Certificate of Analysis
Certified Reference Material

Lipomed Document QC-CA-1893L1
Version: 003-20.Mar.2023 Supersedes: 002-14.Jul.2021

Product Name: **1 ml Norquetiapine.HCl solution**
(1 mg free base/1 ml methanol)
11-(1-Piperazinyl)dibenzo[b,f][1,4]thiazepine.hydrochloride**;** N-Desalkylquetiapine.hydrochloride

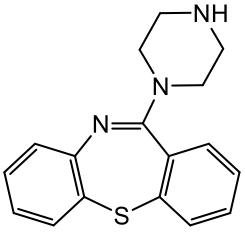
Lot No: 1893.1B1.1L3
Art. No: QUE-1893-HC-1LM

Release Date: January 15, 2020
Last Testing Date: March 20, 2023
Retest Date: **March 2025**

Bulk Product Information: 1893.1B1.1

Chemical Formula: $C_{17}H_{17}N_3S$ Molwt: 295.40
Hydrochloride 331.86

CAS Registry No: 753475-15-9



PARAMETER	SPECIFICATION	RESULT
Certified Concentration	**0.9500 – 1.0500 mg/ml free base**	**0.9944 mg/ml free base**
Combined Uncertainty	**≤ 5.0 %**	**1.4 %**

Certified concentration is verified through duplicate analysis of multiple ampoules representative from the lot compared with 2 independently prepared solutions.
Uncertainty of the certified concentration is an uncertainty determined in accordance with ISO/IEC 17025 and ISO 17034. The calculation was based on the analytical methods applicable to reference standards in solution and incorporates the analytical method uncertainty and the ampoule to ampoule homogeneity (within bottles and between bottles) according to U(y) equation on the last page of this certificate.

Storage Conditions: For maximum stability store airtight at **-18 °C** in a dark location.

Lipomed certifies that this standard meets the specifications stated in this certificate and warrants this product to meet the stated acceptance criteria throughout the retest/expiry date when stored unopened and compliant to the above stated storage conditions. The product should be used shortly after opening to avoid concentration changes due to evaporation. Warranty does not apply to ampoules stored after opening.

FOR ANALYTICAL PURPOSES ONLY: NOT FOR HUMAN OR ANIMAL USE!

Issued by Dr. L. Prévot

Date sign: Arlesheim,

March 20, 2023

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Used Standard Solutions for Calibration:

Solution	Concentration
Reference 1	0.9875 mg/ml
Reference 2	0.9932 mg/ml

Position of Samples	Concentration
Start	0.9917 mg/ml
Middle	0.9977 mg/ml
End	0.9939 mg/ml

Homogeneity:

Lot		Specification	Result
Current	1893.1B1.1L3	RSD ≤ 5.0 %	1.4 %
Comparative	1893.1B1.1L4	RSD ≤ 5.0 %	1.1 %

Lot to Lot Consistency:

Lot		Concentration
Current	1893.1B1.1L3	0.9944 mg/ml free base
Previous	N/A	N/A

Supportive Data:

Parameter	Specification	Result
Appearance	clear colorless solution	conforms
Identity	HPLC R_t corresponds to R_t of reference standard (± 0.5 min)	R_t standard = 8.6 min R_t test = 8.6 min
Solution Purity	HPLC > 95.0 %	96.85930 ± 0.2247 %
Solvent Purity (GC)	methanol > 99.9 %	> 99.9 %
Extractable Volume	> 1 ml	conforms

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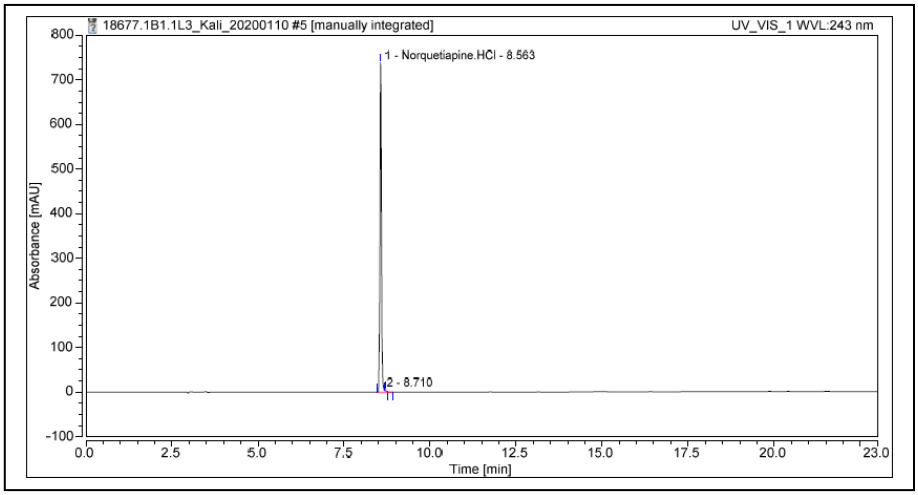
HPLC Data:



