CLARIANT

Bioavailability Enhancement of Poorly Soluble APIs

A WIDE SOLUBILIZERS OFFERING

what is precious to you?

CLARIANT SOLUBILIZERS

Poor bioavailability of API continues to be the biggest challenge to the formulators. Factors affecting the bioavailability of API are related to its solubility, permeability, stability, pharmacokinetic/pharmacodynamic profile (PK/PD), targeted vs. non-targeted drug delivery and formulation. Not all these factors can be equally well influenced. Usually, the main approach in pharmaceutical R&D is to increase the solubility of the API, enhance API stability and optimize the formulation. Improvement of the PK/PD profile may be achieved e.g. via modification of the release profile of a dosage form. To improve the absorption of the API by the body, formulators usually focus on enhancing the solubility and not the permeability of the API as the former can be more easily achieved and represents a major limitation for API bioavailability. By enhancing their bioavailability, more APIs and formulations may reach the market, the R&D costs are reduced, and the time-to-market period is shortened

Solubilizers are still common and first choice adopted by formulators to tackle API solubility issue due to their easy handling and well established safety profile. Clariant offers a wide range of choices of solubilizers which are produced under IPEC GMP standard and naturally compliant to pharmacopoeias. These solubilizers are mainly classified into the category of solvents, PEG-derivatives and Poloxamers.

Types	NAME	PHARMACOPEIAL NAME	MONOGRAPH
Solvents	VitiPure LEX 300/400	Polyethylene Glycol 300/ 400 Macrogol 300/ 400	USP/NF Ph.Eur. JP
PEG-Derivatives	VitiPure HCO 40	Polyoxyl 40 Hydrogenated Castor Oil Macrogolglycerol Hydroxystearate	USP/NF Ph.Eur.
	VitiPure CO 35	Polyoxyl 35 Castor Oil Macrogolglycerol Ricinoleate	USP/NF Ph.Eur.
	VitiPure L 20	Polysorbate 20	USP/NF Ph.Eur.
	VitiPure O 80	Polysorbate 80	USP/NF Ph.Eur.
Poloxamers	VitiPure P 188	Poloxamer 188	USP/NF Ph.Eur.

With our pharmaceutical GMP facilities in Germany, Spain and China Clariant thrives to provide high quality and innovative excipients into various pharmaceutical applications. Clariant is largest supplier of Polyethylene glycols and trusted supplier for pharmaceutical raw material with proven track record.

VITIPURE™ LEX 300 & 400

Polyethylene glycol with stringent control of microbial load for pharmaceutical Industry.

Clariant is a global supplier of pharmaceutical grade polyethylene glycols (PEG). With decades of experience in the production and supply of high-quality PEGs Clariant has further expanded its PEG portfolio with low microbial load variant. VitiPure™ LEX 300 & 400 surpass the current pharmacopoeia requirements and support the needs of customers who require stringent control on microbial load in their formulations.

