Technical Information

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Soluphor® P

Pyrrolidone Ph.Eur.

2-Pyrrolidone as a solvent for the pharmaceutical industry

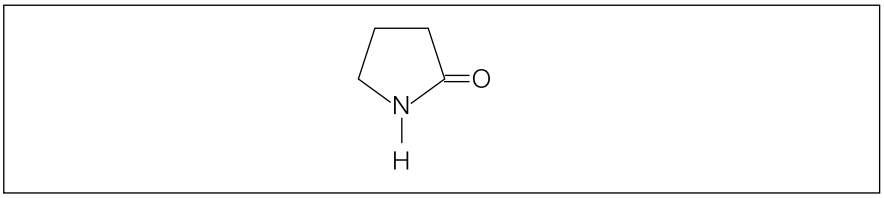
BASF
The Chemical Company

Pharma Ingredients & Services

Chemical nature

Pyrrolidone-2, dist.
C_4H_7NO molecular weight: 85.1

Structural formula



Properties

Soluphor P is a colourless or slightly coloured liquid which solidifies at room temperature and has a characteristic odour. It is soluble in water and a number of organic solvents, e.g. ethanol, isopropyl alcohol and aromatic hydrocarbons. Solutions of Soluphor P in water of up to 50% have a viscosity of no more than 4 mPa s.

Specification

See separate document: "Standard Specification (not for regulatory purposes)“ available via BASF‘s WorldAccount: https://worldaccount.basf.com (registered access).

Regulatory status

Soluphor P is produced in accordance with the GMP guidelines and meets the requirements of the current Ph. Eur. monograph "Pyrrolidone".

Handling recommendations

Before application Soluphor P is to be melted down by careful, possibly lengthy heating and homogenised. Appropriate tests showed after 7 days at 50°C no change in the analytical properties of the product.

Applications

Soluphor P is approved for the use in veterinary medicines. The product is mainly used as a solvent for intravenous applications or topical preparations. Some formulation examples are included below.

Injections

Soluphor P is used in veterinary injection preparations as a solvent together with water and/or in combination with low-molecular polyvinylpyrrolidone (Kollidon® 12 PF or Kollidon 17 PF). Likewise it suggests itself for use in solutions for oral application. In the following table the solubilities of some active ingredients in Soluphor P and Soluphor P mixtures are listed:

Active ingredient	Soluphor P + water (2 + 8)	Soluphor P + water (4 + 6)	Soluphor P + water (4 + 6) + 5% Kollidon 12 PF	Soluphor P
Propanediol	20 mg/ml	140 mg/ml	140 mg/ml	500 mg/ml
Dimetridazole	20 mg/ml	30 mg/ml	30 mg/ml	40 mg/ml
Sulphathiazole	< 10 mg/ml	30 mg/ml	40 mg/ml	220 mg/ml
Chloramphenicol	10 mg/ml	100 mg/ml	150 mg/ml	1,300 mg/ml

The application in connection with oxytetracycline has been described in a patent from which the following example of application of an oxytetracycline retard ampoule was taken [1]:

Oxytetracycline	22.65 g
Magnesium oxide	1.92 g
2-pyrrolidone (e. g. Soluphor P)	40.00 g
Polyvinylpyrrolidone K 17 (e. g. Kollidon® 17 PF)	5.00 g
Magnesium formaldehyde sulphoxylate	0.44 g
2-aminoethanol	3.84 g
Water	q. s. ad 100.00 ml

Water and Soluphor P are mixed and Kollidon 17 PF is dissolved in it; the solution is heated up to 75°C, magnesium formaldehyde sulphoxylate is added and dissolved with stirring. After the suspension of the magnesium oxide, oxytetracycline is slowly stirred in until a clear solution is obtained. After cooling-down the pH value is adjusted to 8.5 with the help of aminoethanol.

By means of the combination of the two substances, polyvinylpyrrolidone and Soluphor P, a parenteral preparation with a long-acting effect can possibly be achieved [2, 3]. In the case of ivermectin injectables also low molecular weight povidone and 1-pyrrolidone are combined [13]. The specific over-sensitivity known for dogs with regard to parenterally administered polyvinylpyrrolidone must be noted in this connection.

A further example of a veterinary injection is the following formulation of a trimethoprim-sulfonamide combination developed on the laboratory scale:

Trimethoprim	2.0 g
Sulfadoxin	10.0 g
Soluphor P	56.0 g
Water	29.0 g
Sodium hydroxide solution	q. s. (pH 8.5)

The two active ingredients are dissolved in Soluphor P, the water is added and the pH value is set to 8.5 with sodium hydroxide solution.

Topical preparations

A number of scientific publications describes the application of Soluphor P as absorption enhancer in topical preparations. The penetration of active ingredients through the human skin is markedly increased by Soluphor P [12] and/or accelerated to the same extent as by dimethyl sulphoxide, dimethyl isosorbide or dimethyl acetamide [4, 10, 14] or even more markedly than by means of dimethyl formamide [6-9]. This effect is also described for transdermal systems [5] and for the transmucosal application [11].

Preservation

Soluphor P shows strong antimicrobial effectiveness against gram-positive and gram-negative bacteria and moulds. This results in additional preservation of the application formulation possibly no longer being necessary.

Stability

The product can be kept in the unopened original container for at least 12 months at room temperature.

Storage and packaging

In order to avoid discoloration storage below 25°C is recommended.
The sensitivity of the substance to traces of iron is countered by the use of a 200-kg metal drum with a removable PE inner container.

Safety data sheet

A safety data sheet is available.

PRD-No.

30035117

Toxicological data

Reports of the toxicological studies are available on request after having signed a secrecy agreement.

Literature

[1] US Patent 4, 018, 889 (1976), Pfizer

[2] European Patent 0 021 847 (1980), Pfizer

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[4] B. W. Barry, J. Contr. Release **6**, 85-97 (1987)

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[11] Japanese Patent 01160916 (Tanabe, 1989)

[12] T. X. Viegas, A. H. Hikal, A. B. Jones, Int. J. Pharm. **152**, 165-178 (1997)

[13] Int.Patent WO 97/26895 (1997)

[14] V.R. Sinka u. Paul Kaur, Drug Dev. Ind. Pharm., 26 (11) 1131-1140 (2000)

Note

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