Edition: BP 2025 (Ph. Eur. 11.6 update)

Digoxin Injection

General Notices

Action and use

Na/K-ATPase inhibitor; cardiac glycoside.

DEFINITION

Digoxin Injection contains 0.025% w/v of Digoxin in a suitable vehicle.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of digoxin, $C_{41}H_{64}O_{14}$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) has the same retention time as that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 6.7 to 7.3, Appendix V L.

Related substances

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

Solution A 22 volumes of mobile phase B and 78 volumes of mobile phase A.

(1) Dilute a volume of the injection with sufficient mobile phase A to produce a solution containing 0.00625% w/v of Digoxin.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.0005% w/v each of *digoxin EPCRS* and *lanatoside C* (impurity H).
(4) 0.01% w/v of *digoxin for peak identification EPCRS*.
(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable) fitted with a stainless steel guard column (4 mm × 3 mm) packed with the same material.
(b) Use gradient 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 220 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

Mobile phase A 10 volumes of *acetonitrile R1* and 90 volumes of *water*.

Mobile phase B 10 volumes of *water* and 90 volumes of *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	78	22	isocratic
5-15	78→30	22→70	linear gradient
15-16	30→78	70→22	linear gradient
16-21	78	22	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity H and digoxin is at least 1.5.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of digoxin in solution (2).

For the reporting threshold, use the concentration of digoxin in solution (5).

For peak identification, use solution (4).

Digoxin retention time: about 4 minutes; relative retention: impurity C, about 0.3; impurity E, about 0.5; impurity F, about 0.6; impurity G, about 0.8; impurity H, about 0.9; impurity K, about 1.6; impurity B, about 2.1; impurity A, about 2.6.

Correction factors: impurity C, multiply by 0.7.

LIMITS

— impurity F: not more than 2.5%;

— impurities E and K: not more than 1.0% of each;

— impurity G: not more than 0.8%;

— unspecified impurities: for each impurity, not more than 0.5%;

— total impurities: not more than 3.5%;

— reporting threshold: 0.1%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in solution A as described under Related substances.

(1) Dilute a volume of the injection with sufficient volume to produce a solution expected to contain 0.00125% w/v of Digoxin.
(2) 0.00125% w/v of *digoxin EPCRS*.
(3) 0.0005% w/v each of *digoxin EPCRS* and *lanatoside C*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity H and digoxin is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of digoxin, $C_{41}H_{64}O_{14}$, in the injection from the chromatograms obtained and using the declared content of $C_{41}H_{64}O_{14}$ in *digoxin EPCRS*.

STORAGE

Digoxin Injection should be protected from light.

IMPURITIES

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