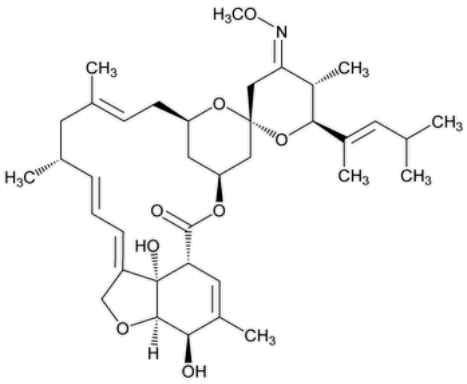
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-56CD88AE-F246-42AA-9EAF-83750D745EDD_5_en-US
DOI: https://doi.org/10.31003/USPNF_M54920_05_01
DOI Ref: v3a2y



# Moxidectin



$C_{37}H_{53}NO_8$ 639.82

(6*R*,25*S*)-5-*O*-Demethyl-28-deoxy-25-[(*E*)-1,3-dimethyl-1-butenyl]-6,28-epoxy-23-oxomilbemycin B 23-(*E*)-(*O*-methyloxime); (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-6'-[(*E*)-1,3-Dimethyl-1-butenyl]-5',6,6',7,10,11,14,15,17a,20,20a,20b-dodecahydro-20,20b-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime) CAS RN®: 113507-06-5; UNII: NGU5H31YO9.

## DEFINITION

Moxidectin contains NLT 92.0% and NMT 102.0% of moxidectin ($C_{37}H_{53}NO_8$), calculated on the anhydrous basis. It may contain a suitable antioxidant.

## IDENTIFICATION

***Change to read:***

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **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**

**Buffer:** Dissolve 7.7 g of ammonium acetate in 400 mL of water, and adjust with glacial acetic acid to a pH of 4.8.

**Mobile phase:** Acetonitrile and *Buffer* (60:40)

**Standard solution:** 1.0 mg/mL of USP Moxidectin RS in acetonitrile. Sonicate if necessary to facilitate dissolution.

**Sample solution:** 1.0 mg/mL of Moxidectin in acetonitrile. Sonicate if necessary to facilitate dissolution.

**Chromatographic system**

(See *Chromatography ⟨621⟩, System Suitability*.)

**Mode:** LC

**Detector:** UV 242 nm

**Column:** 3.9-mm × 15-cm; 4-µm packing L1

**Column temperature:** 50°

**Flow rate:** 2.5 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Relative standard deviation:** NMT 1%, for 4 replicate injections

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of moxidectin ($C_{37}H_{53}NO_8$) in the portion of Moxidectin 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 Moxidectin RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Moxidectin in the *Sample solution* (mg/mL)

**Acceptance criteria:** 92.0%–102.0% on the anhydrous basis

**IMPURITIES**

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

***Delete the following:***

▲• **Heavy Metals,** *Method II* ⟨231⟩**:** NMT 20 ppm▲ (Official 1-Jan-2018)

• **Organic Impurities: Early-Eluting Impurities**

**Buffer, Mobile phase, Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**System suitability solution:** 1.0 mg/mL of USP Moxidectin System Suitability Mixture RS in acetonitrile. Sonicate if necessary to facilitate dissolution.

**Standard solution:** 0.01 mg/mL of Moxidectin in acetonitrile from the *Sample solution*

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Peak-to-valley ratio:** NLT 3.0 between moxidectin 17a-epimer and moxidectin

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each early-eluting impurity in the portion of Moxidectin taken:

$$\text{Result} = (r_U/r_S) \times F \times D \times 100$$

$r_U$ = peak response of each early-eluting impurity from the *Sample solution*

$r_S$ = peak response of moxidectin from the *Standard solution*

$F$ = *Assay* value expressed as a decimal

$D$ = dilution factor used to prepare the *Standard solution*, 0.01

**Acceptance criteria:** See *Table 1*.

The reporting level for impurities is 0.1%. Disregard the peak due to the stabilizer (identify this peak, where applicable, by injecting a suitable reference solution).

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Moxidectin butenyl analog[a] | 0.5 | 1.5 |
| 5'-Demethyl moxidectin[b] | 0.7 | 0.5 |
| Moxidectin pentenyl analog[c] | 0.75 | 1.5 |
| Moxidectin 17a-epimer[d] | 0.9 | 2.5 |
| Moxidectin | 1.0 | — |
| Sum of moxidectin 19-*S*-17a-ene[e] and moxidectin ethyl isomers[f] | 1.3–1.5 | 1.7[g] |
| Milbemycin B analog (moxidectin open ring)[h] | 1.6 | 1.5 |
| Any other individual impurity eluting before milbemycin B analog | — | 0.5 |

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| (moxidectin open ring) | | |

[a] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-6'-[(*E*)-But-2-en-2-yl]-5',6,6',7,10,11,14,15,17a,20,20a,20b-dodecahydro-20,20b-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[b] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,17a,20,20a,20b-Dodecahydro-20,20b-dihydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-6,8,19-trimethylspiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2'-[2*H*]pyran]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[c] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,17a,20,20a,20b-Dodecahydro-20,20b-dihydroxy-5',6,8,19-tetramethyl-6'-[(*E*)-pent-2-en-2-yl]spiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*pq*][2,6]benzodioxacyclooctadecin-13,2'-[2*H*]pyran]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[d] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*S*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,17a,20,20a,20b-Dodecahydro-20,20b-dihydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[e] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,19*S*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,19,20,20a,20b-Dodecahydro-20,20b-dihydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[f] Mixture of five possible isomers, where one methyl group in the analyte is replaced with an ethyl group.

