EUDA
EUROPEAN UNION DRUGS AGENCY

EU Early Warning System: Formal Notification

Formal notification of 2-amino-*N*-[4-chloro-2-(2-chlorobenzoyl)phenyl]acetamide (Diclazafone desglycyl) by Denmark as a new psychoactive substance under the terms of Regulation (EU) No 2023/1322 and Council Framework Decision 2004/757/JHA

Date issued	**RCS ID**
09.09.2024	EU-EWS-RCS-FN-2024-0028
Issued by	**Transmitted by**
EUDA	Action on New Drugs Sector, EUDA

1. Read me first

This document provides formal notification of the analytical identification of 2-amino-*N*-[4-chloro-2-(2-chlorobenzoyl)phenyl]acetamide (Diclazafone desglycyl) for the first time in Europe.

There is limited information available on the pharmacology and toxicology of Diclazafone desglycyl. Based on its chemical structure, and the fact that it is a pro-drug of the benzodiazepine Delorazepam, 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

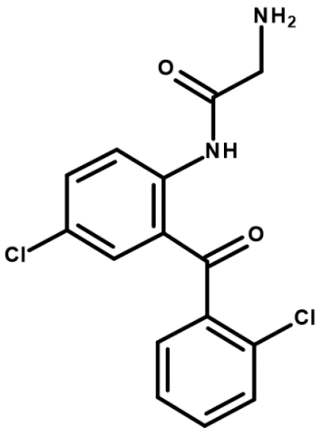
2. Data use restrictions

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*-[4-chloro-2-(2-chlorobenzoyl)phenyl]acetamide
- **Chemical names:** *N*-[4-chloro-2-(2-chlorobenzoyl)phenyl]glycinamide; 2-amino-4′-chloro-2′-(o-chlorobenzoyl)-acetanilide
- **Common name:** Diclazafone desglycyl
- **Other names:** Desglycyldiclazafone
- **Chemical formula:** $C_{15}H_{12}Cl_2N_2O_2$
- **Molecular weight:** 323.17
- **CAS Registry number:** 5600-85-1 (base); 3029269-95-9 (hydrochloride)
- **InChIKey:** YGKSPOBIXHTPMV-UHFFFAOYSA-N

Molecular structure:



4. Substance classification

Other

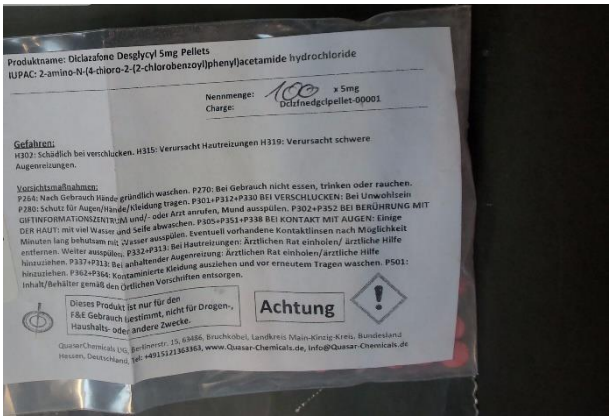
5. Detection

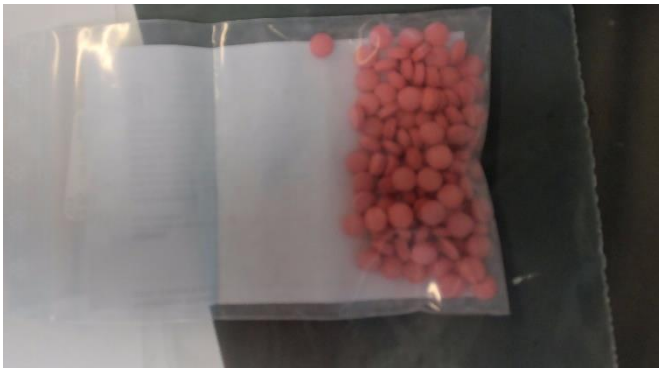
Type: Seizure

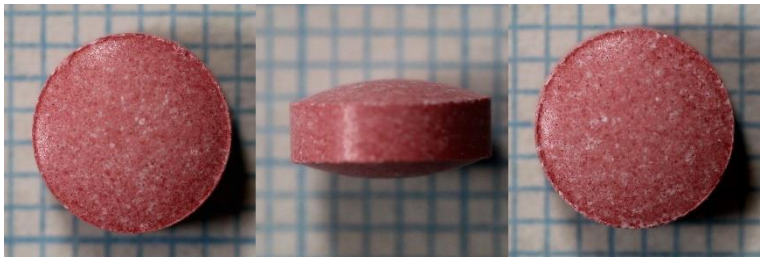
Case Report identifier: EDND-CR-2024-326

Details: Diclazafone desglycyl was identified in 103 tablets seized in Copenhagen by Danish Customs, on 11 March 2024. In the same seizure, Rilmazafone was identified in 1 gram of powder.

Diclazafone desglycyl was analytically confirmed by using GC-MS and UPLC-TOF-MS by the Section of Forensic Chemistry, University of Copenhagen.







Other detections

Type: Collected sample

Case Report identifier: EDND-CR-2024-382

Details: Diclazafone desglycyl was identified in a test purchase of 500 mg of yellow powder, collected by University Medical Center Freiburg, Institute of Forensic Medicine, Forensic Toxicology Department, on 1 December 2023.

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

6. Chemistry and Analysis

Chemical classification: Unclassified

Diclazafone desglycyl is a benzophenone and the ring-opened derivative of internationally controlled Delorazepam (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 Delorazepam. Diclazafone desglycyl is also a precursor of Delorazepam.

Diclazafone desglycyl is a pro-drug of Delorazepam. It has been observed that, after intake, Diclazafone desglycyl can be metabolised *in vivo* into Delorazepam, 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, Delorazepam was detected as an artifact in the GC-MS and UPLC-TOF-MS.

A reference standard is available for the hydrochloride form of Diclazafone desglycyl [4]. Diclazafone desglycyl is reported as being sparingly soluble in DMSO (1-10 mg/ml) and slightly soluble in ethanol (0.1-1 mg/ml) [4].

7. Pharmacology and toxicology

Pharmacological classification: Anxiolytic or Sedative-Hypnotic

There is limited information available on the pharmacology and toxicology of Diclazafone 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 Diclazafone desglycyl is a pro-drug of Delorazepam, it is expected to have low affinity for benzodiazepine receptors and to elicit anxiolytic or sedative-hypnotic effects after being metabolized into Delorazepam.

8. Further information

Further information on this substance is available on the EDND profile:
https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1490

9. Acknowledgements

The Danish National Focal Point, the Danish Customs, the Section of Forensic Chemistry, University of Copenhagen, 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/35688/delorazepam-uncyclized-intermediate-(hydrochloride)