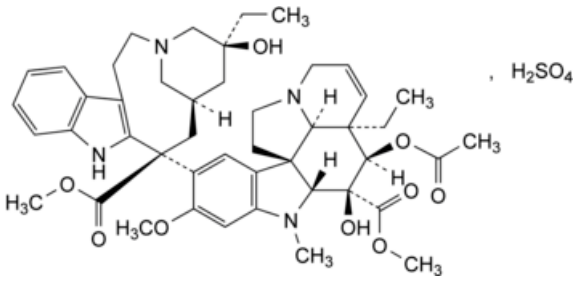
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Vinblastine Sulfate

General Notices

Vinblastine Sulphate

*(Ph. Eur. monograph 0748)*



$C_{46}H_{60}N_4O_{13}S$ 909 *143-67-9*

**Action and use**

Vinca alkaloid cytotoxic.

**Preparation**

Vinblastine Injection

Ph Eur

## DEFINITION

Vinblastine sulfate contains not less than 95.0 per cent and not more than the equivalent of 104.0 per cent of methyl (3a*R*,4*R*,5*S*,5a*R*,10b*R*,13a*R*)-4-(acetyloxy)-3a-ethyl-9-[(5*S*,7*R*,9*S*)5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2*H*-3,7-methanoazacycloundecino[5,4-*b*]indol-9-yl]-5-hydroxy-8-methoxy-6-methyl-3a,4,5,5a,6,11,12,13a-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate sulfate, calculated with reference to the dried substance.

## CHARACTERS

A white or slightly yellowish, crystalline powder, very hygroscopic, freely soluble in water, practically insoluble in ethanol (96 per cent).

## IDENTIFICATION

A. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the *Ph. Eur. reference spectrum of vinblastine sulfate*.
B. Examine the chromatograms obtained in the assay. The principal peak in the chromatogram obtained with the test solution is similar in position and approximate size to the principal peak in the chromatogram obtained with reference

solution (a).

## TESTS

### Solution S

Dissolve 50.0 mg in *carbon dioxide-free water R* and dilute to 10.0 mL with the same solvent.

### Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution $Y_7$ (*2.2.2, Method I*).

### pH (*2.2.3*)

Dilute 3 mL of solution S to 10 mL with *carbon dioxide-free water R*. The pH of this solution is 3.5 to 5.0.

### Related substances

Examine the chromatograms obtained in the assay. In the chromatogram obtained with the test solution, the area of any peak apart from the principal peak is not greater than the area of the principal peak in the chromatogram obtained with reference solution (c) (2.0 per cent) and the sum of the areas of any such peaks is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (5.0 per cent). Disregard any peak with an area less than that of the peak in the chromatogram obtained with reference solution (d).

### Loss on drying

Not more than 15.0 per cent, determined on 3 mg by thermogravimetry (*2.2.34*). Heat to 200 °C at a rate of 5 °C/min, under a stream of *nitrogen for chromatography R*, at a flow rate of 40 mL/min.

## ASSAY

Examine by liquid chromatography (*2.2.29*).

*Keep the solutions in iced water before use*.

*Test solution* Dilute 1.0 mL of solution S (see Tests) to 5.0 mL with *water R*.

*Reference solution (a)* Dissolve the contents of a vial of *vinblastine sulfate CRS* in 5.0 mL of *water R* to obtain a concentration of 1.0 mg/mL.

*Reference solution (b)* Dissolve 1.0 mg of *vincristine sulfate CRS* in 1.0 mL of reference solution (a).

*Reference solution (c)* Dilute 1.0 mL of reference solution (a) to 50.0 mL with *water R*.

*Reference solution (d)* Dilute 1.0 mL of reference solution (c) to 20.0 mL with *water R*.

The chromatographic procedure may be carried out using:

— a stainless steel column 0.25 m long and 4.6 mm in internal diameter packed with *octylsilyl silica gel for chromatography R* (5 µm). Place between the injector and the column a precolumn packed with suitable silica gel,

— as mobile phase at a flow rate of 1.0 mL/min a mixture of 38 volumes of a 1.5 per cent *V/V* solution of *diethylamine R* adjusted to pH 7.5 with *phosphoric acid R*, 12 volumes of *acetonitrile R* and 50 volumes of *methanol R*,

— as detector a spectrophotometer set at 262 nm,

— a loop injector.

Inject 10 µL of each solution and record the chromatograms for 3 times the retention time of the peak due to vinblastine. The assay is not valid unless: in the chromatogram obtained with reference solution (b) the resolution between the peaks

due to vincristine and vinblastine is not less than 4; the peak in the chromatogram obtained with reference solution (d) has a signal-to-noise ratio not less than 5. Calculate the percentage content of $C_{46}H_{60}N_4O_{13}S$ from the area of the principal peak in each of the chromatograms obtained with the test solution and reference solution (a) and from the declared content of *vinblastine sulfate CRS*.

## STORAGE

Store in an airtight, glass container, protected from light, at a temperature not exceeding -20 °C. If the substance is sterile, store in a sterile, airtight, tamper-evident glass container.

---

Ph Eur