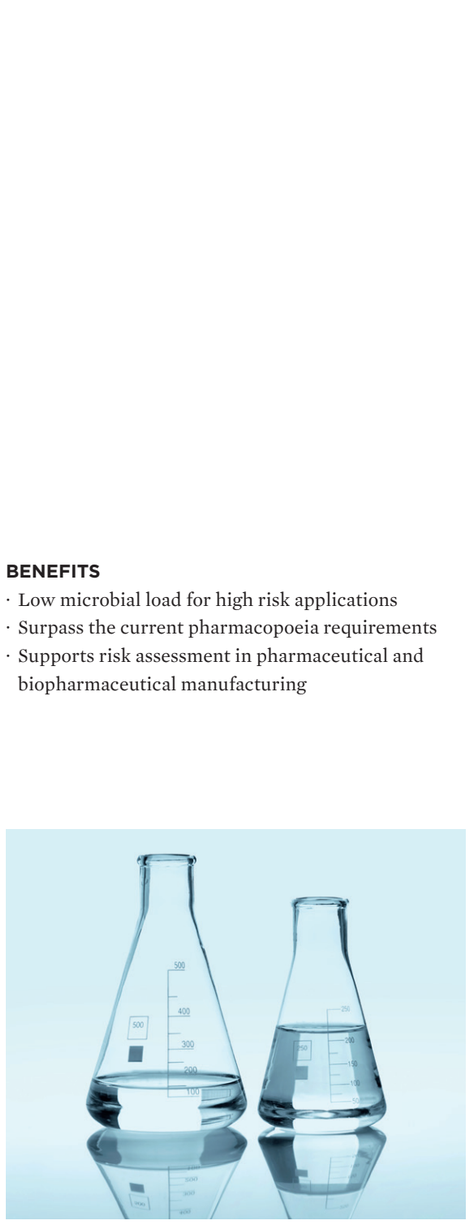
KEY INFORMATION – MICROBIAL LOAD

Endotoxin: max. 1 IU/ml
TAMC: max. 50 cfu/g
TYMC: max. 50 cuf/g
Salmonella: absent
Staphylococcus aureus: absent
Escherichia coli: absent
Pseudomonas aeruginosa: absent

BENEFITS

- Low microbial load for high risk applications
- Surpass the current pharmacopoeia requirements
- Supports risk assessment in pharmaceutical and biopharmaceutical manufacturing

Description	
CAS-No.	25322-68-3
Chemical name	Polyethylene Glycol 300 & Polyethylene Glycol 400
Pharmacopoeia	Meets the requirement of the current monographs for Macrogol in Ph.Eur., JP and Polyethylene glycol in USP/NF
Appearance	Clear liquid
GMP	IPEC-GMP (excipients)
ICHQ3D	Metal impurity statement is available on request
Packaging material	Stainless steel drum with PE-inliner
Packaging	220kg, 30kg
Retest Period	730 days (in unopened original container)



APPLICATION & FUNCTIONALITY

- Safe and widely used pharmaceutical solvents for varieties of different APIs which are difficult to dissolve in water
- Applied in liquid and semi-solid formulations
- Excellent hygroscopicity, perfect as humectants

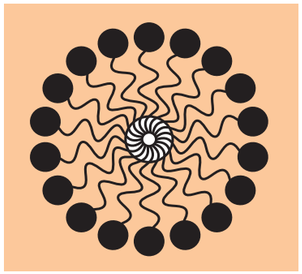
VITIPURE™ HCO 40

Versatile solubilizer and emulsifier enhancing the solubility and bioavailability of hydrophobic APIs and vitamins.

BENEFITS
- Ideal excipient for hydrophobic APIs and vitamins
- Well established safety and toxicology via a variety of traded drugs
- Suitable for SEDDS and SMEDDS formulations*
- Zero taste and odour: perfect for oral applications

KEY INFORMATION
- Type: Non ionic surfactant
- Generic names: Polyoxyl 40 Hydrogenated Castor Oil (USP), Macrogolglycerol Hydroxystearate (Ph. Ur.)
- CAS Number: 61788-85-0
- Retest period: 2 years
- Packaging sizes: 100kg steel drum (epoxy coated in-liner) and 25kg steel drum (epoxy coated in-liner).
- Sample size: 0.5kg

SAFETY
- World-wide several registered Pharmaceutical OTC and prescription medicines
- Listed in the inactive ingredient database of the FDA



SOLUBILITY OF API IN SURFACTANTS
The solubilizing effect of surfactants is associated with the number and size of micelles formed. The solubility of hydrophobic APIs would increase with increasing concentration of surfactants above the critical micelle concentration (CMC). For VitiPure™ HCO 40 it is 0.03% w/w at 37°C.

