LAMIVUDINE

(LAMIVUDINUM)

Draft proposal for revision for The International Pharmacopoeia

(July 2019)

DRAFT FOR COMMENTS

Please send any comments you may have on this draft working document to Dr Herbert Schmidt, Technical Officer, Medicines Quality Assurance, Technologies Standards and Norms (email: schmidt@who.int) by 30 September 2019.

Working documents are sent out electronically and they will also be placed on the WHO Medicines website (http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en/) for comments under the “Current projects” link. If you wish to receive our draft guidelines, please send your e-mail address to jonessi@who.int and your name will be added to our electronic mailing list.

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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/19.784:

LAMIVUDINE
(LAMIVUDINUM

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<tr>
<td>Drafting of the revision.</td>
<td>January 2019</td>
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<tr>
<td>Discussion at the informal Consultation on Screening Technologies and Pharmacopoeial Specifications for Medicines.</td>
<td>2 – 3 May 2019</td>
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<tr>
<td>Draft revision sent out for public consultation</td>
<td>August – September 2019</td>
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<td>Presentation to the Fifty-fourth WHO Expert Committee on Specifications for Pharmaceutical Preparations.</td>
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[Note from the Secretariat. It is proposed to revise the monograph on Lamivudine as follows:

- addition of a test for lamivudine enantiomer (impurity D),
- revision of the test for related substances,
- addition of an alternative assay by HPLC.

The proposal is based on laboratory investigations and on information found in other pharmacopoeias.

Changes from the current monograph are indicated in the text by insert or delete.]
LAMIVUDINE
(LAMIVUDINUM)

Molecular formula. \( \text{C}_8\text{H}_{11}\text{N}_3\text{O}_3\text{S} \)

Relative molecular mass. 229.3

Graphic formula

![Graphic formula of Lamivudine]

Chemical name. (-)-4-Amino-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidin-2(1H)-one; CAS Reg. No. 134678-17-4.

Description. A white or almost white powder.

Solubility. Soluble in water; sparingly soluble in methanol R; slightly soluble in dehydrated ethanol R; practically insoluble in acetone R.

Category. Antiretroviral (Nucleoside/Nucleotide Reverse Transcriptase Inhibitor).

Storage. Lamivudine should be kept in a well-closed container, protected from light.

Additional information. Lamivudine may exhibit polymorphism.

Requirements

Definition. Lamivudine contains not less than 97.5% and not more than 102.0% (“Assay”, Method A) or not less than 97.0% and not more than 103.0% (“Assay”, Method B) of \( \text{C}_8\text{H}_{11}\text{N}_3\text{O}_3\text{S} \), calculated with reference to the dried substance.
Identity tests

• Either tests A and D, or tests B and D, or tests C and D may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from lamivudine RS or with the reference spectrum of lamivudine.

If the spectra thus obtained are not concordant, repeat the test using the residues obtained by separately dissolving the test substance and lamivudine RS in a small amount of methanol R and evaporating to dryness. The infrared absorption spectrum is concordant with the spectrum obtained from lamivudine RS.

B. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R6 as the coating substance and a mixture of 67 volumes of dichloromethane R, 20 volumes of acetonitrile R, 10 volumes of methanol R and 3 volumes of ammonia (~260 g/L) TS as the mobile phase. Apply separately to the plate 10 μl of each of the following two solutions in methanol containing (A) 1 mg of the test substance per mL and (B) 1 mg of lamivudine RS per mL. After removing the plate from the chromatographic chamber, allow it to dry exhaustively in air or in a current of cool air. Examine the chromatogram in ultraviolet light (254 nm). The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

Spray the plate with vanillin/sulfuric acid TS1 and heat it for a few minutes at 120 °C. Examine the chromatogram in daylight. The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

C. Carry out test C.1 or, where HPLC with a diode array detector is available, test C.2.

C.1 Carry out the test as described under 1.14.4 High-performance liquid chromatography using the conditions given under “Assay”, Method A. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to lamivudine in the chromatogram obtained with solution (2).
The absorption spectrum (1.6) of the final solution prepared for “Assay”, Method B, when observed between 210 nm and 300 nm, exhibits one maximum at about 280 nm.

