Certificate of Analysis
Certified Reference Material

Lipomed Document QC-CA-74L1
Version: 002-14.Sep.2018 Supersedes: 001-26.Jul.2016

Product name: **1 ml 7-Aminoflunitrazepam solution**
(1 mg free base/1 ml acetonitrile)
9-Amino-6-(2-fluorophenyl)-2-methyl-2,5-diazabicyclo[5.4.0]undeca-5,8,10,12-tetraen-3-one

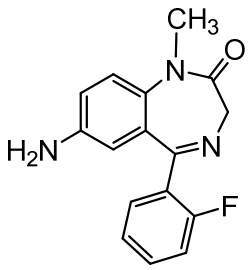
Lot Nr: 74.1B3.2L1
Art. Nr: FLU-74-FB-1LA

Release date: June 07, 2016
Last testing date: N/A
Expiry date: **June 2026**

Bulk Product Information: 74.1B3.2

Chemical formula: $C_{16}H_{14}FN_3O$ Molwt: 283.31

CAS Registry Nr: 34084-50-9



TEST	SPECIFICATIONS	RESULTS
1. Appearance	clear colorless solution	conforms
2. Identity	HPLC R_t corresponds to R_t of reference standard (± 0.5 min)	R_t standard = 10.7 min R_t test = 10.6 min
3. Solution Purity	HPLC > 98.5 %	99.4599 ± 0.0107 %
4. Certified Concentration	0.9500 – 1.0500 mg/ml free base	0.9753 ± 0.0475 mg/ml (mean value) free base
5. Solvent purity (GC)	acetonitrile > 99.9 %	> 99.9 %
6. Extractable volume	> 1 ml	conforms

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

Storage conditions: For maximum stability store air-tight at 2 - 8 °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 through the retest date when stored unopened as recommended. The product should be used shortly after opening to avoid concentration changes due to evaporation. Warranty does not apply to ampoules stored after opening.

Issued by Dr. L. Prévot

Date sign: Arlesheim,

September 14, 2018

Lipomed AG
Fabrikmattenweg 4
4144 Arlesheim
Switzerland
Tel. +41 61 702 02 00
Fax +41 61 702 02 20

Lipomed GmbH
Hegenheimer Str. 2
79576 Weil am Rhein
Germany
+49 7621 1693 473
+49 7621 1693 474

Lipomed Inc.
150 Cambridge Park Drive, Suite 705
Cambridge, MA 02140
U.S.A.
+1 (617) 577 7222
+1 (617) 577 1776

www.lipomed.com
lipomed@lipomed.com

Standard Solution Calibration:

Bulk Reference Solutions	Prepared concentration in mg/ml
Reference 1	1.0175 mg/ml
Reference 2	1.0180 mg/ml

Fill position	Analyzed concentration in mg/ml
Early	0.9753 mg/ml
Middle	0.9735 mg/ml
Late	0.9771 mg/ml

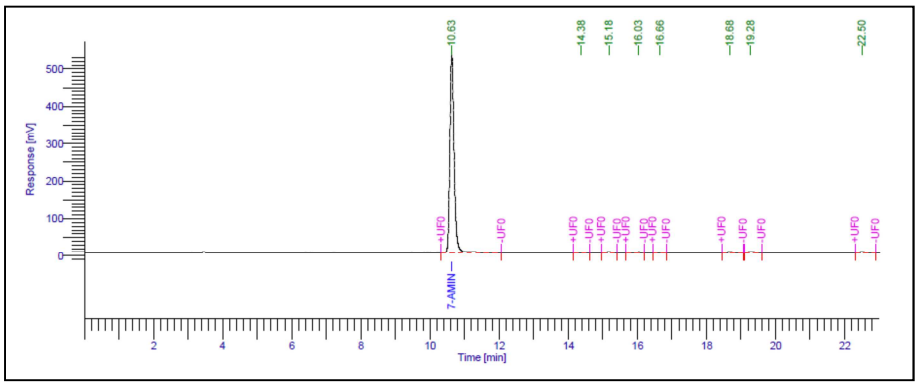
Homogeneity:

	Specification	Result
% RSD	< 5 %	2.4 %

Lot to Lot Consistency:

