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Doxycycline Compounded Oral Suspension, Veterinary

DEFINITION

Change to read:

Doxycycline Compounded Oral Suspension, Veterinary contains NLT 90.0% and NMT 110.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$). Prepare Oral Suspension, Veterinary 50 mg/mL ▲in a paraben solution▲ (USP 1-May-2020) as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩). For this preparation, a *Paraben solution* needs to be separately prepared.

Methylparaben	25 mg
Propylparaben	12.5 mg
Purified Water, a sufficient quantity to make	50 mL

Prepare a *Paraben solution* by dissolving the *Methylparaben* and *Propylparaben* in a sufficient amount of Purified Water to bring to final volume.

Doxycycline (as Doxycycline Hyclate) powder▲▲ (USP 1-May-2020)	2.5 g of doxycycline (calculate)[a]
Calcium Hydroxide▲▲ (USP 1-May-2020)	Calculate (see below)[b]
Glycerin	12.5 mL
Polysorbate 20▲▲ (USP 1-May-2020)	0.063 mL
Sodium Metabisulfite▲▲ (USP 1-May-2020) (granular)	0.05 g
Carboxymethylcellulose Sodium▲▲ (USP 1-May-2020) (medium viscosity)	0.25 g
Steviol Glycosides 95%	0.15 g
Paraben solution, a sufficient quantity to make	50 mL

[a] Calculate the amount of *Doxycycline Hyclate* powder required by dividing the weight of doxycycline required by the potency of the *Doxycycline Hyclate* powder obtained from the Certificate of Analysis. ▲[NOTE—Unit conversion is needed in the calculation.]▲ (USP 1-May-2020)

[b] Calculate the amount of *Calcium Hydroxide* needed, in grams, by multiplying the amount of *Doxycycline Hyclate* needed, in grams, by 0.21.

Pour the calculated amount of *Doxycycline Hyclate* powder into a suitable mortar, and mix with about 12.5 mL of *Paraben solution* until all the solids are dissolved. Do not use more than 5 mL of *Paraben solution* for each gram of the calculated amount of *Doxycycline Hyclate*. Add the calculated amount of *Calcium Hydroxide* to the mortar, and mix with the pestle until the mixture thickens up and has a pasty consistency. [NOTE—Reaction may take a few minutes to occur. The pasty mixture may look dry and harden up which is an indication that the reaction is complete.]

In a separate beaker, mix *Glycerin* and *Polysorbate 20* with about 30 mL of the *Paraben solution*. Add *Sodium Metabisulfite* to the mixture of *Glycerin*, *Polysorbate 20*, and *Paraben solution* with mixing.

Add approximately two thirds of the separately prepared mixture of *Glycerin*, *Polysorbate 20*, *Sodium Metabisulfite*, and *Paraben solution* to the mortar in small increments with continuous mixing to make an even mixture free of lumps. Transfer the doxycycline mixture from the mortar to an appropriately sized beaker. Rinse the mortar three times, each time with one third of the remaining *Glycerin*, *Polysorbate 20*, *Sodium Metabisulfite*, and *Paraben solution*, and combine with the doxycycline mixture in the beaker. Add *Steviol Glycosides 95%* to the beaker.

Disperse *Carboxymethylcellulose Sodium* through a 40-mesh sieve, and mix into the suspension until homogenous. Add sufficient *Paraben solution* to bring to final volume. Mix well.

▲Prepare Oral Suspension, Veterinary 100 mg/mL in a fixed oil base as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

Doxycycline (as Doxycycline Hyclate) powder	10 g of doxycycline (calculate)[a]
Steviol Glycosides 95%	0.3 g
Acesulfame Potassium	0.3 g
Flavor (chicken, grilled, natural, oil miscible)[b]	3 mL
PCCA Fixed Oil Suspension Vehicle,[b] a sufficient quantity to make	100 mL

[a] Calculate the amount of *Doxycycline Hyclate* powder required by dividing the weight of doxycycline required by the potency of the *Doxycycline Hyclate* powder obtained from the Certificate of Analysis. [NOTE—Unit conversion is needed in the calculation.]

[b] PCCA, Houston, TX.

