



European Monitoring Centre  
for Drugs and Drug Addiction

## EU Early Warning System Alert

**Issued: 22/04/2015 by Rachel Christie, EMCDDA**

**Subject: Death in Belgium associated with ocfentanil (*N*-(2-fluorophenyl)-2-methoxy-*N*-[1-(2-phenylethyl)-4-piperidyl]acetamide)**

### Summary

The Belgian National Focal Point has reported a death associated with ocfentanil which occurred in March 2015. This is the first such case to be reported to the EU Early Warning System.

### Case Details

The decedent was found dead at home. Ocfentanil was identified in post-mortem blood samples, but has not yet been quantified (GC-MS analysis was performed). Examination of the nasal tract suggests that the ocfentanil was snorted; no needle or injection sites were identified on the body. The decedent had no known previous history of heroin usage. A small zip-locked plastic bag containing 2.07 grams of a brown powder was recovered from the scene (Figure 1). Analysis of a sample of the powder identified ocfentanil as the main psychoactive ingredient; caffeine and paracetamol were also detected. The source of the ocfentanil has not been confirmed yet, but one possible scenario is that the decedent purchased the ocfentanil through the Internet, and possibly from a darknet site.



Figure 1: Zip-locked plastic bag containing a brown powder that was recovered from the scene. Analysis of a sample of the powder identified ocfentanil as the main psychoactive ingredient; caffeine and paracetamol were also present.

### Overview of detections in Europe

Ocfentanil has been reported in one previous seizure in Europe in the Netherlands in 2013 where it was sold as synthetic heroin. The seizure also contained paracetamol and caffeine which was confirmed by both GC-MS and NMR analysis.

## Chemical and analytical details

The molecular structure of ocfentanil is provided in Figure 2. Synthesis and analytical characterisation of ocfentanil has been reported by Filer *et al.*, [1].

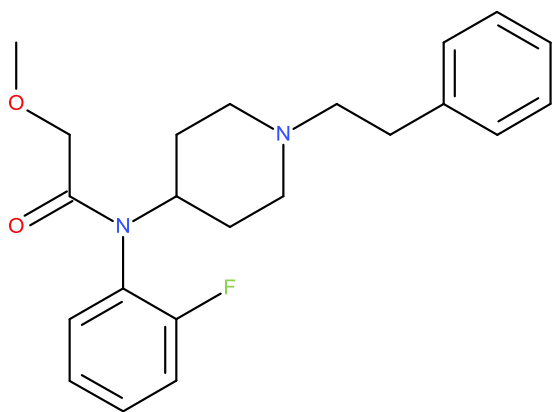


Figure 2: Molecular structure of ocfentanil.

Other names and abbreviations: Ocfentanilum; A-3217; A3217.

## Pharmacology and Toxicology

Ocfentanil is a potent synthetic opioid structurally related to fentanyl [2,3]. According to Fletcher *et al.*, it was developed as one of a series of potent naloxone-reversible opioids in an attempt to obtain an opioid that had better therapeutic indices in terms of cardiovascular effects and respiratory depression as compared to fentanyl [3].

Study of the analgesic activity of ocfentanil using the mouse hot plate test (55°C) gave an ED<sub>50</sub> of 0.007 mg/kg compared to 0.018 mg/kg for fentanyl; ocfentanil being approximately 2.5 times as potent as fentanyl in this test [2].

In human volunteers ocfentanil induces effective analgesia at 1 µg/kg, while in doses up to 3 µg/kg, analgesia and respiratory depression occurred in a dose-dependent manner [3]. While a further study suggests that ocfentanil may be as effective as morphine in post-operative relief [4]. Ocfentanil was also studied as a supplement to general anaesthesia, in which the researchers concluded that it appears to be similar in action to fentanyl, with 3 µg/kg of ocfentanil approximately equivalent to 5 µg/kg of fentanyl [2].

Further details on the pharmacology and toxicology of ocfentanil are available in the references [2-5].

## **Epidemiology**

No information is currently available.

## **EDND profile**

[https://ednd.emcdda.europa.eu/html.cfm/index7246EN.html?SUB\\_ID=355&detail](https://ednd.emcdda.europa.eu/html.cfm/index7246EN.html?SUB_ID=355&detail)

## **Please note**

The details provided above for the death and seized material must not be made public and should be restricted to relevant members of the EWS network; these include toxicology services, poison information services, healthcare professionals, law enforcement and policy makers.

As with all alerts transmitted by the EWS, please remember that they may contain information that could be regarded as sensitive. Should you provide some of the information to other groups we would ask that you exercise your best judgement on what information needs to be provided. If you have any questions in this respect, please do contact us.

We would be grateful if you could forward any further information that you have on ocfentanil to: [ews@emcdda.europa.eu](mailto:ews@emcdda.europa.eu)

## **References**

- [1]. Filer CN, et al. The synthesis of [fluorophenyl-3H(N)] ocfentanil and [fluorophenyl-3H(N)] brifentanil. *Journal of Labelled Compounds and Radiopharmaceuticals*, 1995, 36(11), 1019–27.
- [2]. Bagley J. R. et al., Evolution of the 4-Anilidopiperidine Class of Opioid Analgesics. *Medicinal Research Reviews*, 1991, 11(4), 403-436.
- [3]. Fletcher JE, Sebel PS, Murphy MR, Mick SA, Fein S. Comparison of ocfentanil and fentanyl as supplements to general anesthesia. *Anesthesia and Analgesia*, 1991, 73(5), 622-6.
- [4]. Glass P, et al. The analgesic efficacy of A3217. *Anesthesiology*, 1989, 71(3a), A321.
- [5]. Ebrahim Z, et al. Multiple dose evaluation of the efficacy of ocfentanil hydrochloride (A3217) to produce postoperative analgesia. *Anesthesia and Analgesia*, 1991, 72, S63.