LTS Lohmann Therapie-Systeme AG, Germany
Quality Control Department

Certificate of Analysis

PRODUCT / MATERIAL:

Buprenorphine (according to the monograph of the Ph. Eur.)

LTS - article no.:	**6506481**	**LTS - batch no.:**	**7645916**
LTS specification :	**2001525-cv**	**Manufacturer batch no.:**	**A16CB1357**

Test parameters	Specified	Result
Appearance / Description	White or almost white powder	complies
Identification	IR corresponds to reference	complies
Appearance of solution	Clear and colourless	complies
Specific optical rotation	-103° to -107°	M.V. = -107°
Impurities / related substances Ph. Eur 2.2.29		
Impurity H[1] according to Ph. Eur.	nmt 0.25 [%]	< 0.05 %
Impurity A, B, F, J[1] according to Ph. Eur.	nmt 0.2 [%]	< 0.1 %
Impurity G[1] according to Ph. Eur.	nmt 0.15 [%]	< 0.05 %
Unspecified impurities / any other unknown[1] & [2] according to Ph. Eur.	nmt 0.10 [%]	< 0.05 %
Total impurities[1] according to Ph. Eur.	nmt 0.7 [%]	< 0.1 %
Loss on Drying	nmt 0.5 [%]*	M.V. = < 0.1 %
Assay	98.5 – 101.5 [%]	M.V. = 99.8 %

Abbreviations: lt = less than; M.V. = mean value; nmt = not more than; n.d. = not detected

[1] Limit value test - the acceptance criteria for the related substances are expressed in the Buprenorphine monograph (1180) in terms of comparison of peak areas (comparative tests).

[2] Under this point also the other detectable impurities C, D, E and I are covered. As they are limited by the general acceptance criterion for other/unspecified impurities

* Tighter than Ph. Eur. monograph (1180); according to CEP/ASMF

The material / product is tested according to the current version of the specification / pharmacopoeia monograph at the time of testing.

Product and documentation were tested according to the relevant SOP´s and conform to the requirements.

Comments:

Date: 15. APR. 2019 **Signature**

Dr. Joscha Kotthaus
Head of the Quality Control Department

The original CoA´s for routine testing will show another format and is in German language.

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JANSSEN PHARMACEUTICA NV
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C16047001/4

Certificate of Analysis

Name of Product :	BUPRENORPHINE, 2 (N*)		
Product Code :	497074	Date of Manufacture :	10-MAR-2016
Batch Number :	A16CB1357	Retest date :	10-MAR-2019
Manufacturing Site :	Geel		

Test	Specification	Result
Appearance	A white or almost white crystalline powder.	Pass
Identification		
IR	Complies with reference spectrum.	Pass
HPLC	The retention time of R371605 in the sample solution must be within ± 5% of the retention time of R371605 in the specificity solution.	Pass
Chromatographic purity (HPLC1 - DS-TMD-9348)		
Norbuprenorphine	< 0.10 %	<0.05 %
N-methyl-nor-buprenorphine (R314053)	< 0.10 %	<0.05 %
6-O-desmethylbuprenorphine (R314050)	< 0.10 %	<0.05 %
5,19-anhydrobuprenorphine (R313514)	<= 0.10 %	<0.05 %
3-O-methyl-N-cyano-nor-buprenorphine (R314047)	< 0.10 %	<0.05 %
N-but-3-enylnorbuprenorphine (R314052)	<= 0.15 %	<0.05 %
3-O-methylbuprenorphine (T002713)	< 0.10 %	<0.05 %
Unspecified impurity	<= 0.10 %	<0.05 %
Chromatographic purity (HPLC1 - DS-TMD-15989)		
Norbuprenorphine	< 0.10 %	<0.05 %
N-methyl-nor-buprenorphine (R314053)	< 0.10 %	<0.05 %
6-O-desmethylbuprenorphine (R314050)	< 0.10 %	<0.05 %
5,19-anhydrobuprenorphine (R313514)	<= 0.10 %	<0.05 %
3-O-methyl-N-cyano-nor-buprenorphine (R314047)	< 0.10 %	<0.05 %
N-but-3-enylnorbuprenorphine (R314052)	<= 0.15 %	<0.05 %
3-O-methylbuprenorphine (T002713)	< 0.10 %	<0.05 %
Unspecified impurity	<= 0.10 %	<0.05 %
Chromatographic purity (HPLC2 - DS-TMD-6533)		
15,16-dehydrobuprenorphine (R314054) and/or 17,18-dehydrobuprenorphine (R314058)	< 0.10 %	<0.05 %

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Manufacturing Site :	Geel		

Test	Specification	Result
Chromatographic purity (HPLC1 - DS-TMD-9348 + HPLC2 - DS-TMD-6533)		
Total impurities	<= 0.65 %	0.00 %
Chromatographic purity (HPLC1 - DS-TMD-15989 + HPLC2 - DS-TMD-6533)		
Total impurities	<= 0.65 %	0.00 %
Appearance of solution	Clear and colorless.	Pass
Loss on drying	<= 0.5 %	0.1 %
Specific optical rotation (calculated on the dry basis)	-107 degree to -103 degree	-105 degree
Assay Base Titration (calculated on the dry basis)	98.5 % to 101.0 %	100.1 %
Particle size Laser diffraction		
d! 10	<= 600 µm	590 µm
Residual Solvent GC		
Methanol	<= 250 ppm	<99 ppm
Ethanol	<= 1000 ppm	<99 ppm
Dichloromethane	<= 600 ppm	<100 ppm

Information

Specification Report : DS-SPE-23958 (1.0)

Conclusion: Approved

Remark: ONLY FOR THE APPROVED MARKE TS

This batch has been manufactured, including packaging and quality control, in accordance with the GMP requirements and complies with the requirements in the above Specification Report.

This certificate of analysis has been produced on 08-SEP-2016 and originally electronically signed for approval by Ewoud Somers (ESOMERS3) on 02-AUG-2016. This certificate is produced by a validated Laboratory Information Management System and therefore bears no handwritten signature. The release of this certificate is under the supervision of Jelle Van Gauwbergen, Director Quality Assurance.