SPECIFICATION

Glycerol Ph. Eur. * / USP* / JP* 99.7% (synth.) LA

parenteral grade

OPTIM™ Plus Glycerine 99.7% USP/EP **Product code: 014**

Testing specifications: Ph. Eur.* / USP* / JP* / LSM 014* / LSM 015*

The material meets all requirements of Ph. Eur.*, USP*, JP*, FCC*, 21 CFR 182.1320, (EU) No 231/2012 (E422)

Parameter	Specification	Method
Purity	≥ 99.7 % (m/m)	GC, LSM 015*

Parameter	Ph. Eur.*		USP*		JP*	
	Specification	Method	Specification	Method	Specification	Method
Description / Characters	viscous, colorless, clear,very hygroscopic	Ph. Eur.*	—	—	clear,colorless, viscous	JP*
Assay	98.0 –101.0 %	Ph. Eur.*	99.0-101.0 %	USP*	98.0-101.0 %	JP*
Identification	A / B / C	Ph. Eur.*	A / B / C	USP*	FT-IR	JP*
Appearance of solution	clear, colourless	Ph. Eur.*	—	—	—	—
Color	—	—	conforms USP*	USP*	conforms JP*	JP*
Acidity or alkalinity	≤ 0.2 ml 0.1N NaOH	Ph. Eur.*	—	—	conforms JP*	JP*
Esters (Ph. Eur.*) Fatty acids and esters (USP*/JP*)	conforms Ph. Eur.*	Ph. Eur.*	conforms USP*	USP*	conforms JP*	JP*
Halogenated compounds (Ph. Eur.*) / Limit of chlorinated compounds (USP*)	≤ 35 ppm	Ph. Eur.*	≤ 30 ppm	USP*	—	—
Aldehydes	≤ 10 ppm	Ph. Eur.*	—	—	—	—
Acrolein, glucose, or other reducing substances	—	—	—	—	conforms JP*	JP*
Calcium	—	—	—	—	conforms JP*	JP*
Arsenic	—	—	—	—	≤ 2 ppm	JP*
Sugars	conforms Ph. Eur.*	Ph. Eur.*	—	—	—	—
Chloride(s)	≤ 10 ppm	Ph. Eur.*	≤ 10 ppm	USP*	≤ 0.001 %	JP*
Sulfate	—	—	≤ 20 ppm	USP*	≤ 0.002 %	JP*
Ammonium	—	—	—	—	conforms JP*	JP*
Heavy metals	—	—	—	—	≤ 5 ppm	JP*
Specific gravity (USP /JP) Relative density (Ph. Eur.)	d_{20}^{20} 1.258 – 1.268	Ph. Eur.*	$d_{25}^{25} \geq 1.249$	USP*	$d_{20}^{20} \geq 1.258$	JP*
Refractive index n_D^{20}	1.470 – 1.475	Ph. Eur.*	—	—	≥ 1.470	JP*
Readily carbonizable substances	—	—	—	—	conforms JP*	JP*
Residue on ignition	—	—	≤ 0.01 %	USP*	≤ 0.01%	JP*
Sulphated ash	≤ 0.01 % m/m	Ph. Eur.*	—	—	—	—
Water[1]	≤ 2.0 %	Ph. Eur.*	≤ 5.0 %	USP*	≤ 2.0 %	JP*

[1] The limits are given in the monographs; actually the product contains not more than 0.3% water.

*current version

Compiled by: 09.11.2018	Approved by: 12.11.2018	Released by: 23.11.2018	Effective:	Supersedes:
Dr. Philipp Hoch QA/QC-Manager	Elisabeth Bartel Qualified Person (GMP)	Dr. Frank Milek Qualified Person (GMP)	01.01.2019	25.09.2017

