

Polyoxyethylene Stearates

1 Nonproprietary Names

The polyoxyethylene stearates are a series of polyethoxylated derivatives of stearic acid. Of the large number of different materials commercially available, one type is listed in the USPNF 20.

JP: Polyoxyl 40 stearate

USPNF: Polyoxyl 40 stearate

See also Sections 2, 3, 4 and 5.

2 Synonyms

Ethoxylated fatty acid esters; macrogol stearates; *Marlosol*; PEG fatty acid esters; PEG stearates; polyethylene glycol stearates; poly(oxy-1,2-ethanediyl) α -hydro- ω -hydroxyoctadecanoate; polyoxyethylene glycol stearates.

Polyoxyethylene stearates are nonionic surfactants produced by polyethoxylation of stearic acid. Two systems of nomenclature are used for these materials. The number '8' in the names 'polyoxyl 8 stearate' or 'polyoxyethylene 8 stearate' refers to the approximate polymer length in oxyethylene units. The same material may also be designated 'polyoxyethylene glycol 400 stearate' or 'macrogol stearate 400' in which case, the number '400' refers to the average molecular weight of the polymer chain.

For synonyms applicable to specific polyoxyethylene stearates, see Table I.

3 Chemical Name and CAS Registry Number

Polyethylene glycol stearate [9004-99-3]

Polyethylene glycol distearate [9005-08-7]

4 Empirical Formula Molecular Weight

See Table II.

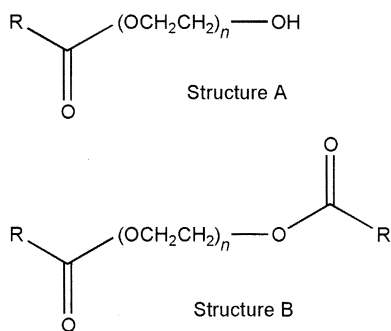
Table II: Empirical formulas and molecular weights of selected polyoxyethylene stearates.

Name	Empirical formula	Molecular weight
Polyoxyl 6 stearate	C ₃₀ H ₆₀ O ₈	548.80
Polyoxyl 8 stearate	C ₃₄ H ₆₈ O ₁₀	636.91
Polyoxyl 12 stearate	C ₄₂ H ₈₄ O ₁₄	813.12
Polyoxyl 20 stearate	C ₅₈ H ₁₁₆ O ₂₂	1165.55
Polyoxyl 40 stearate	C ₉₈ H ₁₉₆ O ₄₂	2046.61
Polyoxyl 50 stearate	C ₁₁₈ H ₂₃₆ O ₅₂	2487.15
Polyoxyl 100 stearate	C ₂₁₈ H ₄₃₆ O ₁₀₂	4689.80

Table I: Synonyms of selected polyoxyethylene stearates and distearates.

Name	Synonym
Polyoxyl 2 stearate	<i>Hodag DGS; Lipo DGS; PEG-2 stearate</i>
Polyoxyl 4 stearate	<i>Acconon 200-MS; Hodag 20-S; PEG-4 stearate; polyethylene glycol 200 monostearate; polyoxyethylene (4) monostearate; Protamate 200-DPS</i>
Polyoxyl 6 stearate	<i>Cerasynt 616; Kessco PEG 300 Monostearate; Lipal 300S; Lipo PEG 3-S; PEG-6 stearate; polyethylene glycol 300 monostearate; polyoxyethylene (6) monostearate; Polystate C; Protamate 300-DPS</i>
Polyoxyl 8 stearate	<i>Acconon 400-MS; Cerasynt 660; Cithrol 4MS; Crodet S8; Emerest 2640; Grocor 400; Hodag 40-S; Kessco PEG-400 Monostearate; Lipo-PEG 4-S; macrogol stearate 400; Myrj 45; PEG-8 stearate; Pegospense 400 MS; polyethylene glycol 400 monostearate; polyoxyethylene (8) monostearate; Protamate 400-DPS; Ritapeg 400 MS</i>
Polyoxyl 12 stearate	<i>Hodag 60-S; Kessco PEG 600 Monostearate; Lipo-PEG 6-S; PEG-12 stearate; Pegospense 600 MS; polyethylene glycol 600 monostearate; polyoxyethylene (12) monostearate; Protamate 600-DPS</i>
Polyoxyl 20 stearate	<i>Cerasynt 840; Hodag 100-S; Kessco PEG 1000 Monostearate; Lipo-PEG 10-S; Myrj 49; Pegospense 1000 MS; PEG-20 stearate; polyethylene glycol 1000 monostearate; polyoxyethylene (20) monostearate; Protamate 1000-DPS</i>
Polyoxyl 30 stearate	<i>Myrj 51; PEG-30 stearate; polyoxyethylene (30) stearate</i>
Polyoxyl 40 stearate	<i>Crodet S40; E431; Emerest 2672; Hodag POE (40) MS; Lipal 395; Lipo-PEG 39-S; macrogol stearate 2000; Myrj 52; PEG-40 stearate; polyoxyethylene glycol 2000 monostearate; polyoxyethylene (40) monostearate; Protamate 2000-DPS; Ritox 52</i>
Polyoxyl 50 stearate	<i>Atlas G-2153; Crodet S50; Lipal 505; Myrj 53; PEG-50 stearate; polyoxyethylene (50) monostearate</i>
Polyoxyl 100 stearate	<i>Lipo-PEG 100-S; Myrj 59; PEG-100 stearate; polyethylene glycol 4400 monostearate; polyoxyethylene (100) monostearate; Protamate 4400-DPS; Ritox 53</i>
Polyoxyl 150 stearate	<i>Hodag 600-S; PEG-150 stearate; Ritox 59</i>
Polyoxyl 4 distearate	<i>Hodag 22-S; PEG-4 distearate</i>
Polyoxyl 8 distearate	<i>Hodag 42-S; Kessco PEG 400 DS; PEG-8 distearate; polyethylene glycol 400 distearate; Protamate 400-DS</i>
Polyoxyl 12 distearate	<i>Hodag 62-S; Kessco PEG 600 Distearate; PEG-12 distearate; polyethylene (12) distearate; polyethylene glycol 600 distearate; Protamate 600-DS</i>
Polyoxyl 32 distearate	<i>Hodag 154-S; Kessco PEG 1540 Distearate; PEG-32 distearate; polyethylene glycol 1540 distearate; polyoxyethylene (32) distearate</i>
Polyoxyl 150 distearate	<i>Hodag 602-S; Kessco PEG 6000 DS; Lipo-PEG 6000-DS; PEG-150 distearate; polyethylene glycol 6000 distearate; polyoxyethylene (150) distearate; Protamate 6000-DS</i>