Place the calculated amount of *Doxycycline Hyclate* powder, *Steviol Glycosides 95%*, and *Acesulfame Potassium* into a suitable container and triturate to a fine powder. Add a sufficient amount of *PCCA Fixed Oil Suspension Vehicle* to form a smooth paste. Add *Flavor* and mix thoroughly. Add a sufficient amount of *PCCA Fixed Oil Suspension Vehicle* to make the contents pourable. Transfer the contents, stepwise and quantitatively, to a calibrated container using the *PCCA Fixed Oil Suspension Vehicle*. Add sufficient *PCCA Fixed Oil Suspension Vehicle* to bring to final volume, and mix well.▲ (USP 1-May-2020)

ASSAY

Change to read:

• **PROCEDURE ▲1: ORAL SUSPENSION IN PARABEN SOLUTION▲** (USP 1-MAY-2020)

Solution A: 20 mM monobasic sodium phosphate containing 0.74 g/L of sodium hydroxide. Adjust with phosphoric acid to a pH of 7.0.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Acetonitrile (%)	Solution A (%)
0	1	99
7	80	20
8	80	20
8.1	1	99
14	1	99

Diluent: Acetonitrile and 1 N hydrochloric acid (50:50)

Standard solution: 0.5 mg/mL of doxycycline prepared from USP Doxycycline Hyclate RS in *Diluent*

Sample solution: Shake each bottle of Oral Suspension, Veterinary thoroughly. Transfer 0.5 mL of Oral Suspension, Veterinary to a 50-mL volumetric flask, add approximately 10 mL of *Diluent*, and vortex for 30 s. Dilute with *Diluent* to volume, and mix well.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for doxycycline is about 4.7 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) in the portion of Oral Suspension, Veterinary taken:

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

r_U = peak response of doxycycline from the *Sample solution*

r_S = peak response of doxycycline from the *Standard solution*

C_S = concentration of doxycycline in the *Standard solution* (mg/mL)

C_U = nominal concentration of doxycycline in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

Add the following:

▲• **Procedure 2: Oral Suspension in Fixed Oil**

Solution A: 1 mg/mL of trifluoroacetic acid in water

Solution B: 1 mg/mL of trifluoroacetic acid in acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2.6	70	30
2.8	10	90
3.0	90	10

Standard solution: 0.125 mg/mL of doxycycline prepared from USP Doxycycline Hyclate RS in methanol

Sample solution: Transfer 0.5 mL of Oral Suspension, Veterinary to a centrifuge tube and add 39.5 mL of methanol. Vortex for 1 min, sonicate for 2 min, and vortex again for 1 min until the solution is mixed well. Centrifuge this solution for 10 min. Transfer 1 mL of the supernatant to a 10-mL volumetric flask and add sufficient methanol to bring to volume. Centrifuge again for 10 min.

Chromatographic system

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

Mode: LC

Detector: UV 350 nm

Column: 2.1-mm × 50-mm; 1.7-µm packing L1

Autosampler temperature: 4°

Flow rate: 0.7 mL/min

Injection volume: 1.0 µL

System suitability

Sample: *Standard solution*

[Note—The retention time for doxycycline is about 2.7 min.]

Suitability requirements

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) in the portion of Oral Suspension, Veterinary taken:

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

r_U = peak response of doxycycline from the *Sample solution*

r_S = peak response of doxycycline from the *Standard solution*

C_S = concentration of doxycycline in the *Standard solution* (mg/mL)

C_U = nominal concentration of doxycycline in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%▲ (USP 1-May-2020)

SPECIFIC TESTS

Change to read:

• **pH** ⟨791⟩

▲**Oral Suspension in paraben solution:**▲ (USP 1-May-2020)

6.0–7.0

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Package in tight, light-resistant containers. ▲Store the Oral Suspension, Veterinary in paraben solution in a refrigerator. Store the Oral Suspension, Veterinary in fixed oil at controlled room temperature, or in a refrigerator.▲ (USP 1-May-2020)

• **Labeling:** Label it to indicate that it is to be well shaken before use, and to state the *Beyond-Use Date*. Label it to state that it is for veterinary use only.

Change to read:

• **Beyond-Use Date**

▲**Oral Suspension, Veterinary in paraben solution:** NMT 30 days after the date on which it was compounded when stored in a refrigerator

Oral Suspension, Veterinary in fixed oil: NMT 60 days after the date on which it was compounded when stored at controlled room temperature or in a refrigerator▲ (USP 1-May-2020)

• **USP Reference Standards** ⟨11⟩

USP Doxycycline Hyclate RS

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

Topic/Question	Contact	Expert Committee
DOXYCYCLINE COMPOUNDED ORAL SUSPENSION, VETERINARY	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

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