FOR FORMULATORS	
HLB value	14 - 16
Physical properties	yellowish to white paste at 20°C
Organoleptic properties	practically no odor or taste
Solubility	forms clear solutions in water, ethanol, 2-propanol, n-propanol, ethyl-acetate, chloroform, carbon tetrachloride, toluene and xylene
Stability	pure VitiPure™ HCO 40 is stable in aqueous or alcoholic solutions.
Sterilization	by heating to 120°C

FUNCTIONS IN FORMULATIONS	Liquid formulations	Semi-solid formulations	Solid formulations
Solubilizer	●	●	●
Emulsifier	●	●	
Wettability improvement	●	●	
Sedimentation reduction	●		

FDA PUBLISHED APPLICATIONS Dosage & Applications*	
Capsule	3319 mg MDE**
Opthalmic	0.5 – 1% w/v
Oral solution	0.5 – 45%
Tablet	120 mg MDE
Cream	1% w/w

* SEDDS: self-emulsifying drug delivery systems / SMEDDS: self-microemulsifying drug delivery systems
** MDE: Maximum daily exposure

VITIPURE™ CO 35

Solubiliser and emulsifying agent for the human and veterinary pharmaceutical industries

KEY INFORMATION
- Generic names: Polyoxyl 35 Castor Oil (USP)
  Macrogolglycerol Ricinoleate (Ph. Eur.)
- Chemical nature: VitiPure CO 35 is a nonionic solubiliser and emulsifier made by reacting 1 mole of castor oil with 35 moles of ethylene oxide
- CAS no.: 61791-12-6
- GMP: IPEC
- Retest period: 2 years
- Packaging sizes: 100 kg steel drum (epoxy coated in-liner) and 25kg steel drum (epoxy coated in-liner)
- Sample size: 0.5 kg

SAFETY
- World-wide several registered Pharmaceutical OTC and prescription medicines
- Listed in the inactive ingredient database of the FDA

KEY BENEFITS
- Increases bioavailability when used in SEDDS
- Emulsifies or solubilizes the fat-soluble vitamins A, D, E and K in aqueous solutions for oral and topical administration.
- Aqueous solutions of hydrophobic drugs (e.g. Miconazole, Hexedetine, Clotrimazole, Benzocaine etc.) can be prepared using VitiPure CO 35

FOR FORMULATORS	
HLB value	12 - 14
Physical properties	Pale yellow or clear liquid depending on the temperature
Critical micelle concentration	0.02 % w/v
Organoleptic properties	Faint characteristics odor
Solubility	forms clear solutions in water, ethanol, 2-propanol, n-propanol, ethyl-acetate, chloroform, carbon tetrachloride, trichloroethylene, toluene and xylene
Stability	VitiPure CO 35 can be sterilized by heating to 120°C for 30 min.

FDA PUBLISHED APPLICATIONS Dosage & Applications*	
Oral Solutions	upto. 515 mg/1ml
Ophthalmics	upto. 5% w/v
Tablets/Capsules	upto. 599.4 mg
Creams	upto. 4% w/w
Injection	IV upto. 52.75% w/v 24945mg (MDE)**

* Published in Inactive Ingredients Database by FDA per unit dose MDE: Maximum daily exposure
** Requires parenteral grade
** IV: Intravenous

VITIPURE™ L 20 / O 80

Most widely used surfactants in biopharmaceutical formulations

KEY INFORMATION

- Generic names: Polysorbate 20 (USP/NF; Ph. Eur.)
  Polysorbate 80 (USP/NF; Ph. Eur.)
- Type: Non-ionic surfactant
- CAS no. VitiPure L 20: (9005-65-5)
- CAS no. VitiPure O 80 (9005-65-6)
- GMP: IPEC
- Retest period: 2 years
- Packaging sizes: 100kg steel drum (epoxy coated in-liner) and 25 kg steel drum (epoxy coated in-liner)
- Sample size 0.5 kg

SAFETY

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FOR FORMULATORS	
HLB value	16.7 (VitiPure™ L20) / 15.0 (VitiPure™ O80)
Physical properties	Viscous clear liquid
Critical micelle concentration	0.006% (VitiPure™ L20) / 0.002% (VitiPure™ O80)
Solubility	It is readily soluble in water and alcohols, it is insoluble in oils.