5 Structural Formula



Structure A applies to the monostearate; where the average value of *n* is 6 for polyoxyl 6 stearate, 8 for polyoxyl 8 stearate, and so on.

Structure B applies to the distearate; where the average value of *n* is 12 for polyoxyl 12 distearate, 32 for polyoxyl 32 distearate, and so on.

In both structures, R represents the alkyl group of the parent fatty acid. With stearic acid, R is CH₃(CH₂)₁₆. However, it should be noted that stearic acid usually contains other fatty acids, primarily palmitic acid, and consequently a polyoxyethylene stearate may also contain varying amounts of other fatty acid derivatives such as palmitates.

6 Functional Category

Emulsifying agent; solubilizing agent; wetting agent.

7 Applications in Pharmaceutical Formulation or Technology

Polyoxyethylene stearates are generally used as emulsifiers in oil-in-water-type creams and lotions. Their hydrophilicity or lipophilicity depends on the number of ethylene oxide units present: the larger the number, the greater the hydrophilic properties. Polyoxyl 40 stearate has been used as an emulsifying agent in intravenous infusions.⁽¹⁾

Polyoxyethylene stearates are particularly useful as emulsifying agents when astringent salts or other strong electrolytes are present. They can also be blended with other surfactants to obtain any hydrophilic-lipophilic balance for lotions or ointment formulations. See Table III.

Table III: Uses of polyoxyethylene stearates.

Use	Concentration (%)
Auxiliary emulsifier for o/w intravenous fat emulsion	0.5-5
Emulsifier for o/w creams or lotions	0.5-10
Ophthalmic ointment	7
Suppository component	1-10
Tablet lubricant	1-2

8 Description

See Table IV.

Table IV: Description of various polyoxyethylene stearates.

Name	Description
Polyoxyl 6 stearate	Soft solid
Polyoxyl 8 stearate	Waxy cream
Polyoxyl 12 stearate	Pasty solid
Polyoxyl 20 stearate	Waxy solid
Polyoxyl 40 stearate	Waxy solid, with a faint, bland, fatlike odor, off-white to light tan in color
Polyoxyl 50 stearate	Solid, with a bland, fatlike odor or odorless
Polyoxyl 100 stearate	Solid
Polyoxyl 12 distearate	Paste
Polyoxyl 32 distearate	Solid
Polyoxyl 150 distearate	Solid

9 Pharmacopeial Specifications

See Table V.

Table V: Pharmacopeial specifications for polyoxyethylene stearates.

Test	JP 2001	USPNF 20
	Polyoxyl 40 stearate	Polyoxyl 40 stearate
Identification	+	+
Clarity and color of solution	+	—
Congealing range	39-44°C	37-47°C
Congealing point of the fatty acid	≥53 °C	—
Residue on ignition	≤0.10%	—
Water	—	≤3.0%
Arsenic	≤3 ppm	—
Heavy metals	≤10 ppm	≤0.001%
Acid value	≤1	≤2
Hydroxyl value	—	25-40
Saponification value	25-35	25-35
Free polyethylene glycols	—	17-27%
Organic volatile impurities	—	+

10 Typical Properties

Flash point: >149°C for polyoxyl 8 stearate (*Myrj 45*).