Analytical Conditions:

Column
YMC Pack Pro C18, (250*4.6) mm, 5 um
Mobile Phase
A: 0.1 % H3PO4 in water
B: 0.1 % H3PO4 in acetonitrile
Gradient:
10 min (equilib.) 90% A/10% B
1 min 90% A/10% B
19 min 30% A/70% B
22 min 30% A/70% B
Flow rate: 1 ml/min
Wavelength: 243 nm
Injection volume: 1 ul

Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %
1	Norquetiapine.HCl	8.56	35.704	738.8	99.71988
2		8.71	0.100	3.0	0.28012
Total:			**35.804**	**741.742**	**100.00000**

Stability:

Short Term Stability: Short term stability studies have been performed at -18°C and +40°C during a period of 2 weeks. No decrease in purity was observed at -18°C. A decrease of 6.8% has been observed at +40°C. These data support transport of this product in cold conditions.

Long Term Stability: Long term stability studies have been performed in freezer (-18°C). A stability of 62 months has been established. A decrease of 2.9% in purity has been observed during this period.

Based on these stability values, shipping uncertainty has been considered insignificant to the overall uncertainty.

Document History:

Version	Change	Date
Version 1	New version	January 30, 2020
Version 2	Long term stability has been updated to 42 months after release date.	July 14, 2021
Version 3	Solution purity specification has been updated to > 95.0%. Long term stability has been updated to 62 months after release date.	March 20, 2023

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GENERAL INFORMATION

Quality Documentation:

This certificate is designed in accordance with ISO Guide 31 (Reference Materials – Contents of Certificates and Labels) and ISO Guide 35 (Reference Materials – General and Statistical Principles for Certification).

Quality Standards for Arlesheim production site:

ISO 9001 Quality Management System. Manufacturing, analysis, packaging and distribution of Analytical Reference Materials and Pharmaceuticals. IQNet/SQS Certification: 37199

ISO/IEC 17025 General requirements for the competence of Testing Analytical Reference Standards. ANAB Certificate number: AT-1760

ISO 17034 General requirements for the competence of Reference Material Producer. ANAB Certificate number: AR-1761

Quality Control Assessment:

The product quality is controlled by regularly performed analytical control tests/retests.

Intended Use:

The product covered by this certificate is designed for calibration or for use in quality control procedures for the specified chemical compound listed on the first page. This product can be used for quantification and/or identification. All solutions should be thoroughly mixed prior to use. If dilution is required, use only diluent compatible with the substance and solvent in this preparation.

Expiration/Retest Date:

Expiration/retest date of the unopened ampoule stored at the recommended storage conditions is the last day of the month.

A retest will be performed 6 months prior to the stated retest date. Upon successful retesting, a new retest date or expiration date is set for the product. The certificate of analysis is then updated and made available on our website. For our products, the extension of the shelf life is capped to 10 years after release as the maximum period.

Gravimetric Preparation:

All balances are calibrated annually by an ISO/IEC 17025 accredited calibration service. Calibration verification is performed weekly with certified and traceable weights. For each balance, a minimum weighing value has been assigned.

Purity:

- Purity and/or chemical identity are determined by one or more of the following techniques: HPLC/UV, GC/FID, LC/MS, IR, UV, 1H NMR, Karl Fischer, melting point, and optical rotation if applicable
- Purity of isomeric compounds is reported as the sum of the isomers
- Purity values are rounded to the last decimal place given
- The salt form, purity, residual water, and residual solvents are already taken into account for the given content value.

Uncertainty Statistics:

The uncertainties are determined in accordance with ISO 17034 and ISO/IEC 17025. Uncertainty is given for a minimum injection volume of 1 µl. The certified uncertainty value (including characterization uncertainty, homogeneity between ampoules uncertainty, storage stability uncertainty and shipping stability uncertainty) is combined using the following formula:

$$U(y) = \sqrt{U^2_{characterization} + U^2_{homogeneity} + U^2_{storage\ stability} + U^2_{shipping\ stability}}$$

For expanded uncertainty with confidence interval of 95% multiply combined uncertainty, here above, by coverage factor k=2. The filling volume is the minimum sample size for which the uncertainty is valid. The ampoules are over-filled to ensure that the minimum filling volume can be sufficiently transferred.

Homogeneity:

Homogeneity of the lot is confirmed by a duplicate analysis of at least 12 ampoules. At least 4 ampoules are taken at start, middle and end of the filling process. The number of ampoules to be analyzed depends on the lot size. The analyzed concentration at each position is the average value obtained from duplicate analysis of 4 ampoules.

Stability:

The manufacturer guarantees the stability of this product throughout its intended shelf life, when handled and stored accordingly to the given storage conditions.

Legal and Safety Notice:

This product is for routine laboratory analysis and research purposes only. Due to the hazardous nature, only trained personnel should handle this product. The General Terms and Conditions of Lipomed apply.

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