

Drug Status Report

Drug: Sufentanil citrate related substances

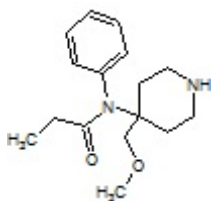
A client requested the status of nine sufentanil citrate related substances (A - I) in the European Pharmacopoeia monograph.

Drug Name Status:

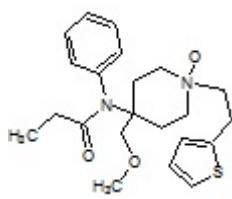
- (A) N-[4-(methoxymethyl)piperidin-4-yl]-N-phenylpropanamide
- (B) cis-4-(methoxymethyl)-4-(phenylpropanoylamino)-1-[2-(thiophen-2-yl)ethyl]piperidine 1-oxide
- (C) [4-(phenylamino)-1-[2-(thiophen-2-yl)ethyl]piperidin-4-yl]methanol
- (D) N-[4-(methoxymethyl)-1-[2-thiophen-2-yl)ethyl]piperidin-4-yl]-N-phenylacetamide
- (E) 4-(methoxymethyl)-N-phenyl-1-[2-thiophen-2-yl)ethyl]piperidin-4-amine
- (F) N-[4-(methoxymethyl)-1-[2-thiophen-3-yl)ethyl]piperidin-4-yl]-N-phenylpropanamide
- (G) [4-(phenylpropanoylamino)-1-[2-thiophen-2-yl)ethyl]piperidin-4-yl]methyl propanoate
- (H) N-[4-(methoxymethyl)-1-[2-thiophen-2-yl)ethyl]piperidin-4-yl]-N-phenylbutanamide
- (I) trans-4-(methoxymethyl)-4-(phenylpropanoylamino)-1-[2-(thiophen-2-yl)ethyl]piperidine 1-oxide

These are the chemical names. Related substances B and I are geometric isomers; stereochemistry is not shown in the chemical structures.

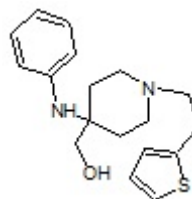
Chemical structure:



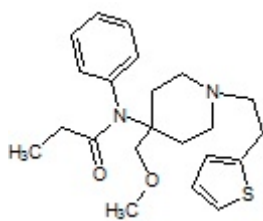
A



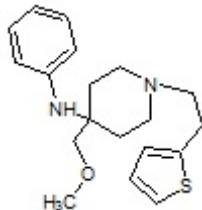
B-cis



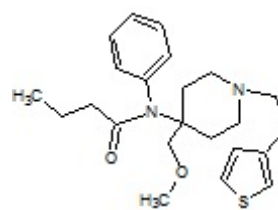
C



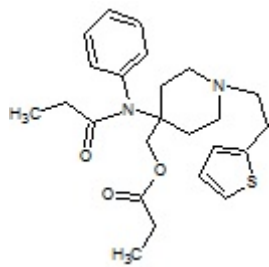
D



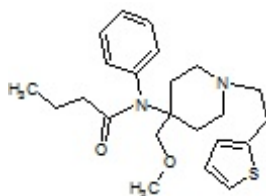
E



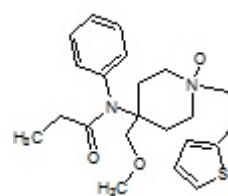
F



G



H



I-trans

Molecular Formula: (A) $C_{16}H_{24}N_2O_2$; (B) $C_{22}H_{30}N_2O_3S$; (C) $C_{18}H_{24}N_2OS$; (D) $C_{22}H_{30}N_2O_2S$; (E) $C_{19}H_{26}N_2OS$; (F) $C_{23}H_{32}N_2O_2S$; (G) $C_{24}H_{32}N_2O_3S$; (H) $C_{23}H_{32}N_2O_2S$; (I) $C_{22}H_{30}N_2O_3S$

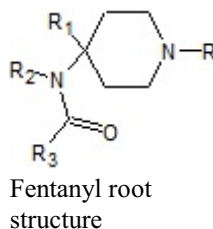
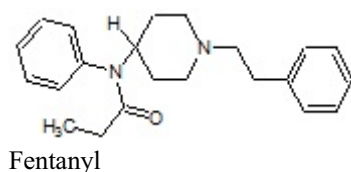
Pharmacological class / Application: pharmaceutical related substance

International status:

US: The substances are not currently listed on the US Controlled Substances Act and are not mentioned on the DEA website.

United Nations: The substances are not listed on the Yellow List - List of Narcotic Drugs under International Control nor the Green List - List of Psychotropic Substances under International Control.

Canadian Status: Item 16 of Schedule I is "Fentanyls, their salts, derivatives and analogues and salts of derivatives and analogues." The structure of fentanyl is shown below. A review of the current family of fentanyls indicates that all members have one common root structure. This fentanyl root structure is shown below and must be considered essential in order to consider a substance a member of the fentanyl family of drugs and hence included in this item of Schedule I. The substituents R may be alkyl, aralkyl and substituted alkyl groups. Substituents R_1 to R_3 may be hydrogen, alkyl or aryl groups.



Related substance A does not contain a substituent on the nitrogen in the piperidine ring. Related substances C and E lack the necessary amide element on the nitrogen at the four position of the piperidine ring. Related substances B, D, F, G, H and I all contain the essential structural elements of the fentanyl root structure and therefore should be considered to be included in item 16 of Schedule I.

Recommendation: Related substances A, C and E are not included in item 16 of Schedule I and are not controlled substances.

Related substances B, D, F, G, H and I are included in item 16 of Schedule I to the CDSA and are controlled substances.

September 23, 2007