C.2 Carry out the test as described under 1.14.4 High-performance liquid chromatography using the conditions given under “Assay”, Method A. The retention time and the UV spectrum of the principal peak in the chromatogram obtained with solution (1) correspond to the retention time and the UV spectrum of the peak due to lamivudine in the chromatogram obtained with solution (2).

D. Carry out test D.1 or, where a HPLC and the indicated chiral columns is available, test D.2.

D.1 Determine the specific optical rotation (1.4) using a 10 mg/mL solution in methanol R and calculate with reference to the dried substance; \([\alpha]_{D}^{25^\circ C} = -135\) to -144.

D.2 Carry out the test as described under 1.14.4 High-performance liquid chromatography using the conditions and solutions given under “Impurity D (lamivudine enantiomer)”. The retention time of the principal peak obtained with solution (1) correspond to the retention time of the peak due to lamivudine in the chromatogram obtained with solution (2).

Heavy metals (2.2.3). Use 1.000 g of the test substance for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals, procedure 4. Determine the heavy metals content according to method A; not more than 20 μg/g.

Sulfated ash (2.3). Not more than 1.0 mg/g.

Loss on drying. Dry 1.000 g of the test substance for 3 hours at 105 °C; it loses not more than 5 mg/g.

Impurity D (lamivudine enantiomer). Carry out the test as described under 1.14.4 High-performance liquid chromatography using a stainless steel column (25 cm x 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded 2-
hydroxypropyl-β-cyclodextrin, (5 µm). As mobile phase, use a mixture of 5 volumes of methanol R and 95 volumes of a 7.7 g/L solution of ammonium acetate R.

Operate at a flow rate of 1.0 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of 270 nm. Maintain the column temperature between 15 °C and 30 °C. The temperature may be adjusted to optimize the resolution between lamivudine and impurity D; a lower temperature may improve resolution.

Prepare the following solutions in water. For solution (1), dissolve 25.0 mg of the test substance and dilute to 100.0 mL. For solution (2), dissolve the content of a vial lamivudine for peak identification RS (containing lamivudine and impurity D) and dilute to 1.0 mL.

Inject 10 µL each of solutions (1) and (2). Record the chromatograms for about twice the retention time of lamivudine.

The impurities, if present, are eluted at the following relative retentions with reference to lamivudine (retention time about 8 minutes): impurity D (lamivudine enantiomer) about 1.2; impurity B and enantiomer about 1.3 and 1.5.

The test is not valid unless the peak-to-valley ratio (Hp/Hv) is at least 15.0, where Hp is the height above the baseline of the peak due to impurity D and Hv is the height above the baseline of the lowest point of the curve separating this peak from the peak due to lamivudine.

Calculate the sum of the percentage contents of impurity B and enantiomer and impurity D.

Subtract the percentage content of impurity B as obtained in the test for related substances.

The concentration of impurity D is not greater than 0.1%.

**Related substances.** Carry out the test as described under [1.14.4 High-performance liquid chromatography](#) using a stainless steel column (25cm x 4.6mm) packed with base deactivated particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups (5 µm). As the mobile phase, use a mixture of 5 volumes of methanol R and 95 volumes of an acetate buffer pH 3.8. Prepare the buffer by dissolving 1.9 g of

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1 A Cyclobond 1-SP or I2000SP or I-RSP or I2000-RSP column was found suitable.
2 A Hypersil BDS column was found suitable.
ammonium acetate R in 900 mL of water R, adjust to pH 3.8 with glacial acetic acid R and dilute to 1000 mL.

