# Bisacodyl Gastro-resistant Tablets

Bisacodyl Tablets

Gastro-resistant Bisacodyl Tablets

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

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| **Notes** | Revised monograph<br>**Related substances** Impurity D limit and method revised in line with updated Ph. Eur. monograph, and other limits revised in line with ICH.<br>If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. |



### Action and use

Stimulant laxative.

## DEFINITION

Bisacodyl Gastro-resistant Tablets contain Bisacodyl. They are made gastro-resistant by enteric coating or by other means.

*The tablets comply with the requirements stated under Tablets and with the following requirements.*

### Content of bisacodyl, $C_{22}H_{19}NO_4$

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

A. 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).

B. Extract a quantity of the powdered tablets containing 50 mg of Bisacodyl with 20 mL of *dichloromethane*, filter, evaporate the filtrate to dryness and dissolve the residue in 10 mL of a 0.5% v/v solution of *sulfuric acid*. To 2 mL of the solution obtained add *sulfuric acid*. A reddish violet colour is produced on addition of the concentrated acid.

C. Boil 2 mL of the solution obtained in test B with a little *nitric acid*; a yellow colour is produced. Cool and add 5M *sodium hydroxide*; the colour becomes yellowish brown.

# TESTS

## Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

*First stage*

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.

(b) Use 500 mL of *0.1M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 2 hours, withdraw a 10-mL sample of the medium.

(2) Dissolve 50 mg of *bisacodyl BPCRS* in 50 mL of *methanol* containing a drop of *orthophosphoric acid*. Dilute with *0.1M hydrochloric acid* to produce a solution containing 0.00005% w/v of *bisacodyl BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.0 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).

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

(c) Use a flow rate of 0.8 mL per minute.

(d) Use a column temperature of 40°.

(e) Use a detection wavelength of 230 nm.

(f) Inject 20 µL of each solution.

MOBILE PHASE

350 volumes of a 0.1% w/v solution of *ammonium acetate*, adjusted to pH 8.0 with *dilute ammonia solution* and 650 volumes of *acetonitrile*.

DETERMINATION OF CONTENT

Calculate the total content of $C_{22}H_{19}NO_4$ in the medium using the declared content of $C_{22}H_{19}NO_4$ in *bisacodyl BPCRS*.

LIMITS

The amount of bisacodyl released is not more than 5% of the stated amount.

After completion of the first stage, remove the basket from the vessel and dip once into a 100-mL beaker containing 80 mL of *water*. After the water has drained from the basket, transfer the tablet to Apparatus 2 and carry out the procedure described under Final stage.

*Final stage*

*Solution A:* Dissolve 8.9 g of *disodium hydrogen orthophosphate* and 10 g of *sodium lauryl sulfate* in 800 mL of *water*. Adjust to pH 7.5 with 0.1M *hydrochloric acid* and dilute to 1000 mL with *water*.

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.

(b) Use 900 mL of solution A, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 60 minutes, withdraw a 10-mL sample of the medium and filter through a 0.45-µm filter, discarding the first 3 mL.

(2) Dissolve 50 mg of *bisacodyl BPCRS* in 50 mL of *methanol* containing a drop of *orthophosphoric acid*. Dilute with solution A to produce a solution containing 0.00056% w/v of *bisacodyl BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution – First stage may be used.

DETERMINATION OF CONTENT

Calculate the total content of $C_{22}H_{19}NO_4$ in the medium using the declared content of $C_{22}H_{19}NO_4$ in *bisacodyl BPCRS*.

LIMITS

The amount of bisacodyl released is not less than 75% (Q) of the stated amount.

## Related substances

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

*Solution B:* A mixture of 4 volumes of *glacial acetic acid*, 30 volumes of *acetonitrile* and 66 volumes of *water*.

(1) Shake a quantity of the powdered tablets containing 25 mg of Bisacodyl with 40 mL of solution B, dilute to 50 mL with solution B and filter.

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

(3) Dissolve the contents of a vial of *bisacodyl for system suitability A EPCRS* in 1 mL of *acetonitrile* and mix with 1 mL of solution B.

(4) Dissolve 5 mg of *bisacodyl for peak identification EPCRS* in 2.5 mL of *acetonitrile* and dilute to 5 mL with solution B.

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

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable).

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

(c) Use a flow rate of 1.5 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 265 nm.

(f) Inject 20 µL of each solution.

(g) For solution (1), allow the chromatography to proceed for 3.5 times the retention time of the principal peak.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of 0.025M *ammonium formate* previously adjusted to pH 5.0 with *anhydrous formic acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to bisacodyl (retention time about 13 minutes) are: impurity A, about 0.2; impurity B, about 0.4; impurity C, about 0.45; impurity E, about 0.9; impurity F, about 2.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained solution (3), the *peak-to-valley ratio* is at least 1.5, where $H_p$ is the height above the baseline of the peak due to impurity E and $H_v$ is the height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

LIMITS

In the chromatogram obtained with solution (1):

identify any peak corresponding to impurity A using solution (3) and multiply the area of this peak by a correction factor of 0.7;

the area of any peak corresponding to impurity C is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of any peak corresponding to impurity A is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.8%);

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

the area of any peak corresponding to impurity F is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any other *secondary peak* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (5) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

## ASSAY

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

*Solution B:* A mixture of 4 volumes of *glacial acetic acid*, 30 volumes of *acetonitrile* and 66 volumes of *water*.

(1) Shake a quantity of the powdered tablets containing 10 mg of Bisacodyl with 40 mL of solution B, dilute to 50 mL and filter. Further dilute 1 volume to 4 volumes with solution B.

(2) 0.005% w/v of *bisacodyl BPCRS* in solution B.

(3) Dissolve the contents of a vial of *bisacodyl for system suitability A EPCRS* in 1 mL of *acetonitrile* and mix with 1 mL of solution B.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained solution (3), the *peak-to-valley ratio* is at least 1.5, where $H_p$ is the height above the baseline of the peak due to impurity E and $H_v$ is the height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

DETERMINATION OF CONTENT

Calculate the total content of bisacodyl, $C_{22}H_{19}NO_4$, in the tablets using the chromatograms obtained and the declared content of $C_{22}H_{19}NO_4$ in *bisacodyl BPCRS*.

## IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Bisacodyl.