Standard solution	Lot Number	Concentration
Actual Lot	74.1B3.2L1	0.9753 ± 0.0475 mg/ml free base
Previous Lot	74.1B2.1L6	0.9737 ± 0.0007 mg/ml free base

HPLC Data:



Analytical conditions:

column:
YMC Pack Pro C18 5um (250*4.6)mm
mobile phase:
A: water
B: acetonitrile
1 min 75%A / 25%B
18 min 35%A / 65%B
3 min 35%A / 65%B
flow rate: 1.0 ml/min
wavelength: 265 nm
injection volume: 2 ul

Peak #	Component Name	Time [min]	Area [uV*sec]	Area [%]
1	7-Aminoflunitrazepam	10.63	4456908.2	99.47689
2		14.38	1008.0	0.02250
3		15.18	3155.2	0.07042
4		16.03	2252.2	0.05027
5		16.66	1066.5	0.02380
6		18.68	4503.6	0.10052
7		19.28	9228.3	0.20597
8		22.50	2223.3	0.04962

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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. These data support transport of this product at ambient temperature.

Long term stability: Long term stability studies have been performed in refrigerator (+2°C to +8°C) over a period of more than 5 years. No decrease in purity has been observed during this period. Based on this stability data, an expiry date 10 years after release date has been set.

Based on these stability values, storage uncertainty and shipping uncertainty have been considered insignificant to the overall uncertainty.

Document history:

Version	Change	Date
Version 1	New version	July 26, 2016
Version 2	Long term stability updated to 10 years after release	September 14, 2018

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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:

ISO 9001:2015	Quality Management System. Manufacturing, analysis, packaging and distribution of Analytical Reference Materials and Pharmaceuticals. IQNet/SQS Certification: 37199
ISO/IEC 17025:2005	General requirements for the competence of Testing Analytical Reference Standards. ANAB Certificate number: AT-1760
ISO Guide 34:2009	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 quality 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 page 1. This product can be used for quantification and/or identification. If dilution is required use only diluent compatible with all certified analyses in this preparation. All solutions should be thoroughly mixed prior to use.

Expiration/Retest dates:

Expiration date/Retest date of the unopened ampoule stored at the recommended storage condition is the last day of the month listed page 1.

A retest is performed 6 months prior to the stated retest date. Upon successful retesting, a new retest date or expiration date is set for the product. A maximum shelf-life of 10 years after the release date can be stated. The certificate of analysis is then updated and made available on our web-site.

Uncertainty, concentration and Expiration/Retest dates of the Reference Material are based on the unopened ampoule being stored according to the recommended condition found in the storage field.

Gravimetric preparation:

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

Purity:

- Purity and/or chemical identity are determined by one or more of the following techniques: HPLC, GC/FID, LC/MS, IR, UV, 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 up to the third decimal place
- The content is already corrected from the salt form, the purity, residual water and residual solvents.

Uncertainty Statistics and Confidence limits:

The uncertainties are determined in accordance with ISO Guide 34 and 17025. The certified combined stressed uncertainty value (includes gravimetric uncertainty, homogeneity between ampoules uncertainty, storage stability uncertainty and shipping stability uncertainty) were combined using the following formula:

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

K is a coverage factor of 2, which gives the level of confidence of approximately 95%.
The packaged amount is the minimum sample size for which uncertainty is valid. The ampoules are over-filled to ensure that the minimum packaged amount can be sufficiently transferred.

Homogeneity:

Homogeneity of the lot is confirmed by a duplicate analysis of 12 ampoules. 4 ampoules are taken in each early, middle and late fill position. The analyzed concentration in each early, middle and late fill position is the average value obtained from duplicate analysis of 4 ampoules

Stability:

The manufacturer guarantees the stability of this solution through the date stated on page 1 of the certificate when handled and stored accordingly to the conditions stated page 1.

Legal Notice and Limit of Liability:

This product is for routine laboratory analysis and research proposal only. Due to the hazardous nature, only trained personnel should handle this product. The company's liability will be limited to replacement of product or refund or purchase price. Notice of claims must be made within thirty (30) days from date of delivery.

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