USP 31

Amifostine

C_H2_N_O_3PS · 3H_2O 268.27

Ethanol, 2-[(3-aminopropyl)amino]-dihydrogen phosphate (ester), trihydrate.
S-[(3-Aminopropyl)amino]ethyl dihydrogen phosphorothioate, trihydrate [112901-68-5].

> Amifostine contains not less than 78.0 percent and not more than 82.0 percent of C_H2_N_O_3PS, calculated on the as-is basis.

Packaging and storage—Preserve in tight, light-resistant containers, and store in a refrigerator.

USP Reference standards (11)—USP Amifostine RS. USP Amifostine Thiol RS.

Identification—
A: Infrared Absorption (197K).
B: The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.
X-ray diﬀraction (941)—Its X-ray diﬀraction pattern conforms to that of USP Amifostine RS, similarly determined.

pH (791): between 6.5 and 7.5, in a solution (5 in 100).

Water, Method Ic (921): between 19.2% and 21.2%, the assay for this impurity is 1.0 mL per minute. Chromatograph the sample solution and record the chromatograms, and measure the responses of all the peaks, excluding the peaks corresponding to those obtained from the Blank solution. Calculate the percentage of amifostine thiol in the portion of Amifostine taken by the formula:

100(r / r_s)

in which r and r_s are the peak responses for each impurity and amifostine thiol, respectively, obtained from the Test solution; and r_U and r_S are the amifostine thiol peak responses obtained from the Test solution and the Standard thiol solution, respectively. Calculate the percentage of each of the other impurities in the portion of Amifostine taken by the formula:

100(r / r_s)

in which r and r_s are the peak responses for each impurity and amifostine thiol, respectively, obtained from the Test solution; and r_U and r_S are the amifostine thiol peak responses obtained from the Test solution and the Standard thiol solution, respectively.

Organic volatile impurities, Method V (467): meets the requirements.

(Official until July 1, 2008)

Assay—
Mobile phase—Dissolve 1.0 mL of nonafluorobutane sulfonic acid in 1200 mL of HPLC grade water. Prepare a degassed mixture of this solution and acetonitrile (90:10).

Standard preparation—Transfer about 30 mg of USP Amifostine RS, accurately weighed, to a 10-mL volumetric flask. Dissolve in and dilute with water to volume, mix. [NOTE—Inject immediately after preparation, or reﬂux until use. The solution is stable for 48 hours if maintained at about 5°.]

Assay preparation—Transfer about 30 mg of Amifostine, accurately weighed, to a 10-mL volumetric ﬂask. Dissolve in and dilute with water to volume, and mix. [NOTE—Inject immediately after preparation, or reﬂux until use. The solution is stable for 48 hours if maintained at about 5°.]

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm x 25-cm column that contains packing L1. The column temperature is maintained at 30°, and the temperature of the solution to be injected is maintained at 2-° to 8°. The flow rate is about 1.0 mL per minute. Chromatograph the System suitability solution and the Standard thiol solution, and record the peak responses as directed for Procedure: the resolution, R, between amifostine and amifostine thiol is not less than 2.0; the column eﬃciency calculated for the amifostine thiol peak is not less than 2300 theoretical plates; the tailing factor is not more than 4.0; the capacity factor, k, is more than 0.5; and the relative standard deviation for replicate injections is not more than 4.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the Standard thiol solution, the Test solution, and the Blank solution into the chromatograph, record the chromatograms, and measure the responses of all the peaks, excluding the peaks corresponding to those obtained from the Blank solution. Calculate the percentage of amifostine thiol in the portion of Amifostine taken by the formula:

100(C / W)(r_C / r_S)

in which C is the concentration, in mg per mL, of USP Amifostine RS in the Standard preparation; and r_C and r_S are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.