



Specifications  
for the Active Ingredient

PIROCTONE OLAMINE

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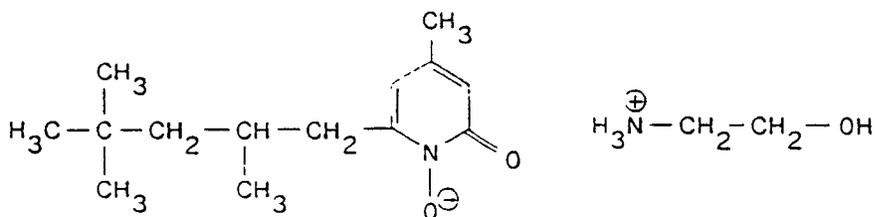
Chemical name:

1-Hydroxy-4-methyl-6-(2,4,4-trimethyl-  
pentyl)-2-(1H)pyridone ethanolamine  
salt

Synonyma:

H 72 6146 A  
Octopirox<sup>(R)</sup>

Formula:



Sum formula:

C<sub>16</sub> H<sub>30</sub> N<sub>2</sub> O<sub>3</sub>

Molecular weight:

298,4

Description:

white or faintly yellow crystalline  
powder

Solubility:

Water: very slightly soluble  
Ethanol: freely soluble  
Chloroform: freely soluble  
Ether: very slightly soluble

Specifications for the Active Ingredient / PIROCTONE OLAMIN

Identity:

1. Add 1 ml of diluted acetic acid and 5 drops of ferrous sulfate solution (5 % w/v) to a solution of 10 mg of sample in 5 ml methanol. An orange-red color develops.
2. The infrared spectrum must show the same peaks as that of authentic substance.

Solution in methanol:                      Should be clear and colorless to  
(1 g + 10 ml)                                      slightly yellow

pH of a suspension in water:    8,5 - 10,0  
(1 % w/v)

Heavy metals:                                      Not more than 20 ppm

Test solution:

Dissolve the residue of sulfate ash in 0,5 ml hydrochloric acid (25 % w/v). After evaporating to dryness the residue is dissolved in 2 ml of water, add a drop of conc. hydrochlorid acid. After addition of phenolphthaleine and dilution with water up to 15 ml the solution is neutralized with 2 N sodium hydroxide. 12 ml of this solution must pass the limit test on heavy metals, following Ph.Eur.

Specific extinction in 0,1 N  
methanolic sodium hydroxide  
at 317 nm:                                      214 - 236

Loss on drying:                                      not more than 2 %  
(vacuum at room temp., 6 hours)

Sulphated ash:                                      not more than 0,2 %  
(from 1,5 g)

Specifications for the Active Ingredient / PIROCTONE OLAMIN

Thin layer chromatography:

Stationary phase: Prefabricated glass plates, type polyamide 11 F254 (Merck, Darmstadt, Fed. Rep. of Germany).

Mobile Phase: 0,2 M disodium edetate solution 40  
methanol 37  
acetone 21  
strong ammonia solution 2

The chamber must be vapor-saturated

Quantities applied: A) 10 µl of a solution of Piroctone olamin (4 % w/v methanol)  
B) 10 µl of a solution of Piroctone olamin standard substance (4 % w/v methanol)  
C) 10 µl of a solution of Piroctone olamin standard substance (0,02 % w/v methanol)

Distance from start to solvent front: approx. 15 cm

Detection: UV (254 nm)

Evaluation: The main spots from samples A and B should show the same Rf-value. From sample A no spot of byproducts should be more intensive than spot C.

0,2 M disodium edetate solution:

74,448 g disodium edetate dihydrate and 10 g sodium hydroxide are dissolved in water up to 1000 ml (e.g. = Idranal III, Riedel de Haen, Fed. Rep. of Germany).

In the routinetest we usually apply a diluted solution of the active ingredient (= solution C). Under the above TLC-conditions the separation of the precursor - [4-Methyl-6-(2,4,4-trimethyl-pentyl)-2-(1H)-pyron] - and the theoretical degradationproduct [4-Methyl-6-(2,4,4-trimethyl-pentyl)-2-(1H)-pyridon] shows the following Rf-values:

Piroctone olamin Rf ~ 0,35  
Pyron Rf ~ 0,19  
Pyridon Rf ~ 0,21

Specifications for the active ingredient / PIROCTONE OLAMIN

Aminoethanol content:

Dissolve about 200 mg Piroctone olamin, exactly weighed, in acetic acid and titrate potentiometrically with 0,1 N perchloric acid.

1 ml 0,1 N perchloric acid corresponds to 6,108 mg aminoethanol.

Limits: between 20,1 and 20,9 % aminoethanol, relating to dry substance.

Coefficient of variation of the method: 0,8 %.

Content:

Dissolve about 150 mg Piroctone olamin, exactly weighed, in 35 ml dimethylformamide and under nitrogen cover titrate with 0,1 N lithium methylate using three drops of thymol blue solution as indicator; the indicator changes from yellow to blue.

Titrate a blank under the same conditions.

1 ml 0,1 N lithium methylate corresponds to 29,84 mg  $C_{16} H_{30} N_2 O_3$ .

Limits: between 98,0 and 101,5 %, related to the dry substance.

Coefficient of variation of the method: 0,2 %

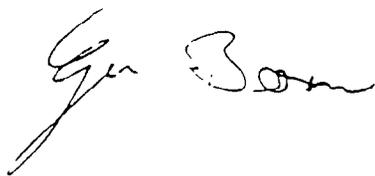
Lithium methylate solution:

produce according to BP 80.

Indicator:

0,3 % solution of thymol blue in dimethylformamide.

PHARMA QUALITY CONTROL DEPARTMENT  
Chemistry Group, Dec. 14, 1983  
Ap.Bo/Ra Nr. 564

A handwritten signature in black ink, appearing to read "Gen. B. B. B.", is written over the typed text of the document.