Prepare the following solutions in mobile phase. For solution (1), dissolve 50.0 mg of the test substance and dilute to 100.0 mL. For solution (2), dilute 1.0 mL of solution (1) to 100 mL. For solution (3), dilute 1.0 mL of solution (2) to 10.0 mL. For solution (4), dissolve 5 mg of salicylic acid R in 100.0 mL. Dilute 1.0 mL of this solution to 100.0 mL. For solution (5), dissolve 5 mg of cytosine R and 5 mg of uracil R and dilute to 100.0 mL. Dilute 2.0 mL of this solution to 10.0 mL. For solution (6), dissolve 5 mg of lamivudine for system suitability RS (containing lamivudine and lamivudine impurities A and B) in 2 mL, add 1 mL of solution (5) and dilute to 10 mL.

Operate with a flow rate of 1.0 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of about 277 nm. For identity test C.2, use a diode array detector in the range of 210 to 300 nm. Maintain the temperature of the column at 35 °C.

Inject alternately 10 μl each of solutions (1), (2), (3), (4) and (6).

Record the chromatograms for about three times the retention time of lamivudine. Use the chromatogram supplied with lamivudine for system suitability RS and the chromatograms obtained with solutions (4) and (6) to identify the peaks due to impurities A, B, C, E and F. The impurity peaks are eluted at the following relative retention times with reference to lamivudine (retention time about 9 minutes): impurity E (cytosine) about 0.28; impurity F (uracil) about 0.32; impurity A about 0.36; impurity B about 0.91; impurity J about 1.45; impurity C (salicylic acid) about 2.32.

The test is not valid unless, in the chromatogram obtained with solution (6), the resolution factor between the peaks due to impurity B and lamivudine is at least 1.5. Also, the test is not valid unless, in the chromatogram obtained with solution (3), the peak due to lamivudine is detected with a signal-to-noise ratio of at least 20.

In the chromatogram obtained with solution (1):

- the area of any peak corresponding to impurity A is not greater than three times the area of the peak due to lamivudine in the chromatogram obtained with solution (3) (0.3%);
the area of any peak corresponding to impurity B is not greater than twice the area of the
peak due to lamivudine in the chromatogram obtained with solution (3) (0.2%);

- the area of any peak corresponding to impurity C is not greater than the peak due to
  salicylic acid in the chromatogram obtained with solution (4) (0.1%);

- the area of any peak corresponding to impurity E, when multiplied by a correction factor
  of 0.6, is not greater than the area of the peak due to lamivudine in the chromatogram
  obtained with solution (3) (0.1%);

- the area of any peak corresponding to either impurities F or J, when multiplied by a
  correction factor of 2.2, is not greater than the area of the peak due to lamivudine in the
  chromatogram obtained with solution (3) (0.1%);

- the area of any other impurity peak is not greater than the area of the peak due to
  lamivudine in the chromatogram obtained with solution (3) (0.1%);

- the sum of the corrected areas of any peaks corresponding to impurities E, F or J and the
  areas of all other impurity peaks is not greater than 0.6 times the area of the peak due to
  lamivudine in the chromatogram obtained with solution (2) (0.6%). Disregard any peak
  with an area less than 0.5 times the area of the principal peak obtained with solution (3)
  (0.05%).

**Assay**

- Either method A or method B may be applied.

**A.** Carry out the test as described under 1.14.4 High-performance liquid chromatography,
  using the conditions given under “Related substances” with the following modifications.

  - Use solution (1) as described under “Related substances”. For solution (2), dissolve 50.0
    mg of lamivudine RS in mobile phase and dilute to 100.0 mL with the same solvent.
  - Inject alternately 10 μL each of solutions (1) and (2).

