C_i = concentration of alprazolam in the *Sample solution* at the specified time point (mg/mL)
V = volume of *Medium*, 500 mL
L = label claim (mg/Tablet)
V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 5*.

Table 5

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	NMT 25
2	4	40–65
3	8	65–95
4	16	NLT 85

The percentages of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$) released at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

Buffer: 5.4 g/L of monobasic potassium phosphate (KH_2PO_4) in water. Adjust with phosphoric acid to a pH of 3.4.
Solution A: Acetonitrile, methanol, and *Buffer* (27:10:63)
Solution B: Acetonitrile, methanol, and *Buffer* (7:3:10)
Mobile phase: See *Table 6*.

Table 6

Time (min)	Solution A (%)	Solution B (%)
0	95	5
22	95	5
25	15	85
60	15	85
60.1	95	5
70	95	5

System suitability solution: 1 µg/mL each of USP Chlordiazepoxide Related Compound A RS, USP Alprazolam Related Compound A RS, and USP Nordazepam RS; and 0.4 µg/mL of USP Alprazolam RS in methanol
Standard solution: 0.4 µg/mL of USP Alprazolam RS in methanol
Sample solution: From NLT 20 Tablets ground to a fine powder, transfer an amount of powder to a suitable flask to obtain a nominal concentration of 0.2 mg/mL of alprazolam in methanol. [NOTE—Sonicate for 15 min to dissolve the contents.] Filter a portion, and discard the first 1 mL of filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 230 nm
Column: 4.6-mm × 25-cm; 5-µm packing L7
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times are listed in *Table 7*.]
Suitability requirements
Resolution: NLT 1.5 between nordazepam and alprazolam; NLT 1.5 between chlordiazepoxide related compound A and alprazolam related compound A, *System suitability solution*
Tailing factor: NMT 2.0 for the alprazolam peak, *System suitability solution*
Relative standard deviation: NMT 5%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of the impurity from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Alprazolam RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of alprazolam in the *Sample solution* (mg/mL)
F = relative response factor (see *Table 7*)
Acceptance criteria: See *Table 7*.

Table 7

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Chlordiazepoxide related compound A[a]	0.36	1.0	0.2
Alprazolam related compound A	0.45	0.7	0.5
Nordazepam[a,b]	0.8	1.0	0.2
Alprazolam	1.0	—	—
2-Amino-5-chloro-benzophenone	1.8	0.9	0.5
Amino-derivative[c]	2.2	1.2	0.5
Any other individual degradation product	—	1.0	0.2
Total impurities	—	—	2.0

[a] If possible from the manufacturing process.
[b] 7-Chloro-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.
[c] 7-Chloro-1-methyl-5-phenyl[1,2,4]triazolo[4,3-*a*]quinolin-4-amine.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at room temperature.
- **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards ⟨11⟩**

USP Alprazolam RS
USP Alprazolam Related Compound A RS
2-(2-Acetylhydrazino)-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine.
$C_{17}H_{15}ClN_4O$ 326.78
USP Chlordiazepoxide Related Compound A RS
7-Chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one 4-oxide.
$C_{15}H_{11}ClN_2O_2$ 286.71
USP Nordazepam RS

Alprazolam Orally Disintegrating Tablets

DEFINITION

Alprazolam Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$).