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Parameter	Ph. Eur.*		USP*		JP*	
	Specification	Method	Specification	Method	Specification	Method
Limit of diethylene glycol and ethylene glycol: - DEG - EG	—	—	 ≤ 0.10 % ≤ 0.10 %	USP*	—	—
Related compounds: - total impurities - any individual impurity	—	—	≤ 1.0 % ≤ 0.1 % each	USP*	—	—
Impurity A and related substances: - ∑ Impurities with Rt > Rt of glycerol - each impurity with Rt < Rt of glycerol - Diethylene glycol (Impurity A)	≤ 0.5 % m/m ≤ 0.1 % m/m ≤ 0.1 % m/m	Ph. Eur.*	—	—	—	—
Ethylene glycol, diethylene glycol and related substances: - Ethylene glycol - Diethylene glycol - ∑ Impurities - each other related substance	—	—	—	—	 ≤ 0.1 % ≤ 0.1 % ≤ 1.0 % ≤ 0.1 %	JP*

Microbiological Specification		
Parameter	**Specification**	**Method**
Bioburden (∑ Total aerobic microbial count + Total yeast mould count)	≤ 100 CFU/g	Ph. Eur.* 2.6.12 / USP* <61>/ JP* (harmonised method)
Endotoxins	≤ 0.5 IU/mg	Ph. Eur.* / USP* / JP* (LAL, kinetic-turbidimetric method)

HPLC Aldehyde Specification		
Parameter	**Specification**	**Method**
Glyceraldehyde	≤ 5 ppm	LSM 015* (HPLC)
Dihydroxyacetone	≤ 5 ppm	LSM 015* (HPLC)
Hydroxyacetone	≤ 5 ppm	LSM 015* (HPLC)
Formaldehyde	≤ 2 ppm	LSM 015* (HPLC)

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Quality Assurance and Quality Control	
Process/Operation	**Standard / Requirement**
Production	IPEC PQG – GMP Guidelines for Pharmaceutical Excipients
Supply chain	WHO – GTDP Guidelines for Pharmaceutical Starting Materials
Analytical quality control	Full analysis of specification for each batch in a GMP qualified laboratory
Batch release	Qualified Person according to EU-GMP (2001/83/EC; Articles 48 & 49)
Packaging	Class D (100,000) clean room according to GMP (EU-GMP Part I Annex 1, US cGMP)
Packaging	Extended supervision of repackaging process by chemist or pharmacist
Primary packaging material	Specified packaging materials from audited suppliers: 1 L, 2.5 L Amber Glass Bottles 5L, 10L HDPE Containers 200 L HDPE-Steel Combi-drums 1000 L HDPE EVOH Intermediate Bulk Container with diffusion barrier
Labelling of seal caps	Labelling with filling date and batch no.
Packaging material reconciliation	Full seal cap and label reconciliation
End control of filled containers	First and last container of filling process (water content, color; IR-spectrum)

Storage: It is recommended to store the material in closed containers, below 30°C

Shelf life: 24 months (HPLC aldehyde specification is excluded)

Manufacturer and manufacturing site: Blue Cube Germany Assets GmbH & Co. KG, Stade (Germany)

Manufacturing process: synthetic, key raw material: epichlorohydrin

Regulatory Compliance:

Low aldehyde content:

The certified low aldehyde content of Glycerol 99.7% Ph. Eur.* / USP* / JP* (synth.) (LA / parenteral grade) is advantageous for aldehyde sensitive pharmaceuticals such as biopharmaceutical formulations containing polypeptide based active pharmaceutical ingredients.

BSE/GMO/Kosher status/Aflatoxins:

The material has no BSE risk, is not derived from GMO, is kosher and complies with the German “Aflatoxin Verbotsverordnung”.

Residual solvents (Ph. Eur.* 5.4 / USP* <467> / ICH Q3C):

Based on the process knowledge only one Class 3 solvent is likely to be present. The level of this Residual Solvent is less than 100 ppm.

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Elemental Impurities (Ph. Eur.* 5.20 / ICH Q3D):

At least three independent batches have been analysed for elemental impurities according to guideline ICH Q3D. All determined values of elemental impurities were below the level of 30% of the permitted concentrations for parenteral application according to table A.2.2 of the guideline ICH Q3D. More detailed information is available upon request.

Batch certification:

Every batch is analysed according to all parameters of this specification (except Description / Characters). The Certificate of Analysis (CoA) provides all results like above including analysis date, date of manufacture and residual solvents statement. All CoAs are signed by a Qualified Person according to EU-GMP or a responsible QA/QC-Manager.

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