  Measure the areas of the peaks corresponding to lamivudine obtained in the
  chromatograms of solution (1) and (2) and calculate the percentage content of
  C₈H₁₁N₃O₃S, using the declared content of C₈H₁₁N₃O₃S in lamivudine RS.
B. **Transfer 50.0 mg of the test substance into a 500 mL volumetric flask and dissolve in about 400 mL of water R. Sonicate, if necessary. Cool to room temperature, dilute to volume with water R and mix. Dilute 5 mL of this solution to 50 mL with sulfuric acid (0.1 mol/l) VS and mix.**

Measure the absorbance \((1.6)\) of a 1.0 cm layer of the final solution at a maximum about 280 nm using a solution prepared by mixing 5 mL of water R with 50 mL of sulfuric acid (0.1 mol/l) VS as a blank. Calculate the content of \(\text{C}_8\text{H}_{11}\text{N}_3\text{O}_3\text{S}\) using the absorptivity value of 60.7 \(\left(\frac{A}{c \cdot l}\right) = 607\).

**Impurities**

A. \((2\text{RS},5\text{SR})-5-(4\text{-amino-2-oxopyrimidin-1(2H)}-\text{-yl})-1,3\text{-oxathiolane-2-carboxylic acid (lamivudine carboxylic acid)} (synthesis related impurity).\)

![](image)

B. \(4\text{-amino-1-[(2\text{RS},5\text{RS})-2-(hydroxymethyl)-1,3\text{-oxathiolan-5-yl}]pyrimidin-2(1H)-one, (lamivudine diastereomer, (+/-)-trans-lamivudine)} (synthesis related impurity).\)

![](image)
C. 2-hydroxybenzoic acid (salicylic acid) (synthesis related impurity).

D. (+)-4-amino-1-[(2S,5R)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidin-2(1H)-one (ent-lamivudine) (synthesis related impurity).

E. 4-aminopyrimidin-2(1H)-one (cytosine) (synthesis related impurity, degradation product).

F. Pyrimidine-2,4(1H,3H)-dione (uracil) (synthesis related impurity, degradation product).
G. 4-amino-1-[(2R,3S,5S)-2-(hydroxymethyl)-3-oxo-1,3\(\lambda^4\)-oxathiolan-5-yl]pyrimidin-2(1\(H\))-one (lamivudine S-sulfoxide) (synthesis related impurity, degradation product).

H. 4-amino-1-[(2R,3R,5S)-2-(hydroxymethyl)-3-oxo-1,3\(\lambda^4\)-oxathiolan-5-yl]pyrimidin-2(1\(H\))-one (lamivudine R-sulfoxide) (synthesis related impurity, degradation product).

I. (+)-4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-oxathiolan-4-yl]pyrimidin-2(1\(H\))-one.
J. 1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidine-2,4(1H,3H)-dione; 1-
[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5yl]uracil (lamivudine uracil derivative)
(degradation product).

Reference substances invoked

Lamivudine RS
Established ICRS.

Lamivudine for system suitability (containing lamivudine and impurities A and B) RS
Established ICRS.

Lamivudine for peak identification (containing lamivudine and impurity D) RS

It is intended to refer to Lamivudine for system suitability 2 CRS established by the European
Pharmacopoeia.

Lamivudine (Lamivudinum)

\[
\text{C}_8\text{H}_{11}\text{N}_3\text{O}_3\text{S}
\]

Relative molecular mass. 229.3

Chemical name. (+)-4-Amino 1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidine-
2(1H)-one; CAS Reg. No. 134678-17-4.
**Description.** A white or almost white powder.

**Solubility.** Soluble in water; sparingly soluble in methanol R; practically insoluble in acetone R.

**Category.** Antiretroviral (Nucleoside Reverse Transcriptase Inhibitor).

**Storage.** Lamivudine should be kept in a well-closed container, protected from light.

**Additional information.** Lamivudine may exhibit polymorphism.

**Requirements**

**Definition.** Lamivudine contains not less than 97.0% and not more than 103.0% of C$_8$H$_{11}$N$_3$O$_3$S, calculated with reference to the dried substance.

**Manufacture.** The production method is validated to demonstrate that the substance, if tested, would comply with a limit of not more than 0.3% for the (2S,5R)-enantiomer using a suitable chiral chromatographic method.

