

**Pharmacopoeias.** In *Jpn.* Also in *USNF*.

**USNF 26** (Polyoxyl 40 Stearate). A mixture of the mono- and di-esters of stearic acid and mixed macrogols, the average polymer length being about 40 oxyethylene units. It contains not less than 17% and not more than 27% of free macrogols. It is a waxy, white to light tan solid, odourless or with a faint fat-like odour. Congealing range 37° to 47°. Soluble in water, in alcohol, in acetone, and in ether; insoluble in liquid paraffin and in vegetable oils. Store in airtight containers.

**Incompatibility.** Macrogol stearates have been reported to be generally stable with electrolytes and weak acids or bases although strong acids or bases may cause hydrolysis and saponification. Discoloration or precipitation may occur with phenolic substances and complexation with preservatives. Decrease in the antimicrobial activity of bacitracin, chloramphenicol, phenoxymethylpenicillin, and tetracycline has been stated to occur with concentrations of macrogol stearates exceeding 5%.

#### Profile

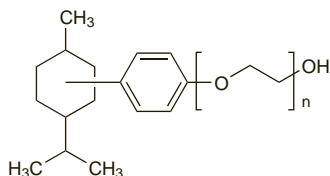
Macrogol stearates are macrogol esters that are used as emulsifying and solubilising agents.

#### Menfegol (rINN)

Menfégol; Menfegolum; Menpegol.  $\alpha$ -[p-(p-Menthyl)phenyl]- $\omega$ -hydroxypoly(oxyethylene).

Менфегол

CAS — 57821-32-6.



#### Profile

Menfegol consists of menthylphenyl ethers of macrogols represented by the formula  $C_{16}H_{23}(OCH_2CH_2)_nOH$ . It is a nonionic surfactant used as a spermicide.

**Adverse effects.** Frequent use of menfegol in spermicidal foaming tablets has been associated with a high incidence of genital ulceration, which could increase the risk of infection by HIV.<sup>1</sup>

- Goeman, J. *et al.* Frequent use of menfegol spermicidal vaginal foaming tablets associated with a high incidence of genital lesions. *J Infect Dis* 1995; **171**: 1611–14.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Hong Kong:** Neo Sampoo; **Malaysia:** Neo Sampoo; **Philipp.:** Neo Sampoo; **Singapore:** Neo Sampoo.

#### Mono- and Di-glycerides

E471 (mono- and di-glycerides of fatty acids); Mono y diglicerídicos.

Моно- и Диглицириды

**Pharmacopoeias.** In *USNF*.

**USNF 26** (Mono- and Di-glycerides). A mixture of glycerol mono- and di-esters, with minor amounts of tri-esters, of fatty acids from edible oils. It contains not less than 40% of monoglycerides. It may contain suitable stabilisers. Store in airtight containers. Protect from light.

#### Profile

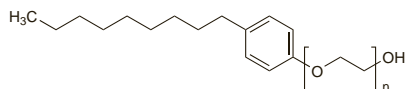
A mixture of mono- and di-glycerides is used as an emulsifying agent and food additive.

#### Nonoxinols

Macrogol Nonylphenyl Ethers; Nonoxinols; Nonoxynols.  $\alpha$ -(4-Nonylphenyl)- $\omega$ -hydroxypoly(oxyethylene).

Ноноксинолы

CAS — 26027-38-3.



**Nomenclature.** Nonoxinols are a series of nonylphenyl ethers of macrogols of differing chain lengths, represented by the formula  $C_{15}H_{23}[O.CH_2.CH_2]_n.OH$ . Nonoxinol is *BAN* and *rINN*. The name may be followed by a figure indicating the approximate number of oxyethylene groups in the polyoxyethylene chain. *USAN* specifies Nonoxynol 4, Nonoxynol 9, Nonoxynol 15, and Nonoxynol 30.

The symbol † denotes a preparation no longer actively marketed

#### Nonoxinol 9 (BAN, rINN)

Nonoxinol-9; Nonoxinol-9; Nonoxinolum 9; Nonoxynol 9 (*USAN*).  $\alpha$ -(4-Nonylphenyl)- $\omega$ -hydroxynona(oxyethylene).

Ноноксинол 9

$C_{33}H_{60}O_{10}$  (nominal) = 616.8.

**Pharmacopoeias.** In *Eur.* (see p.vii), *Int.*, and *US*.

**Ph. Eur. 6.2** (Nonoxinol 9). A mixture consisting mainly of monononylphenyl ethers of macrogols corresponding to the formula:  $C_{15}H_{23}[O.CH_2.CH_2]_n.OH$  where the average value of *n* is 9. A clear, colourless to light yellow, viscous liquid. Miscible with water, with alcohol, and with vegetable oils. Store in airtight containers.

**USP 31** (Nonoxynol 9). An anhydrous liquid mixture consisting chiefly of monononylphenyl ethers of macrogols corresponding to the formula  $C_{15}H_{23}[O.CH_2.CH_2]_n.OH$ , in which the average value of *n* is about 9. A clear, colourless to light yellow, viscous liquid. Soluble in water, in alcohol, and in maize oil. Store in airtight containers.

