

# Ethyl Oleate

## 1 Nonproprietary Names

BP: Ethyl oleate  
PhEur: Ethylis oleas  
USPNF: Ethyl oleate

## 2 Synonyms

Ethyl 9-octadecenoate; *Kessco EO*; oleic acid, ethyl ester.

## 3 Chemical Name and CAS Registry Number

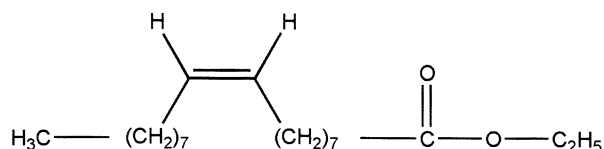
(Z)-9-Octadecenoic acid, ethyl ester [111-62-6]

## 4 Empirical Formula Molecular Weight

$C_{20}H_{38}O_2$

310.51

## 5 Structural Formula



## 6 Functional Category

Oleaginous vehicle; solvent.

## 7 Applications in Pharmaceutical Formulation or Technology

Ethyl oleate is primarily used as a vehicle in certain parenteral preparations intended for intramuscular administration. It has also been used as a solvent for drugs formulated as biodegradable capsules for subdermal implantation<sup>(1)</sup> and in the preparation of microemulsions containing cyclosporin.<sup>(2)</sup>

Ethyl oleate is a suitable solvent for steroids and other lipophilic drugs. Its properties are similar to those of almond oil and peanut oil. However, it has the advantage that it is less viscous than fixed oils and is more rapidly absorbed by body tissues.<sup>(3)</sup>

Ethyl oleate has also been evaluated as a vehicle for subcutaneous injection.<sup>(4)</sup>

## 8 Description

Ethyl oleate occurs as a pale yellow to almost colorless, mobile, oily liquid with a taste resembling that of olive oil and a slight, but not rancid odor.

Ethyl oleate consists of the ethyl esters of oleic acid and related high molecular weight fatty acids. A suitable antioxidant may be included.

## 9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for ethyl oleate.

Test	PhEur 2002	USPNF 20
Characters	+	—
Specific gravity	0.866–0.874	0.866–0.874
Viscosity	—	≥ 5.15 mPa s
Refractive index	—	1.443–1.450
Acid value	≤ 0.5	≤ 0.5
Iodine value	75–90	75–85
Saponification value	177–188	177–188
Peroxide value	≤ 10	—
Oleic acid	+	—
Water content	≤ 1.0%	—
Total ash	≤ 0.1%	—

## 10 Typical Properties

Boiling point: 205–208 °C (some decomposition)

Flash point: 175.3 °C

Freezing point: ≈ –32 °C

Moisture content: at 20 °C and 52% relative humidity, the equilibrium moisture content of ethyl oleate is 0.08%.

Solubility: miscible with chloroform, ethanol (95%), ether, fixed oils, liquid paraffin, and most other organic solvents; practically insoluble in water.

Surface tension: 32.3 mN/m (32.3 dynes/cm) at 25 °C<sup>(3)</sup>

Viscosity (dynamic): 3.9 mPa s (3.9 cP) at 25 °C<sup>(3)</sup>

Viscosity (kinematic): 0.046 mm<sup>2</sup>/s (4.6 cSt) at 25 °C<sup>(3)</sup>

## 11 Stability and Storage Conditions

Ethyl oleate should be stored in a cool, dry place in a small, well-filled, well-closed container, protected from light. When a partially filled container is used, the air should be replaced by nitrogen or another inert gas. Ethyl oleate oxidizes on exposure to air, resulting in an increase in the peroxide value. It remains clear at 5 °C, but darkens in color on standing. Antioxidants are frequently used to extend the shelf life of ethyl oleate. Protection from oxidation for over 2 years has been achieved by storage in amber glass bottles with the addition of combinations of propyl gallate, butylated hydroxyanisole, butylated hydroxytoluene, and citric or ascorbic acid.<sup>(5,6)</sup> A concentration of 0.03% w/v of a mixture of propyl gallate (37.5%), butylated hydroxytoluene (37.5%), and butylated hydroxyanisole (25%) was found to be the best antioxidant for ethyl oleate.<sup>(6)</sup>

Ethyl oleate may be sterilized by heating at 150 °C for 1 hour.

## 12 Incompatibilities

Ethyl oleate dissolves certain types of rubber and causes others to swell.<sup>(7,8)</sup> It may also react with oxidizing agents.

**13 Method of Manufacture**

Ethyl oleate is prepared by the reaction of ethanol with oleoyl chloride in the presence of a suitable hydrogen chloride acceptor.

**14 Safety**

Ethyl oleate is generally considered to be of low toxicity but ingestion should be avoided. Ethyl oleate has been found to cause minimal tissue irritation.<sup>(9)</sup> No reports of intramuscular irritation during use have been recorded.

**15 Handling Precautions**

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and nitrile gloves are recommended. Ethyl oleate is flammable.

**16 Regulatory Status**

Included in the FDA Inactive Ingredients Guide (transdermal preparation). Included in parenteral medicines licensed in the UK.

**17 Related Substances**

Methyl oleate; oleic acid.

**Methyl oleate**

Empirical formula: C<sub>19</sub>H<sub>36</sub>O<sub>2</sub>

Molecular weight: 296.49

CAS number: [112-69-9]

Synonyms: methyl 9-octadecenoate; (Z)-9-octadecenoic acid, methyl ester.

Boiling point: 168–170 °C

Density: 0.879 g/cm<sup>3</sup>

Iodine number: 85.6

Refractive index:  $n_D^{26} = 1.4510$

Solubility: miscible with ethanol and ether.

Comments: prepared by refluxing oleic acid with *p*-toluene-sulfonic acid in methanol.

**18 Comments**

The EINECS number for ethyl oleate is 203-889-5.

**19 Specific References**

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- 2 Kim C-K, Ryuu S-A, Park K-M. Preparation and physicochemical characterisation of phase inverted water/oil microemulsion containing cyclosporin A. *Int J Pharm* 1997; **147**: 131–134.
- 3 Howard JR, Hadgraft J. The clearance of oily vehicles following intramuscular and subcutaneous injections in rabbits. *Int J Pharm* 1983; **16**: 31–39.
- 4 Radwan M. *In vivo* screening model for excipients and vehicles used in subcutaneous injections. *Drug Dev Ind Pharm* 1994; **20**: 2753–2762.
- 5 Alemany P, Del Pozo A. Autoxidation of ethyl oleate: protection with antioxidants [in Spanish]. *Galenica Acta* 1963; **16**: 335–338.
- 6 Nikolaeva NM, Gluzman MK. Conditions for stabilizing ethyl oleate during storage [in Russian]. *Farmatsiya* 1977; **26**: 25–28.
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- 8 Halsall KG. Calciferol injection and plastic syringes [letter]. *Pharm J* 1985; **235**: 99.
- 9 Hem SL, Bright DR, Banker GS, Pogue JP. Tissue irritation evaluation of potential parenteral vehicles. *Drug Dev Commun* 1974–75; **1(5)**: 471–477.

**20 General References**

Spiegel AJ, Noseworthy MM. Use of nonaqueous solvents in parenteral products. *J Pharm Sci* 1963; **52**: 917–927.

**21 Authors**

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**22 Date of Revision**

13 June 2002.