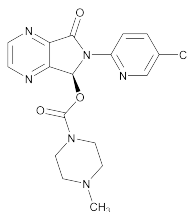


# Eszopiclone.in

Eszopiclone (Imovane, Zopiclone, Lunesta, Zimovane)

## Eszopiclone



$C_{17}H_{17}ClN_6O_3$  388.81  
 1-Piperazinecarboxylic acid, 4-methyl-, (5S)-6-(5-chloro-2-pyridinyl)-6,7-dihydro-7-oxo-5H-pyrrolo[3,4-b]pyrazin-5-yl ester;  
 (+)-(5S)-6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazin-5-yl 4-methylpiperazine-1-carboxylate [138729-47-2].

### DEFINITION

Eszopiclone contains NLT 98.0% and NMT 102.0% of  $C_{17}H_{17}ClN_6O_3$ , calculated on the anhydrous and solvent-free basis.

### IDENTIFICATION

- A. INFRARED ABSORPTION**
- B.** The retention time of the major peak in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

### ASSAY

#### PROCEDURE

**Buffer:** Dissolve 8.1 g of sodium dodecyl sulfate and 1.6 g of monobasic sodium phosphate in 1 L of water. Adjust with 10% phosphoric acid to a pH of 4.0.

**Mobile phase:** Acetonitrile and *Buffer* (38:62)

**Standard solution:** 0.5 mg/mL of USP Eszopiclone RS in *Mobile phase*

**Sample solution:** 0.5 mg/mL of Eszopiclone in *Mobile phase*

### Chromatographic system

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

**Mode:** LC

**Detector:** UV 303 nm

**Column:** 4.6-mm × 25-cm; 5- $\mu$ m packing L1

**Column temperature:** 30°

**Flow rate:** 1.5 mL/min

**Injection size:** 10  $\mu$ L

**Run time:** 2 times the retention time of eszopiclone

### System suitability

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 1.5

**Relative standard deviation:** NMT 1.5%

### Analysis

**Samples:** *Standard solution* and *Sample solution*  
 Calculate the percentage of eszopiclone ( $C_{17}H_{17}ClN_6O_3$ ) in the portion of sample 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 Eszopiclone RS in the *Standard solution* (mg/mL)  
 $C_U$  = concentration of Eszopiclone in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.0%–102.0% on the anhydrous and solvent-free basis

### IMPURITIES

- HEAVY METALS, Method II (231):** NMT 10 ppm
- RESIDUE ON IGNITION (281):** NMT 0.1%
- ORGANIC IMPURITIES**

[NOTE—The *Standard solution* and *Sample solution* are stable for 48 h at refrigerated conditions.]

**Buffer and Mobile phase:** Proceed as directed in the *Assay*.

**Standard solution:** 4.0  $\mu$ g/mL of USP Eszopiclone RS in *Mobile phase*

**System suitability solution:** 0.04 mg/mL of USP Eszopiclone Related Compound A RS and 0.04 mg/mL of USP Eszopiclone RS from the *Standard solution*, in *Mobile phase*

**Sample solution:** 4.0 mg/mL of Eszopiclone in *Mobile phase*

**Chromatographic system:** Proceed as directed in the *Assay*.

**Injection size:** 20  $\mu$ L

### System suitability

**Samples:** *Standard solution* and *System suitability solution*

### Suitability requirements

**Resolution:** NLT 3.0 between eszopiclone related compound A and eszopiclone, *System suitability solution*

**Relative standard deviation:** NMT 5.0%, *Standard solution*

### Analysis

**Samples:** *Standard solution* and *Sample solution*  
 Calculate the percentage of any individual impurity in the portion of Eszopiclone taken:

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

- $r_U$  = peak response of any individual impurity from the *Sample solution*  
 $r_S$  = peak response of eszopiclone from the *Standard solution*  
 $C_S$  = concentration of USP Eszopiclone RS in the *Standard solution* (mg/mL)  
 $C_U$  = concentration of Eszopiclone in the *Sample solution* (mg/mL)  
 $F$  = relative response factor for the corresponding impurity peak (see *Table 1*)

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Acceptance criteria: See Table 1.

**Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Zopiclone alcohol <sup>a</sup>	0.13	1.4	0.15
Pyrolopyrazinone analog <sup>b</sup>	0.24	1.6	0.15
Eszopiclone related compound A <sup>c</sup>	0.60	0.88	0.15
Eszopiclone	1.0	—	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.4

<sup>a</sup> 6-(5-Chloropyridin-2-yl)-7-hydroxy-6,7-dihydro-5H-pyrrolo[3,4-*b*]pyrazin-5-one.

<sup>b</sup> 6-(5-Chloropyridin-2-yl)-6,7-dihydro-5H-pyrrolo[3,4-*b*]pyrazin-5-one.

<sup>c</sup> 6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo [3,4,*b*] pyrazin-5-yl 4-methylpiperazine-1-carboxylate 4-oxide.

### • LIMIT OF ZOPICLONE R-ISOMER

[NOTE—The *Sample solution* is stable for 48 h at refrigerated conditions.]

**Mobile phase:** Absolute alcohol, *n*-hexane, and diethyl amine (700: 300: 0.2)

**System suitability solution:** 0.1 mg/mL each of USP Eszopiclone RS and USP Zopiclone *R*-Isomer RS in methanol

**Sample solution:** 1.0 mg/mL of Eszopiclone in methanol

#### Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

**Mode:** LC

**Detector:** UV 303 nm

**Column:** 4.6-mm × 25-cm; 5-μm packing L##

**Flow rate:** 1 mL/min

**Injection size:** 10 μL

**Run time:** 1.5 times the retention time of eszopiclone

#### System suitability

**Sample:** *System suitability solution*

[NOTE—The relative retention times for zopiclone *R*-isomer and eszopiclone are 0.68 and 1.0, respectively.]

### Suitability requirements

**Resolution:** NLT 2.0 between the zopiclone *R*-isomer and eszopiclone peaks

#### Analysis

**Sample:** *Sample solution*

Calculate the percentage of zopiclone *R*-isomer in the portion of Eszopiclone taken:

$$\text{Result} = (r_U/r_T) \times 100$$

$r_U$  = peak response of zopiclone *R*-isomer from the *Sample solution*

$r_T$  = sum of the peak responses from the *Sample solution*

**Acceptance criteria:** NMT 1.0%

### SPECIFIC TESTS

**WATER DETERMINATION, Method Ia** <921>: NMT 0.5%

### ADDITIONAL REQUIREMENTS

**PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.

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<http://www.eszopiclone.in>