#### Nonoxinol 10 (BAN, rINN)

Nonoxinolum 10; Nonoxynol 10.  $\alpha$ -(4-Nonylphenyl)- $\omega$ -hydroxydecyl(oxyethylene).

Ноноксинол 10

$C_{35}H_{64}O_{11}$  (nominal) = 660.9.

#### Nonoxinol 11 (BAN, rINN)

Nonoxinolum 11; Nonoxynol 11.  $\alpha$ -(4-Nonylphenyl)- $\omega$ -hydroxyundecyl(oxyethylene).

Ноноксинол 11

$C_{37}H_{68}O_{12}$  (nominal) = 704.9.

#### Adverse Effects and Precautions

Nonoxinols used as vaginal spermicides may cause local irritation.

**Genito-urinary infections.** Use of spermicidal foam or jelly containing nonoxinol 9 may disturb the normal vaginal flora and predispose to colonisation with *Escherichia coli* and the development of bacteriuria.<sup>1</sup> An increased risk of acute *E. coli* urinary-tract infection has been reported<sup>2</sup> associated with the use of condoms coated with nonoxinol 9. However, another study<sup>3</sup> of women using nonoxinol-9 spermicidal contraceptives showed that most users experienced minimal disruption to the vaginal microbial ecosystem.

For reference to an increased incidence of some sexually transmitted diseases in women using nonoxinol 9, see Antimicrobial Activity, below.

- Hooton TM, *et al.* *Escherichia coli* bacteriuria and contraceptive method. *JAMA* 1991; **265**: 64–9.
- Fihn SD, *et al.* Association between use of spermicide-coated condoms and *Escherichia coli* urinary tract infection in young women. *Am J Epidemiol* 1996; **144**: 512–20.
- Schreiber CA, *et al.* Effects of long-term use of nonoxynol-9 on vaginal flora. *Obstet Gynecol* 2006; **107**: 136–43.

**Pregnancy.** Maternal use of spermicidal contraceptives has been linked to an increased frequency of congenital abnormalities, including trisomy, but it has been suggested that such studies may be flawed by recall bias.<sup>1</sup> Meta-analysis of 9 studies also supported the view that peri- and postconceptional maternal use of spermicides was not associated with adverse fetal outcome.<sup>2</sup>

- Mishell DR. Contraception. *N Engl J Med* 1989; **320**: 777–87.
- Einarson TR, *et al.* Maternal spermicide use and adverse reproductive outcome: a meta-analysis. *Am J Obstet Gynecol* 1990; **162**: 655–60.

**Toxic shock syndrome.** Toxic shock syndrome has been associated with the use of a vaginal contraceptive sponge impregnated with nonoxinol 9. A review<sup>1</sup> of 13 cases reported in the USA up to November 1984 found that in 4 of the cases there were other predisposing conditions: postpartum use, use during menstruation, and prolonged retention.

- Faich G, *et al.* Toxic shock syndrome and the vaginal contraceptive sponge. *JAMA* 1986; **255**: 216–18.

#### Uses

Nonoxinols have surface active properties and may be used as solubilising agents. Nonoxinol 9 is used as a spermicide (see Contraception, p.2070).

**Antimicrobial activity.** Nonoxinol 9 has activity *in vitro* against a number of bacteria and viruses and it was hoped<sup>1,2</sup> that use of spermicidal contraceptives containing nonoxinol 9 might provide some protection against sexually transmitted diseases, including chlamydial, gonococcal, and HIV infection. However, controlled studies involving HIV-negative female sex workers or other high-risk women have found that use of nonoxinol 9 does not reduce the rate of new HIV,<sup>3,4</sup> or gonorrhoea or chlamydia infection;<sup>5,6</sup> meta-analyses<sup>6,7</sup> including these and other studies have come to similar conclusions. Furthermore, nonoxinol 9 has an irritant action and may increase the risk of genital ulceration, leading to an increased risk of infection by HIV. The United Nations,<sup>8</sup> WHO,<sup>9</sup> and FDA<sup>10</sup> have therefore advised against its use by women at high risk.

- North BB. Vaginal contraceptives: effective protection from sexually transmitted diseases for women? *J Reprod Med* 1988; **33**: 307–311.

