in each tablet from the declared content of $C_{20}H_{28}N_2O_5S\cdot HCl$ in tamsulosin hydrochloride BPCRS.

**ASSAY**

*For tablets containing less than 2 mg and/or less than 2% w/w of tamsulosin hydrochloride*

Use the average of the individual results determined in the test for Uniformity of content.

*For tablets containing 2 mg or more and 2% w/w or more of tamsulosin hydrochloride*

Weigh and powder 20 tablets. Carry out the method for liquid chromatography, Appendix III D, using the following solutions.

1. To a quantity of the powdered tablets containing 1.6 mg of Tamsulosin Hydrochloride add 50 mL of 1M methanolic hydrochloric acid, mix for at least 15 minutes with the aid of ultrasound, cool and add sufficient 1M methanolic hydrochloric acid to produce 100 mL. Filter using a 0.7-µm glass fibre filter and dilute 1 volume of the filtrate to 4 volumes with 0.1M methanolic hydrochloric acid.

2. Prepare a 0.040% w/v solution of tamsulosin hydrochloride BPCRS in methanol with the aid of ultrasound, cool and dilute 1 volume to 100 volumes with 1M methanolic hydrochloric acid.

**CHROMATOGRAPHIC CONDITIONS**

The chromatographic conditions described under Related substances may be used.

**DETERMINATION OF CONTENT**

Calculate the content of $C_{20}H_{28}N_2O_5S\cdot HCl$ in the tablets from the declared content of $C_{20}H_{28}N_2O_5S\cdot HCl$ in tamsulosin hydrochloride BPCRS.

**IMPURITIES**

The impurities limited by the requirements of this monograph include impurities B, E, F and H listed under Tamsulosin Hydrochloride and the following:

1. (2-Ethoxyphenoxy)acetic acid