TYPICAL APPLICATIONS

- Solubilizer / Emulsifier
- Suspension stabilizer
- Skin penetration enhancer
- Solubilizer in solid dispersion
- Protein stabilizers

FDA PUBLISHED APPLICATIONS Dosage & Applications*	
Polysorbate 20	
Auricular (OTIC)	Upto. 0.1% w/v
Ophthalmics	Upto. 0.05 % w/v
Tablets/Capsules	Upto. 4.2 mg
Creams	Upto. 7.8% w/w
Injection**	IM Upto. 18mg IV upto 1%w/v
Suppository	upto. 64.8mg
Nasal	upto. 27mg
Polysorbate 80	
Auricular (OTIC)	Upto. 2.5% w/w
Ophthalmics	Upto. 4 % w/w
Tablets/Capsules	Upto. 418.37mg
Creams	Upto. 15% w/w
Injection**	IA Upto. 5mg IB Upto 0.04%w/v IL Upto 0.19%w/v IM Upto 5% IS Upto 2% IV Upto 69.33% w/v IV Upto 0.02% w/v SC Upto 0.3% w/v
Suppository	upto. 72.15mg
Nasal	upto. 0.02% w/v
Oral Solutions	Upto. 126mg/1ml

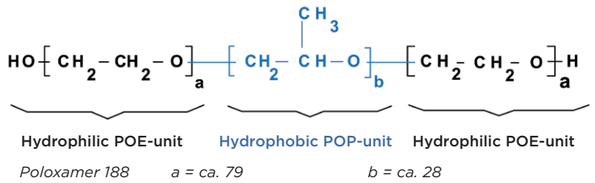
* Published in Inactive Ingredients Database by FDA per unit dose
** Requires parenteral grade
** IA: Intra-articular; IB: Intrabursal; IL: Intralesional; IM: Intramuscular; IS: Intrasynovial; IV: Intravenous; IV:Intravitreal; SC: Subcutaneous

VITIPURE™ P 188

Poloxamer for Pharmaceutical Use

KEY INFORMATION

- Generic names: Poloxamer (USP)
  Poloxamers (Ph. Eur.)
- Chemical nature: VitiPure P 188 is Poloxamer 188. It is a non-ionic solubilizer and synthetic tri-block copolymer of polyoxyethylene (POE) and polyoxypropylene (POP) units represented by following formula:



- CAS no.: 9003-11-6
- GMP: IPEC
- Retest period: 2 years
- Packaging sizes: 100 kg steel drum (epoxy coated in-liner) and 25 kg steel drum (epoxy coated in-liner)
- Sample size: 0.5 kg

SAFETY

- World-wide several registered Pharmaceutical OTC and prescription medicines
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FOR FORMULATORS	
HLB value	29
Physical properties	Waxy Powder (Flakes)
Critical micelle concentration	0.07%
Solubility	Readily soluble in water, Polar and non-polar solvents

TYPICAL APPLICATIONS

- Solubilizers
- Wetting agents
- Gel formers
- Suspension stabilizers
- Melt or spray granulations

KEY BENEFITS

- Multi-talent solubilizer for variety of applications
- Safety & toxicology well established via several marketed drugs world-wide into human and veterinary medicines and nutrition.
- Suitable in solid dispersions and improves the solubility, absorption and bioavailability of low-solubility APIs in solid oral dosage forms.

FDA PUBLISHED APPLICATIONS Dosage & Applications*	
Oral Solutions	upto. 100 mg/1ml
Ophthalmics	upto. 0.1% w/v
Tablets/Capsules	upto. 66.9 mg
Creams	upto. 1% w/w
Injection**	IIM: 0.2% w/v IV: 6mg
Periodontal Gel	upto 55mg

* Published in Inactive Ingredients Database by FDA per unit dose
** Requires parenteral grade

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