Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨**711**⟩

Medium: 3% sodium laur yl sulfate in deaerated water, pH 9.6 to 10.0; 900 mL
Apparatus 1: 100 rpm
Time: 30 min
Determine the amount of $C_{21}H_{26}O_3$ dissolved using the following method.
Standard solution: Transfer about 14 mg of USP Acitretin RS to a 500-mL volumetric flask. Dissolve in 50 mL of alcohol, and dilute with *Medium* to volume.
For Capsules labeled to contain 10 mg: Transfer 20 mL of this solution to a 50-mL volumetric flask, and dilute with *Medium* to volume.
Sample solution: Use portions of the solution under test passed through a suitable filter of 0.45- µm pore size.
Capsule shell solution: Dissolve 6 clean empty-shell Capsules in 900 mL of *Medium.*
Analysis
Samples: *Standard solution*, *Sample solution,* and *Capsule shell solution*
Analytical wavelength: 347 nm
Cell length: 2 mm
Blank: *Medium*
Calculate the amount of $C_{21}H_{26}O_3$ dissolved:

$$\text{Result} = [(A_U - A_{CS})/A_S] \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_{CS} = Capsule shell correction, calculated as shown below
A_S = absorbance of the *Standard solution*
C_S = concentration of the appropriate *Standard solution* (mg/mL)
L = Capsule label claim (mg)
V = volume of *Medium* (mL), 900
The Capsule shell correction, A_{CS}, is calculated as follows:

$$A_{CS} = A_{CSS}/N$$

A_{CSS} = absorbance of the *Capsule shell solution*
N = number of Capsule shells used to prepare the *Capsule shell solution*
Tolerances: NLT 85% (Q) of the labeled amount of $C_{21}H_{26}O_3$ is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

- **PROCEDURE: LIMIT OF DEGRADATION PRODUCTS**

Diluent, Mobile phase, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay.*
Analysis
Sample: *Sample solution*
Calculate the percentage of each degradation product in the portion of Capsules taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each individual impurity
r_T = sum of the responses of all the peaks

Acceptance criteria
Individual impurities: See *Impurity Table 1.*

Impurity Table 1

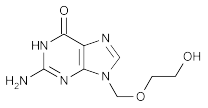
Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acitretin related compound A[a]	0.84	0.5
Acitretin	1.0	—
9-cis isomer[b]	1.09	—
Any unspecified impurity	—	0.4
Total unspecified impurities	—	0.8

[a] [(2*Z*,4*E*,6*E*,8*E*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoic acid] ($C_{21}H_{26}O_3$ 326.43).
[b] (*E,E,Z,E*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Acitretin RS

Acyclovir



$C_8H_{11}N_5O_3$ 225.20
6*H*-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-.
9-[(2-Hydroxyethoxy)methyl]guanine [59277-89-3].

» Acyclovir contains not less than 98.0 per cent and not more than 101.0 per cent of $C_8H_{11}N_5O_3$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers. Store at room temperature. Protect from light and moisture.

USP Reference standards ⟨11⟩**—**
USP Acyclovir 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 and limit for guanine.*

Water, *Method I* ⟨921⟩**:** not more than 6.0%.

Ordinary impurities ⟨466⟩**—**

Test solution: dimethyl sulfoxide.

Standard solution: dimethyl sulfoxide.

Eluant: a mixture of chloroform, methanol, and ammonium hydroxide (80:20:2).

Visualization: 1.

Application volume: 5 µL.

Limit: 1%.

Assay and limit for guanine—

Mobile phase—Prepare a filtered and degassed solution of glacial acetic acid in water (1 in 1000). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution 1—Dissolve accurately weighed quantities of USP Acyclovir RS and guanine in 0.1 N sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having known concentrations of about 0.1 mg of each per mL.

System suitability solution 2—Dissolve an accurately weighed quantity of guanine in 0.1 N sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.7 µg per mL.

Guanine standard preparation—Transfer about 8.75 mg of guanine, accurately weighed, to a 500-mL volumetric flask. Dissolve in 50 mL of 0.1 N sodium hydroxide, dilute with water to volume, and mix. Transfer 2.0 mL of this solution to a 50-mL volumetric flask, dilute with 0.01 N sodium hydroxide to volume, and mix to obtain a solution having a concentration of about 0.7 µg per mL.

