EUDA
EUROPEAN UNION DRUGS AGENCY

EU Early Warning System: Formal Notification

Formal notification of 2-amino-*N*-(2-benzoyl-4-chlorophenyl)acetamide (Noravizafone desglycyl) by Germany as a new psychoactive substance under the terms of Regulation (EU) No 2023/1322 and Council Framework Decision 2004/757/JHA

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09.09.2024	EU-EWS-RCS-FN-2024-0030
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EUDA	Action on New Drugs Sector, EUDA

1. Read me first

This document provides formal notification of the analytical identification of 2-amino-*N*-(2-benzoyl-4-chlorophenyl)acetamide (Noravizafone desglycyl) for the first time in Europe.

There is limited information available on the pharmacology and toxicology of Noravizafone desglycyl. Based on its chemical structure, and the fact that it is a pro-drug of the benzodiazepine Nordazepam, it cannot be excluded that the substance acts as an anxiolytic or sedative-hypnotic, and is therefore formally notified based on a precautionary principle.

Please report any additional data you have on this substance to: ews@euda.europa.eu

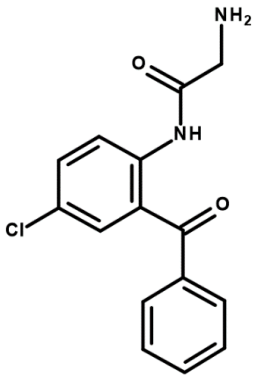
2. Data use restrictions

As with all formal notifications issued by the EU Early Warning System (EWS), remember that they may contain information that could be regarded as sensitive. Should you provide some of the information in this notification to other groups we would ask that you exercise your best judgment on what information needs to be provided. If you have any questions in this respect, please contact us.

3. Names of substance and other identifiers

- **IUPAC name:** 2-amino-*N*-(2-benzoyl-4-chlorophenyl)acetamide
- **Chemical names:** *N*-(2-benzoyl-4-chlorophenyl)glycinamide; 2-aminoacetamido-5-chlorobenzophenone
- **Common name:** Noravizafone desglycyl
- **Other names:** Desglycylnoravizafone
- **Chemical formula:** $C_{15}H_{13}ClN_2O_2$
- **Molecular weight:** 288.73
- **CAS Registry number:** 5504-71-2 (base); 5504-72-3 (hydrochloride)
- **InChIKey:** GIBRATRQHFFRHE-UHFFFAOYSA-N

Molecular structure:



4. Substance classification

Other

5. Detection

Type: Collected sample

Case Report identifier: EDND-CR-2024-380

Details: Noravizafone desglycyl was identified in a test-purchase of 300 mg of white powder, collected by University Medical Center Freiburg, Institute of Forensic Medicine, Forensic Toxicology Department, on 1 December 2023.

The substance was analytically confirmed using (HR)-LC-MS, ATR-IR, Raman spectroscopy and NMR by the EU-project NETZWERK ADEBAR [1]. The hydrochloride salt form of Noravizafone desglycyl was identified in the collected sample.

6. Chemistry and Analysis

Chemical classification: Unclassified

Noravizafone desglycyl is a benzophenone and the ring-open derivative of the internationally controlled benzodiazepine Nordazepam, also known as Nordiazepam (Schedule IV of the 1971 United Nations Single Convention on Psychotropic Substances). It can be formed by acidic hydrolysis and the cleavage of the imine bond on the diazepine ring of Nordazepam. Noravizafone desglycyl is also a precursor of Nordazepam.

Noravizafone desglycyl is a pro-drug of Nordazepam. It has been observed that, after intake, Noravizafone desglycyl can be metabolised *in vivo* into Nordazepam, following a dealkylation of the alkylaminobenzophenone and ring closure into the benzodiazepine [2].

2-Aminoacetoamidobenzophenones undergo spontaneous cyclization to the corresponding benzodiazepine, being the rate of the spontaneous cyclization dependent on the substituents in the phenyl groups [3]. This conversion that can take place during sample preparation and analysis can pose analytical challenges. Actually, Nordazepam was detected as an artifact in the GC-MS-EI and GC-sIR analyses.

A reference standard is available for the hydrochloride form of Noravizafone desglycyl [4]. Noravizafone desglycyl is reported as being soluble in DMSO and Acetonitrile (≥ 10 mg/ml) [4].

7. Pharmacology and toxicology

Pharmacological classification: Anxiolytic or Sedative-Hypnotic

There is limited information available on the pharmacology and toxicology of Noravizafone desglycyl.

The results obtained in a study on the conversion of *N*-alkylaminobenzophenones to benzodiazepines *in vivo* do not prove that the *N*-alkylaminobenzophenones were devoid of activity, but they do suggest that their observed pharmacological activity may be due to the formation of the corresponding benzodiazepines [2].

Based on its chemical structure, and the fact that Noravizafone desglycyl is a pro-drug of Nordazepam, it is expected to have low affinity for benzodiazepine receptors and to elicit anxiolytic or sedative-hypnotic effects after being metabolized into Nordazepam.

8. Further information

Further information on this substance is available on the EDND profile:
https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1498

9. Acknowledgements

The German National Focal Point, the Bavarian State Police State Bureau of Criminal Investigation Schleswig-Holstein, the University Medical Center Freiburg, Institute of Forensic Medicine, Forensic Toxicology Department, and EU-project NETZWERK ADEBAR are kindly acknowledged for the information and analytical data provided.

10. Attachments

None.

11. References

[1] Pulver B, et al. The ADEBAR project: European and international provision of analytical data from structure elucidation and analytical characterization of NPS. Drug Test Anal.2022;14(8):1491-1502.

[2] Lahti RA, et al. Conversion of N-alkylaminobenzophenones to benzodiazepines in vivo. Journal of Medicinal Chemistry. 1976 Aug;19(8):1064-7.

[3] Bundgaard H. The double prodrug concept and its applications. Advanced Drug Delivery Reviews, 1989;3:39-65

[4] https://www.caymanchem.com/product/35679/nordiazepam-uncyclized-intermediate-(hydrochloride)