[g] If present, moxidectin 19-*S*-17a-ene and the moxidectin ethyl isomers may not be completely resolved by the method. These peaks are integrated together to determine conformance.

[h] (2'*R*,3*S*,5'*S*,6'*S*,7*R*,9*E*,12*R*,13*E*,15*E*,16a*S*,18*S*,20a*R*)-16a,18-Dihydroxy-5',10,12,16,19-pentamethyl-6'-[(*E*)-4-methylpent-2-en-2-yl]-3,4,5',6',7,8,11,12,16a,17,18,20a-dodecahydro-1*H*-spiro[3,7-methanobenzo[*g*][1,5]dioxacyclooctadecin-5,2'-[2*H*]pyran]-14'-dione (*E*)-(*O*-methyloxime).

- **Organic Impurities: Late-Eluting Impurities**

**Buffer:** Dissolve 3.8 g of ammonium acetate in 250 mL of water, and adjust with glacial acetic acid to a pH of 4.2.

**Mobile phase:** Acetonitrile and *Buffer* (75:25)

**System suitability solution:** 3.0 mg/mL of USP Moxidectin System Suitability Mixture RS in acetonitrile. Sonicate if necessary to facilitate dissolution.

**Sample solution:** 3.0 mg/mL of Moxidectin in acetonitrile. Sonicate if necessary to facilitate dissolution.

**Standard solution:** 0.03 mg/mL of Moxidectin in acetonitrile from the *Sample solution*

**Chromatographic system**

(See *Chromatography ⟨621⟩, System Suitability*.)

**Mode:** LC

**Detector:** UV 242 nm

**Column:** 3.9-mm × 15-cm; 4-µm packing L1

**Column temperature:** 35°

**Flow rate:** 2 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 10 times the retention time of moxidectin

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 1.0 between moxidectin deoxydiene/methylthiomethoxymoxidectin and 20b-methylthiomoxidectin

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each late-eluting impurity in the portion of Moxidectin taken:

$$\text{Result} = (r_U/r_S) \times F \times D \times 100$$

$r_U$ = peak response of each late-eluting impurity from the *Sample solution*

$r_S$ = peak response of moxidectin from the *Standard solution*

$F$ = *Assay* value expressed as a decimal

$D$ = dilution factor used to prepare the *Standard solution*, 0.01

**Acceptance criteria:** See *Table 2*.

The reporting level for impurities is 0.1%. Disregard the peak due to the stabilizer (identify this peak, where applicable, by injecting a suitable reference solution).

**Table 2**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Moxidectin | 1.0 | — |
| Moxidectin deoxydiene[a] and 4'-methylthiomethoxymoxidectin[b] | 2.0 | 1.0[c] |
| 20b-Methylthiomoxidectin[d] | 2.2 | 0.5 |
| 20-Nitrobenzoylmoxidectin[e] | 3.4 | 0.5 |
| Any other individual impurity eluting after the milbemycin B analog (moxidectin open ring) (≈1.4 RRT) | — | 0.5 |

[a] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,20a,20b-Decahydro-20b-hydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[b] (2a*E*,4*E*,4'*S*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)- 3',4',5',6,6',7,10,11,14,15,17a,20,20a,20b-Tetradecahydro-20,20b-dihydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-4'-methylthiomethoxy-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-one.

[c] If present, impurities moxidectin deoxydiene and 4'-methylthiomethoxymoxidectin may not be completely resolved by the method. These peaks are integrated together to determine conformance.

[d] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,17a,20,20a,20b-Dodecahydro-20-hydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-20b-methylthiomethoxy-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

[e] (2a*E*,4*E*,5'*R*,6*R*,6'*S*,8*E*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-5',6,6',7,10,11,14,15,17a,20,20a,20b-Dodecahydro-20b-hydroxy-6'-[(*E*)-4-methylpent-2-en-2-yl]-20-(4-nitrobenzoyloxy)-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]-4',17(3'*H*)-dione 4'-(*E*)-(*O*-methyloxime).

• **Total Organic Impurities**

**Analysis:** Calculate the sum of all impurities found in the tests for *Organic Impurities: Early-Eluting Impurities* and *Organic Impurities: Late-Eluting Impurities* in the portion of Moxidectin taken.

**Acceptance criteria:** NMT 7.0%

## SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 1.3%

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store in a refrigerator.

***Change to read:***

• **Labeling:** ▲If it is intended for use in animals, it is so labeled.▲ (RB 27-Jun-2018) Label it to state the name(s) and amount(s) of any added substance(s).

• **USP Reference Standards ⟨11⟩**

USP Moxidectin RS

USP Moxidectin System Suitability Mixture RS

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| MOXIDECTIN | Documentary Standards Support | SM32020 Small Molecules 3 |

**Chromatographic Database Information:** Chromatographic Database

**Most Recently Appeared In:**
Pharmacopeial Forum: Volume No. PF 38(5)

**Current DocID: GUID-56CD88AE-F246-42AA-9EAF-83750D745EDD_5_en-US**
**DOI: https://doi.org/10.31003/USPNF_M54920_05_01**
**DOI ref: v3a2y**