**Identity tests**

Either tests A, B and D or tests C and D may be applied.

**A.** Carry out test A.1 or, where UV detection is not available, test A.2.

A.1 Carry out the test as described under **1.14.1 Thin-layer chromatography**, using silica gel R6 as the coating substance and a mixture of 67 volumes of dichloromethane R, 20 volumes of acetonitrile R, 10 volumes of methanol R and 3 volumes of ammonia (~260 g/l) TS as the mobile phase. Apply separately to the plate 5 μl of each of the following 2 solutions in methanol containing (A) 5 mg of the test substance per mL and (B) 5 mg of lamivudine RS per mL. After removing the plate from the chromatographic chamber, allow it to dry exhaustively in air or in a current of cool air. Examine the chromatogram in ultraviolet light (254 nm).

The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.
A.2 Carry out the test as described under 1.14.1 Thin-layer chromatography, using the conditions described above under test A.1 but using silica gel R5 as the coating substance. Spray with vanillin/sulfuric acid TS1. Heat the plate for a few minutes at 120°C. Examine the chromatogram in daylight. The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

B. The absorption spectrum (1.6) of the final solution prepared for the Assay, when observed between 210 nm and 300 nm, exhibits one maximum at about 280 nm; the specific absorbance \( A_{1%}^{1cm} \) is between 577 to 637.

C. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from lamivudine RS or with the reference spectrum of lamivudine. If the spectra thus obtained are not concordant, repeat the test using the residues obtained by separately dissolving the test substance and lamivudine RS in a small amount of methanol R and evaporating to dryness. The infrared absorption spectrum is concordant with the spectrum obtained from lamivudine RS.

D. Determine the specific optical rotation (1.4) using a 10 mg/mL solution in methanol R and calculate with reference to the dried substance; \( [\alpha]_{D}^{25^\circ} = -135^\circ \) to \(-144^\circ\).

Heavy metals. Use 1.0 g for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals, procedure 4. Determine the heavy metals content according to method A; not more than 20 μg/g.

Sulfated ash (2.3). Not more than 2.0 mg/g.

Loss on drying. Dry for 3 hours at 105°C; it loses not more than 5 mg/g.

Related substances. Carry out the test as described under 1.14.4 High-performance liquid chromatography, using a stainless steel column (25cm x 4.6mm) packed with base deactivated particles of silica gel the surface of which has been modified with chemically bonded
octadecylsilyl groups (5μm). As the mobile phase, use a mixture of 5 volumes of methanol R and 95 volumes of buffer pH 3.8 (a 1.9 g/l solution of ammonium acetate R, previously adjusted to pH 3.8 with glacial acetic acid R).

Prepare the following solutions. For solution (1) prepare a 0.5 mg/mL solution of the test substance in the mobile phase. For solution (2) dilute 1.0 mL of solution (1) to 100 mL with mobile phase and then dilute 1.0 mL of this solution to 10 mL. For solution (3) dissolve 25 mg of salicylic acid R in 100 mL of mobile phase, dilute 1.0 mL of the resulting solution to 50 mL with the mobile phase and then further dilute 1.0 mL to 10 mL with the mobile phase. For solution (4) dissolve about 5 mg of lamivudine for system suitability RS (containing lamivudine and lamivudine impurities A and B) in the mobile phase, add 1 mL of solution (CU) prepared as described below and dilute to 10 mL with the mobile phase. For solution (CU) dissolve 25 mg of cytosine R and 25 mg of uracil R in the mobile phase, dilute to 50 mL with the mobile phase and dilute 1 mL of the resulting solution to 10 mL with the mobile phase.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 277 nm.

Maintain the temperature of the column at 35°C.

Inject separately 10 μl each of solutions (1), (2), (3) and (4). Record the chromatograms for about 3 times the retention time of lamivudine. The test is not valid unless in the chromatogram obtained with solution (4) the resolution factor between the peaks due to lamivudine and impurity B is at least 1.5.

