

# Glycofurol

## 1 Nonproprietary Names

None adopted.

## 2 Synonyms

*Glycofurol 75*; tetraglycol;  $\alpha$ -(tetrahydrofuryl)- $\omega$ -hydroxy-poly(oxyethylene); tetrahydrofurfuryl alcohol polyethylene glycol ether.

Note: tetraglycol is also used as a synonym for tetrahydrofurfuryl alcohol.

## 3 Chemical Name and CAS Registry Number

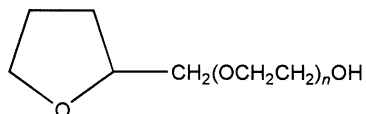
$\alpha$ -[(Tetrahydro-2-furyl)methyl]- $\omega$ -hydroxy-poly(oxy-1,2-ethanediyl) [31692-85-0]

## 4 Empirical Formula      Molecular Weight

C<sub>9</sub>H<sub>18</sub>O<sub>4</sub> (average)

190.24 (average)

## 5 Structural Formula



Glycofurol 75:  $n = 1-2$

## 6 Functional Category

Penetration enhancer; solvent.

## 7 Applications in Pharmaceutical Formulation or Technology

Glycofurol is used as a solvent in parenteral products for intravenous or intramuscular injection in concentrations up to 50% v/v.<sup>(1-5)</sup> It has also been investigated, mainly in animal studies, for use as a penetration enhancer and solvent in topical<sup>(6)</sup> and intranasal formulations.<sup>(7-10)</sup>

## 8 Description

Glycofurol is a clear, colorless, almost odorless liquid, with a bitter taste; it produces a warm sensation on the tongue.

## 9 Pharmacopeial Specifications

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## 10 Typical Properties

Boiling point: 80–100 °C for *Glycofurol 75*

Density: 1.070–1.090 g/cm<sup>3</sup> at 20 °C

Hydroxyl value: 300–400

Moisture content: 0.2–5% at ambient temperature and 30% relative humidity.

Refractive index:  $n_D^{40} = 1.4545$

Solubility: see Table I.

Table I: Solubility of glycofurol.

Solvent	Solubility at 20 °C
Arachis oil	Immiscible
Castor oil	Miscible <sup>(a)</sup>
Ethanol (95%)	Miscible in all proportions
Glycerin	Miscible in all proportions
Isopropyl ether	Immiscible
Petroleum ether	Immiscible
Polyethylene glycol 400	Miscible in all proportions
Propan-2-ol	Miscible in all proportions
Propylene glycol	Miscible in all proportions
Water	Miscible in all proportions <sup>(a)</sup>

<sup>(a)</sup> Cloudiness may occur.

Viscosity (dynamic): 8–18 mPa s (8–18 cP) at 20 °C for *Glycofurol 75*.

## 11 Stability and Storage Conditions

Stable if stored under nitrogen in a well-closed container protected from light, in a cool, dry place.

## 12 Incompatibilities

Incompatible with oxidizing agents.

## 13 Method of Manufacture

Glycofurol is prepared by the reaction of tetrahydrofurfuryl alcohol with ethylene oxide (followed by a special purification process in the case of *Glycofurol 75*).

## 14 Safety

Glycofurol is used as a solvent in parenteral pharmaceutical formulations and is generally regarded as a relatively nontoxic and nonirritant material at the levels used as a pharmaceutical excipient. Glycofurol can be irritant when used undiluted; its tolerability is approximately the same as propylene glycol.<sup>(1,2)</sup>

Glycofurol may have an effect on liver function and may have a low potential for interaction with hepatotoxins or those materials undergoing extensive hepatic metabolism.<sup>(4)</sup>

LD<sub>50</sub> (mouse, IV): 3.5 mL/kg<sup>(2)</sup>

## 15 Handling Precautions

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

**16 Regulatory Status**

Included in parenteral medicines licensed in Europe.

**17 Related Substances**

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**18 Comments**

Grades other than *Glycofurol 75* may contain significant amounts of tetrahydrofurfuryl alcohol and other impurities. *Glycofurol 75* meets an analytical specification which includes a requirement that the fraction in which  $n = 1$  or 2 amounts to a minimum of 95%; see Section 5.

**19 Specific References**

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- 8 Bechgaard E, Gizurarson S, Hjortkjaer RK. Pharmacokinetic and pharmacodynamic response after intranasal administration of diazepam to rabbits. *J Pharm Pharmacol* 1997; 49(8): 747–750.
- 9 Nielson HW, Bechgaard E, Twile B, *et al.* Intranasal administration of different liquid formulations of bumetanide to rabbits. *Int J Pharm* 2000; 204: 35–41.
- 10 Bagger MA, Nielsen HW, Bechgaard E. Nasal bioavailability of peptide T in rabbits: absorption enhancement by sodium glycocholate and glycofurol. *Eur J Pharm Sci* 2001; 14(1): 69–74.

**20 General References**

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**21 Author**

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**22 Date of Revision**

25 April 2002.