- Anonymous. Multipurpose spermicides. *Lancet* 1992; **340**: 211–13.
- Roddy RE, *et al.* A controlled trial of nonoxynol 9 film to reduce male-to-female transmission of sexually transmitted diseases. *N Engl J Med* 1998; **339**: 504–10.
- Van Damme L, *et al.* Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. *Lancet* 2002; **360**: 971–7. Correction. *ibid.*; 1892.
- Roddy RE, *et al.* Effect of nonoxynol-9 gel on urogenital gonorrhoea and chlamydial infection: a randomized controlled trial. *JAMA* 2002; **287**: 1117–22.
- Wilkinson D, *et al.* Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 21/04/08).
- Wilkinson D, *et al.* Nonoxynol-9 for preventing vaginal acquisition of sexually transmitted infections by women from men. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 21/04/08).
- Anonymous. UN warns against use of spermicide. *BMJ* 2000; **321**: 194.
- Anonymous. Nonoxinol 9 ineffective in preventing HIV infection. *WHO Drug Inf* 2002; **16**: 120–1.
- Food and Drug Administration. FDA mandates new warning for nonoxynol 9 OTC contraceptive products (issued 18/12/07). Available at: <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01758.html> (accessed 21/04/08)

#### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Delfen†; Lorphyn; **Austral.:** Lubarol; **Austria:** Delfen†; Patentex; **Braz.:** Pessarios Proflaticos Rendell†; Preserv Nonoxinol-9; **Canada.:** Advantage 24†; Delfen; Gynol II†; K-Y Plus Spermicidal Lubricant; Lifestyle; Ortho-Gynol; Rameses; Sheik; Shields†; Today; Trojan; VCF; **Chile:** Impidol; Supoviol; VCF†; **Cz.:** Delfen†; Patentex Oval N; **Fin.:** Patentex; **Ger.:** Patentex Oval; Patentex†; **Hong Kong:** Patentex; **Hung.:** Patentex; **India:** Delfen; **Ir.:** Patentex†; Gynol II†; Ortho-Creme; **Israel:** Delfen†; **Mex.:** Lorphyn; **NZ:** Lifestyle; Rendells Plus†; **Pol.:** Patentex Oval; Secural; **Port.:** Delfen†; Rendells; **Rus.:** Patentex Oval N (Патентекс Овал Н); **S.Afr.:** Delfen; Gynol II; **Spain:** Nacha†; **Swed.:** Gynol-Plus; **Switz.:** C-Film†; Delfen†; Patentex Oval N; Syn-A-Gen; **Turk.:** Lorphyn; **UK:** Delfen†; Duragel†; Gygel; Gynol II†; Ortho-Creme†; Orthoforms†; Prelude; **USA:** Advantage 24; Delfen; Encare; Gynol II; Semicid; Sheik Elite; Shur-Seal; Today; VCF.

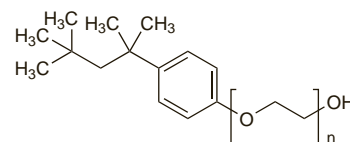
**Multi-ingredient:** **Arg.:** Menthilate Iodopovidona; **Canada.:** Protectaid; **Ger.:** A-gen 53; **Hong Kong:** Protectaid; **Israel:** Glovan; **Mex.:** Nor-forms†; Sin-A-Gen; **Spain:** Lavolen; **Turk.:** Agen; **UK:** Protectaid.

#### Octoxinols

Macrogol Tetramethylbutylphenyl Ethers; Octoxinols; Octoxynols; Octylphenoxy Polyethoxyethanol.  $\alpha$ -(4-(1,1,3,3-Tetramethylbutyl)phenyl)- $\omega$ -hydroxypoly(oxyethylene).

ОКТОКСИНОЛЫ

CAS — 9002-93-1.



**Nomenclature.** Octoxinols are a series of tetramethylbutylphenyl ethers of macrogols of differing chain lengths, represented by the formula  $C_{14}H_{21}[O.CH_2.CH_2]_n.OH$ .

Octoxinol is *BAN* and *rINN*. The name may be followed by a figure indicating the approximate number of oxyethylene groups in the polyoxyethylene chain. *USAN* specifies Octoxynol 9. The name p-di-isobutyl-phenoxypolyethoxyethanol has been used to describe octoxinol 9 but may have also been applied to other octoxinols.

#### Octoxinol 9 (BAN, rINN)

Octoxinolum 9; Octoxynol 9 (*USAN*).

Октоксинол 9

$C_{32}H_{58}O_{10}$  (nominal) = 602.8.

**Pharmacopoeias.** In *USNF*.

**USNF 26** (Octoxynol 9). An anhydrous liquid mixture consisting chiefly of mono-octylphenyl ethers of macrogols, corresponding to the formula  $C_{14}H_{21}[O.CH_2.CH_2]_n.OH$ , in which the average value of *n* is about 9. A clear, pale yellow, viscous liquid with a faint odour. Miscible with water, with alcohol, and with acetone; soluble in toluene and in benzene; practically insoluble in petroleum spirit. Store in airtight containers.

#### Octoxinol 10 (BAN, rINN)

Octoxinolum 10; Oktoksinoli-10; Oktoksinolis 10; Oktoksynol 10; Oktoxinol-10; Oktoxinol 10.

Октоксинол 10

$C_{34}H_{62}O_{11}$  (nominal) = 646.8.

**Pharmacopoeias.** In *Eur.* (see p.vii).

**Ph. Eur. 6.2** (Octoxinol 10). A mixture consisting mainly of mono-octylphenyl ethers of macrogols corresponding to the formula:  $C_{14}H_{21}[O.CH_2.CH_2]_n.OH$  where the average value of *n* is