Use the chromatogram supplied with lamivudine for system suitability RS and the chromatogram obtained with solutions (4) and (3) to identify the peaks due to impurities A, B, E, F and C. The impurity peaks are eluted at the following relative retention times with reference to lamivudine (retention time about 11 to 12 minutes): impurity E (cytosine) about 0.31; impurity F (uracil) about 0.36; impurity A about 0.40; impurity B about 0.9; impurity C (salicylic acid) about 2.6.

In the chromatogram obtained with solution (1):
- the area of any peak corresponding to impurity A is not greater than 3 times the area of the peak in the chromatogram obtained with solution (2) (0.3%),

- the area of any peak corresponding to impurity B is not greater than twice the area of the peak in the chromatogram obtained with solution (2) (0.2%),

- the area of any peak corresponding to impurity C is not greater than that of the principal peak in the chromatogram obtained with solution (3) (0.1%),

- the area of any individual peak corresponding to impurity E, when multiplied by a correction factor of 0.6, is not greater than the area of the peak in the chromatogram obtained with solution (2) (0.1%),

- the area of any individual peak corresponding to impurity F or any peak eluting shortly after the principal peak but well before that, if any, corresponding to impurity C (impurity J), when multiplied by a correction factor of 2.2, is not greater than the area of the peak in the chromatogram obtained with solution (2) (0.1%),

- the area of any other peak, apart from the principal peak, is not greater than the area of the peak in the chromatogram obtained with solution (2) (0.1%),

- the sum of the areas (corrected, where necessary) of all the peaks, apart from the principal peak, is not greater than 6 times the area of the peak obtained with solution (2) (0.6%). Disregard any peak with an area less than 0.5 times the area of the principal peak obtained with solution (2) (0.05%).

Assay. Transfer into a 500-mL volumetric flask about 0.05 g, accurately weighed, and dissolve in about 400 mL of water R using an ultrasonic bath, if necessary. Cool to room temperature and dilute to volume with water R and mix.

Dilute 5 mL of this solution to 50 mL with sulfuric acid (0.1 mol/l) VS and mix. For the blank, use a solution prepared by mixing 5 mL of water R with 50 mL of sulfuric acid (0.1 mol/l) VS.
Measure the absorbance (1.6) of a 1-cm layer of the final solution at a maximum about 280 nm against a solvent cell containing the blank. Calculate the content of C₈H₁₁N₅O₃S using the absorptivity value of 60.7 (A₁%₁cm = 607).

Impurities

A.

\[
\begin{align*}
\text{and enantiomer} \\
\end{align*}
\]

(2RS,5RS)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-1,3-oxathiolane-2-carboxylic acid,

B.

\[
\begin{align*}
\text{and enantiomer} \\
\end{align*}
\]

4-amino-1-\{(2RS,5RS)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl\}pyrimidin-2(1H)-one,

C.

\[
\begin{align*}
\end{align*}
\]

2-hydroxybenzoic acid (salicylic acid),

D.
(+) 4-amino-1-[(2S,5R)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidin-2(1H)-one (ent-lamivudine), [see under Manufacture]

\[\text{H.} \]

4-aminopyrimidin-2(1H)-one (cytosine).

\[\text{F.} \]

pyrimidine-2,4(1H,3H)-dione (uracil).

\[\text{G.} \]

4-amino-1-[(2R,3S,5S)-2-(hydroxymethyl)-3-oxo-1,3\lambda^4-oxathiolan-5-yl]pyrimidin-2(1H)-one.
4-amino-1-[(2R,3R,5S)-2-(hydroxymethyl)-3-oxo-1,3,4-oxathiolan-5-yl]pyrimidin-2(1H)-one.

I. 229.3 C_{8}H_{11}N_{3}O_{3}S

(+)-4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-oxathiolan-4-yl]pyrimidin-2(1H)-one.

J.

1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidine 2,4(1H,3H)-dione.

1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidine 2,4(1H,3H)-dione.