Solubility: see Table VI. See also Table VII.

Table VI: Solubility of polyoxyethylene stearates.

Name	Solvent		
	Ethanol (95%)	Mineral oil	Water
Polyoxyl 6 stearate	S	S	DH
Polyoxyl 8 stearate	S	I	D
Polyoxyl 12 stearate	S	I	S
Polyoxyl 20 stearate	S	I	S
Polyoxyl 40 stearate	S	I	S
Polyoxyl 50 stearate	S	I	S
Polyoxyl 100 stearate	S	I	S
Polyoxyl 12 distearate	S	—	DH
Polyoxyl 32 distearate	S	—	S
Polyoxyl 150 distearate	I	—	S

D = dispersible; I = insoluble; S = soluble; DH = dispersible (with heat).

Table VII: Typical properties of polyoxyethylene stearates.

Name	Acid value	Free ethylene oxide	HLB value	Hydroxyl value	Iodine number	Melting point (°C)	Saponification value	Water content (%)
Polyoxyl 6 stearate	≤5.0	≤100 ppm	9.7	—	≤0.5	28–32	95–110	—
Polyoxyl 8 stearate	≤2.0	≤100 ppm	11.1	87–105	≤1.0	28–33	82–95	≤3.0
Polyoxyl 12 stearate	≤8.5	≤100 ppm	13.6	55–75	≤1.0	≈ 37	62–78	≤1.0
Polyoxyl 20 stearate	≤1.0	≤100 ppm	14	50–62	≤1.0	≈ 28	46–56	≤1.0
Polyoxyl 30 stearate	≤2.0	—	16	35–50	—	—	30–45	≤3.0
Polyoxyl 40 stearate	≤1.0	—	16.9	27–40	—	≈ 38	25–35	≤3.0
Polyoxyl 50 stearate	≤2.0	—	17.9	23–35	—	≈ 42	20–28	≤3.0
Polyoxyl 100 stearate	≤1.0	≤100 ppm	18.8	15–30	—	≈ 46	9–20	≤3.0
Polyoxyl 8 distearate	≤10.0	—	—	≤15	≤0.5	≈ 36	115–124	—
Polyoxyl 12 distearate	≤10.0	≤100 ppm	10.6	≤20	≤1.0	≈ 39	93–102	≤1.0
Polyoxyl 32 distearate	≤10.0	≤100 ppm	14.8	≤20	≤0.25	≈ 45	50–62	≤1.0
Polyoxyl 150 distearate	7–9	≤100 ppm	18.4	≤15	≤0.1	53–57	14–20	≤1.0

11 Stability and Storage Conditions

Polyoxyethylene stearates are generally stable in the presence of electrolytes and weak acids or bases. Strong acids and bases can cause gradual hydrolysis and saponification.

The bulk material should be stored in a well-closed container, in a dry place, at room temperature.

12 Incompatibilities

Polyoxyethylene stearates are unstable in hot alkaline solutions owing to hydrolysis, and will also saponify with strong acids or bases. Discoloration or precipitation can occur with salicylates, phenolic substances, iodine salts, and salts of bismuth, silver, and tannins.^(2–4) Complex formation with preservatives may also occur.⁽⁵⁾ The antimicrobial activity of some materials such as bacitracin, chloramphenicol, phenoxymethylpenicillin, sodium penicillin, and tetracycline may be reduced in the presence of polyoxyethylene stearate concentrations greater than 5% w/w.^(6,7)

13 Method of Manufacture

Polyoxyethylene stearates are prepared by the direct reaction of fatty acids, particularly stearic acid, with ethylene oxide.

14 Safety

Although polyoxyethylene stearates are primarily used as emulsifying agents in topical pharmaceutical formulations, certain materials, particularly polyoxyl 40 stearate, have also been used in intravenous injections and oral preparations.^(1,4)

Polyoxyethylene stearates have been tested extensively for toxicity in animals^(8–13) and are widely used in pharmaceutical formulations and cosmetics. They are generally regarded as essentially nontoxic and nonirritant materials.

Polyoxyl 8 stearate:

LD₅₀ (hamster, oral): 27 g/kg

LD₅₀ (rat, oral): 64 g/kg

Polyoxyl 20 stearate:

LD₅₀ (mouse, IP): 0.2 g/kg

LD₅₀ (mouse, IV): 0.87 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

Polyoxyethylene stearates that contain greater than 100 ppm of free ethylene oxide may present an explosion hazard when stored in a closed container. This is due to the release of ethylene oxide into the container headspace, where it can accumulate and so exceed the explosion limit.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (dental solutions; IV injections; ophthalmic preparations; oral capsules and tablets; otic suspensions; topical creams, emulsions, lotions, ointments, and solutions; and vaginal preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Polyethylene glycol; stearic acid.

18 Comments

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19 Specific References

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20 General References

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21 Author

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22 Date of Revision

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