



STATUS DECISION OF CONTROLLED AND NON-CONTROLLED SUBSTANCE(S)

Substance: Midazolam derivatives

Based on the current information available to the Office of Controlled Substances, it appears that the above substance is:

Controlled [checked]
Not Controlled [unchecked]

under the schedules of the Controlled Drugs and Substances Act (CDSA) for the following reason(s):

- The substances are derivatives of midazolam and therefore included under item 18(22.1) of Schedule IV to the CDSA.

Prepared by: Evelyn Soo Date: Sept 21th 2010

Verified by: Marianne Tang Date:

Approved by: DIRECTOR, OFFICE OF CONTROLLED SUBSTANCES Date:

This status was requested by: "third party information removed as per agreement with applicant"

## Drug Status Report

### Drug:

- I - Midazolam 2,5-dioxide
- II - Midazolam 2,5-dioxide-d6
- III - Midazolam-d5
- IV - Midazolam-d6
- V - 1',4-dihydroxymidazolam
- VI - 1',4-dihydroxymidazolam-d4
- VII - 1'-hydroxy midazolam
- VIII - 1'-hydroxy midazolam-d5
- IX - 1-hydroxy midazolam-13C-3
- X - 1'-hydroxy midazolam-beta-D-glucuronide
- XI - 4-acetoxy midazolam
- XII - 4-hydroxy midazolam
- XIII - 4- hydroxy midazolam-beta-D-glucuronide
- XIV- 5,6- dihydromidazolam

### Drug Name Status:

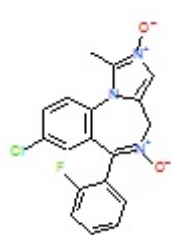
- I - Midazolam 2,5-dioxide
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- XI - 4-acetoxy midazolam
- XII - 4-hydroxy midazolam
- XIII - 4- hydroxy midazolam-beta-D-glucuronide
- XIV- 5,6- dihydromidazolam are common names

### Chemical Name:

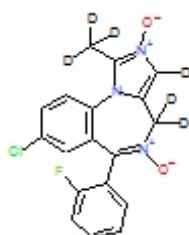
- I - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5- a][1,4]benzodiazepine 2,5-dioxide
- II -8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5- a][1,4]benzodiazepine 2,5-dioxide-d6
- III - 8-chloro-6-(o-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine-d5
- IV - 8-chloro-6-(o-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine-d6
- V - 8-Chloro-6-(2-fluorophenyl)-4-hydroxy-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol
- VI - 8-Chloro-6-(2-fluorophenyl)-4-hydroxy-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-d4

- VII - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol  
 VIII - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-d5  
 IX - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-13C-3  
 X - 8-chloro-6-(2-fluorophenyl)-4H-imidazo[1,5-a][1,4]benzodiazepine-1-methanol-beta-D-glucuronide  
 XI - 4-Acetoxy-8-chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine  
 XII - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepin-4-ol  
 XIII - 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepin-beta-D-glucuronide  
 XIV - 8-Chloro-6-(2-fluorophenyl)-5,6-dihydro-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine

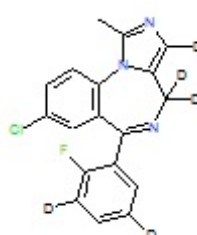
**Chemical structure:**



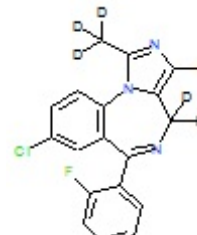
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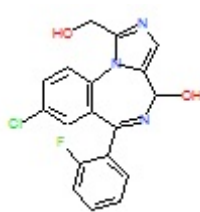
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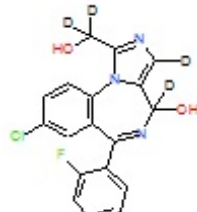
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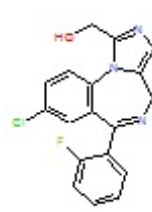
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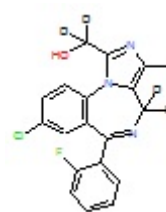
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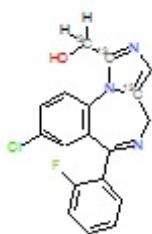
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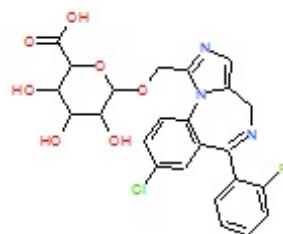
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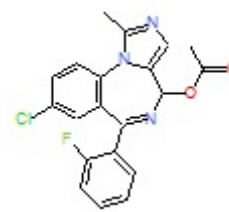
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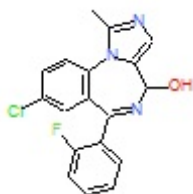
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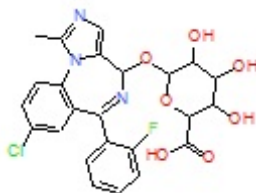
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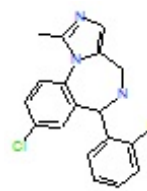
XI



XII



XIII



XIV

**Molecular Formula:** I -  $C_{18}H_{13}ClFN_3O_2$ ; II -  $C_{18}D_6H_7ClFN_3O_2$ ; III -  $C_{18}D_5H_8ClFN_3$ ; IV -  $C_{18}D_6H_7ClFN_3$ ; V -  $C_{18}H_{13}ClFN_3O_2$ ; VI -  $C_{18}D_4H_9ClFN_3O_2$ ; VII -  $C_{18}H_{13}ClFN_3O_2$ ; VIII -  $C_{18}D_4H_9ClFN_3O_2$ ; IX -  $^{13}C_3C_{15}H_{13}ClFN_3O$ ; X -  $C_{24}H_{21}ClFN_3O_7$ ; XI -  $C_{20}H_{15}ClFN_3O_2$ ; XII -  $C_{18}H_{13}ClFN_3O$ ; XIII -  $C_{24}H_{21}ClFN_3O_7$ ; XIV -  $C_{18}H_{15}ClFN_3$

**Pharmacological class / Application:** Pharmaceutical-related substances

**CAS-RN:** I - 59468-87-0; II - 1215321-98-4; III - 59467-70-8; IV - NONE; V - 64740-68-7; VI - NONE; VII - 59468-90-5; VIII - NONE; VIX - NONE; X - 81256-81-7; XI - 59468-84-7; XII - 59468-85-8; XIII - 81256-82-8; XIV - 59468-07-4

#### International status:

US: The substances are not listed specifically in the Controlled Substances Act and are not mentioned anywhere 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: The above substances are all derivatives of midazolam, which is presently listed under as item 18(22.1) in Schedule IV to the CDSA under the item heading "Benzodiazepines, their salts and derivatives, including:". Therefore, the substances must be included under item 18(22.1) of Schedule IV to the CDSA.

**Recommendation:** Midazolam 2,5-dioxide, midazolam 2,5-dioxide-d6, midazolam-d5, midazolam-d6, 1',4-dihydroxymidazolam, 1',4-dihydroxymidazolam-d4, 1'-hydroxy midazolam, 1'-hydroxy midazolam-d5, 1-hydroxy midazolam- $^{13}C$ -3, 1'-hydroxy midazolam-beta-D-glucuronide, 4-acetoxy midazolam, 4-hydroxy midazolam, 4-hydroxy midazolam-beta-D-glucuronide and 5,6-dihydromidazolam are all under item 18(22.1) of Schedule IV to the CDSA and are controlled substances.

**Date:** 21<sup>st</sup> September 2010