Standard preparation—Dissolve about 25 mg of USP Acyclovir RS, accurately weighed, in 5 mL of 0.1 N sodium hydroxide in a 50-mL volumetric flask, dilute with water to volume, and mix. Transfer 10.0 mL of this solution to a 50-mL volumetric flask, dilute with 0.01 N sodium hydroxide to volume, and mix to obtain a solution having a known concentration of about 0.1 mg of USP Acyclovir RS per mL.

Assay preparation—Dissolve about 100 mg of Acyclovir, accurately weighed, in 20 mL of 0.1 N sodium hydroxide in a 200-mL volumetric flask, dilute with water to volume, and mix. Transfer 10.0 mL of this solution to a 50-mL volumetric flask, dilute with 0.01 N sodium hydroxide to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 3 mL per minute. Chromatograph *System suitability solution 1,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between acyclovir and guanine is not less than 2.0; the tailing factor for the analyte peak is not more than 2; and the relative standard deviation for replicate injections for the acyclovir peak is not more than 2.0%. Chromatograph *System suitability solution 2,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation,* the *Guanine standard preparation,* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for all the peaks. Calculate the quantity, in µg, of guanine in the portion of Acyclovir taken by the formula:

$$1000C(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of guanine in the *Guanine standard preparation;* and r_U and r_S are the peak responses due to guanine in the *Assay preparation* and the *Guanine standard preparation,* respectively: not more than 0.7% of guanine is found. Calculate the quantity, in mg, of $C_8H_{11}N_5O_3$ in the portion of Acyclovir taken by the formula:

$$1000C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Acyclovir RS in the *Standard preparation;* and r_U and r_S are the peak responses due to acyclovir in the *Assay preparation* and the *Standard preparation,* respectively.

Acyclovir Capsules

» Acyclovir Capsules contain not less than 93.0 percent and not more than 107.0 per cent of the labeled amount of acyclovir ($C_8H_{11}N_5O_3$).

Packaging and storage—Preserve in tight containers. Store between 15° and 25°. Protect from light and moisture.

USP Reference standards ⟨11⟩**—**
USP Acyclovir RS

Identification—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.*

Uniformity of dosage units ⟨905⟩**:** meet the requirements for *Content Uniformity.*

Dissolution ⟨711⟩**—**

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_8H_{11}N_5O_3$ dissolved from UV absorption at the wavelength of maximum absorbance at about 254 nm on filtered portions of the solution under test, suitably diluted with 0.1 N hydrochloric acid in comparison with a Standard solution having a known concentration of USP Acyclovir RS in the same *Medium.*

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_8H_{11}N_5O_3$ is dissolved in 45 minutes.

Related compounds—

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay.*

Test solution—Use the *Assay preparation.*

Procedure—Inject a volume (about 20 µL) of the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the per centage of each impurity in the portion of Capsules taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity; and r_s is the sum of the responses for all of the peaks: not more than 2.0% of guanine is found; and not more than 0.5% of any individual impurity is found.

Assay—

Mobile phase—Prepare a filtered and degassed solution of 0.02 M acetic acid. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability preparation 1—Dissolve accurately weighed quantities of USP Acyclovir RS and guanine in 0.1 N sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.1 mg of each per mL.

System suitability preparation 2—Dissolve an accurately weighed quantity of guanine in 0.1 N sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 2.0 µg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Acyclovir RS in 0.1 N sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation—Remove, as completely as possible, the contents of not fewer than 10 Capsules. Transfer an accurately weighed portion of the powder, equivalent to about 10 mg of acyclovir, to a 100-mL volumetric flask, dissolve in 10 mL of 0.1 N sodium hydroxide, dilute with water to volume, mix, and filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.2-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph *System suitability preparation 1,* and record the peak responses for acyclovir as directed for *Procedure:* the relative retention times are about 0.6 for guanine and 1.0 for acyclovir; the resolution, *R,* between guanine and acyclovir is not less than 2.0; and the relative stan-