Selamectin

Type of Posting	Revision Bulletin, Postponement
Posting Date	28–April–2017
Official Date	01–May–2017
Expert Committee	Chemical Medicines Monographs 3
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 3 Expert Committee has indefinitely postponed the test for *Organic impurities* in the Selamectin monograph.

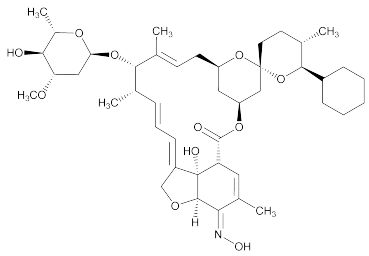
USP has received comments concerning the system suitability resolution requirement in the test for *Organic impurities.* Additional information will be required in order to resolve these concerns. Interested parties are invited to contact USP for additional information on this topic and to get involved in the revision process. If data cannot be obtained to revise the resolution requirement, the Expert Committee will consider removing this criterion from the test for Organic impurities. The process for and timing of any future revision to include the test for *Organic impurities* will be determined following additional consideration by the Expert Committee and USP staff. Please note that other requirements such as those outlined in *General Notices* 5.60 *Impurities and Foreign Substances* and 5.60.10 *Other Impurities in USP and NF Articles* are still applicable.

The Selamectin Revision Bulletin Postponement will supersede the monograph becoming official in *USP 40–NF 35*.

Should you have any questions, please contact Morgan Puderbaugh, Senior Scientific Liaison (301-998-6833 or mxp@usp.org).

Add the following:

▲Selamectin



$C_{43}H_{63}NO_{11}$ *769.96*

25-Cyclohexyl-4′-*O*-de(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-5-demethoxy-25-de(1-methylpropyl)-22,23-dihydro-5-(hydroxyimino)-avermectin A1a;
(2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*R*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-3′,4′,5′,6,6′,7,10,11,14,15,20a,20b-dodecahydro-20b-hydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-17,20(17a*H*)-dione 20-oxime [220119-17-5].

DEFINITION
Selamectin contains NLT 96.0% and NMT 102.0% of selamectin ($C_{43}H_{63}NO_{11}$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197⟩:** [NOTE—Methods described in ⟨197K⟩, ⟨197M⟩, or ⟨197A⟩ may be used.]
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **PROCEDURE**

Mobile phase: Acetonitrile and water (80:20)
Standard solution: 0.2 mg/mL of USP Selamectin RS in *Mobile phase*
Sample solution: 0.2 mg/mL of Selamectin in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 243 nm
Column: 3.9-mm × 15-cm; 4-µm packing L1
Column temperature: 30°
Flow rate: 1.0 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 1.5
Relative standard deviation: NMT 0.73%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of selamectin ($C_{43}H_{63}NO_{11}$) in the portion of Selamectin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Selamectin RS in the *Standard solution* (mg/mL)
C_U = concentration of Selamectin in the *Sample solution* (mg/mL)

Acceptance criteria: 96.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES
- **RESIDUE ON IGNITION ⟨281⟩**

Sample: 1.0 g
Acceptance criteria: NMT 0.1%

Change to read:

- **ORGANIC IMPURITIES**

Solution A: Water
Solution B: Acetonitrile
Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	40	60
28	40	60
45	20	80

Diluent: Acetonitrile and water (60:40)
System suitability solution: 500 µg/mL of USP Selamectin RS in *Diluent*
Standard solution: 2.5 µg/mL of USP Selamectin RS in *Diluent*
Sample solution: 500 µg/mL of Selamectin in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 243 nm
Column: 3.9-mm × 15-cm; 4-µm packing L1
Column temperature: 30°
Flow rate: 2.0 mL/min
Injection volume: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—USP Selamectin RS contains the impurities didehydroselamectin and selamectin aglycone as minor components. The relative retention times for didehydroselamectin and selamectin aglycone are 0.4 and 0.5, respectively.]
Suitability requirements
Resolution: NLT 4.0 between didehydroselamectin and selamectin aglycone, *System suitability solution*
Tailing factor: NMT 1.6 for the selamectin peak, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Selamectin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of selamectin from the *Standard solution*
C_S = concentration of USP Selamectin RS in the *Standard solution* (µg/mL)
C_U = concentration of Selamectin in the *Sample solution* (µg/mL)
F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting level for impurities is 0.2%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Hydroxyselamectin[a]	0.2	1.0	2.0
Didehydroselamectin[b]	0.4	1.0	2.0
Selamectin aglycone[c]	0.5	1.2	1.5
Selamectin	1.0	—	—
α-Oleandrosyl selamectin[d]	1.7	0.67	1.5
Any other individual impurity	—	1.0	1.0
Total impurities	—	—	4.0

[a] (2a*E*,2′*R*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*R*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-3′,4′,5′,6,6′,7,10,11,14,15,20a,20b-dodecahydro-4′,20b-dihydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-17,20(17a*H*)-dione 20-oxime.

[b] (2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-5′,6,6′,7,10,11,14,15,20a,20b-decahydro-20b-hydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-17,20(17a*H*)-dione 20-oxime.

[c] (2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-5′,6,6′,7,10,11,14,15,20a,20b-decahydro-7,20b-dihydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-17,20(17a*H*)-dione 20-oxime.

[d] (2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*R*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-3′,4′,5′,6,6′,7,10,11,14,15,20a,20b-dodecahydro-20b-hydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-17,20(17a*H*)-dione 20-oxime.

•(Postponed indefinitely)• (RB 1-May-2017)

SPECIFIC TESTS

- **WATER DETERMINATION ⟨921⟩,** *Method I, Method Ia*
  Sample: 0.20 g
  Acceptance criteria: NMT 7.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in a tight container.
- **LABELING:** Label it to indicate that it is for veterinary use only.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Selamectin RS

▲*USP40*