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Etodolac Extended-Release Tablets

» Etodolac Extended-Release Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of etodolac ($C_{17}H_{21}NO_3$).

Packaging and storage—Preserve in well-closed containers. Store at controlled room temperature, protected from light.

Labeling—When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

USP Reference standards ⟨11⟩—
USP Etodolac RS
USP Etodolac Related Compound A RS

(±)-8-Ethyl-1-methyl-1,3,4,9-tetrahydropyrano [3,4-*b*]-indole-1-acetic acid.
$C_{16}H_{19}NO_3$ 273.33

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.*

Dissolution ⟨711⟩—

TEST 1—

Medium: 0.05 M phosphate buffer, pH 7.4; 1000 mL.

Apparatus 2: 75 rpm, with USP sinker.

Times: 3, 6, 10, and 16 hours.

Procedure—Determine the amount of $C_{17}H_{21}NO_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 279 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Etodolac RS in the same *Medium.* Use *Medium* as the blank.

Tolerances—The percentages of the labeled amount of $C_{17}H_{21}NO_3$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
3	between 15% and 40%
6	between 35% and 70%
10	between 60% and 95%
16	not less than 80%

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.*

Medium: 0.05 M phosphate buffer, pH 7.5; 1000 mL.

Apparatus 2: 100 rpm.

Times: 2, 4, 8, and 14 hours.

Procedure—Determine the amount of $C_{17}H_{21}NO_3$ dissolved by comparing the difference between the absorbances of the filtered portions of the solution under test determined at 278 nm and 245 nm with the difference between the absorbances of a Standard solution having a known concentration of USP Etodolac RS in the same *Medium* determined at the same wavelengths. Use *Medium* as the blank, and use a 0.05-cm silica cell.

Tolerances—The percentages of the labeled amount of $C_{17}H_{21}NO_3$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
2	between 10% and 35%
4	between 30% and 55%
8	between 60% and 90%
14	not less than 85%

TEST 3—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.05 M phosphate buffer, pH 6.8; 1000 mL.

Apparatus 2: 75 rpm.

Times: 2, 4, 8, and 14 hours.

Procedure—Determine the amount of $C_{17}H_{21}NO_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 278 nm on portions of the solution under test passed through a 10-µm polyethylene filter, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Etodolac RS in the same *Medium*. Use *Medium* as the blank, and use a 0.05-cm silica cell.

Tolerances—The percentages of the labeled amount of $C_{17}H_{21}NO_3$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
2	between 10% and 30%
4	between 30% and 50%
8	between 55% and 75%
14	not less than 80%

TEST 4—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.05 M phosphate buffer, pH 6.8; 900 mL.

Apparatus 2: 75 rpm, with a wire helix sinker.

Times: 2, 4, 8, and 18 hours.

Test solution— Pass a portion of the solution under test through a suitable 70-µm filter.

Standard solution—From a solution containing about 4 mg per mL of USP Etodolac RS in *Mobile phase*, make dilutions with *Medium* to obtain a solution with a final concentration of about *L*/1500 mg per mL, where *L* is the tablet label claim, in mg.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and concentrated phosphoric acid (500:500:0.25). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Chromatographic system (see Chromatography ⟨621⟩)— The liquid chromatograph is equipped with a 274-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. The column is maintained at 25°. Chromatograph the *Standard solution*, 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 10 µL) of the *Standard solution* and *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of etodolac dissolved at the times specified.

Tolerances—The percentages of the labeled amount of $C_{17}H_{21}NO_3$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
2	between 10% and 30%
4	between 20% and 45%

Time (hours)	Amount dissolved
8	between 40% and 65%
18	not less than 80%

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

Chromatographic purity—

Diluent, Mobile phase, and *System suitability solution*—Proceed as directed in the *Assay.*

Test solution—Use the *Assay preparation*.

Chromatographic system—Prepare as directed in the *Assay.* Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 for etodolac related compound A and 1.0 for etodolac; the resolution, *R,* between etodolac related compound A and etodolac is not less than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Inject a volume (about 10 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure all of the peak areas. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the peak area for each impurity, and r_S is the sum of the areas of all the peaks: not more than 0.2% of any individual impurity is found; and not more than 0.75% of total impurities is found.

Assay—

Diluent—Use acetonitrile.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and phosphoric acid (500:500:0.25). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

System suitability solution—Dissolve accurately weighed quantities of USP Etodolac RS and USP Etodolac Related Compound A RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having known concentrations of about 0.48 mg per mL and 0.05 mg per mL, respectively.

Standard preparation—Dissolve an accurately weighed quantity of USP Etodolac RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having a known concentration of about 0.6 mg per mL.

Assay preparation—[Note—Do not finely powder Tablets.] Weigh and powder not fewer than 20 Tablets, and transfer an accurately weighed portion of the powder, equivalent to about 600 mg of etodolac, to a 200-mL volumetric flask. Add about 100 mL of *Diluent,* mix, and shake for 40 minutes by mechanical means. Dilute with *Diluent* to volume, and mix. Pass through a filter having a 0.45-µm porosity, discarding the first 3 mL of the filtrate. Transfer 2.0 mL of the filtrate to a 10-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 274-nm detector, a 4.0-mm × 4.0-cm guard column that contains 5-µm packing L7, and a 4.0-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 for etodolac related compound A and 1.0 for etodolac; the resolution, *R,* between etodolac related compound A and etodolac is not less than 2.5; and the tailing factor is not more than 2.0. Chromatograph the *Standard preparation,* 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 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of etodolac ($C_{17}H_{21}NO_3$) in the portion of Tablets taken by the formula:

$$1000C(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Etodolac RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
ETODOLAC EXTENDED-RELEASE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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