

Established acceptable intake for other nitroso-structures in medicines

Last updated

TBA 2026

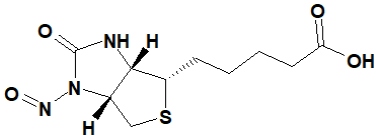
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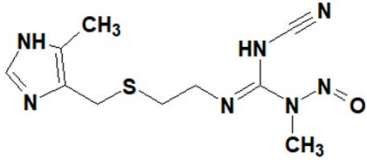
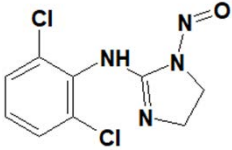
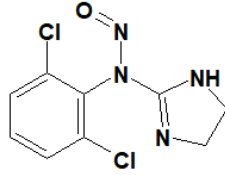
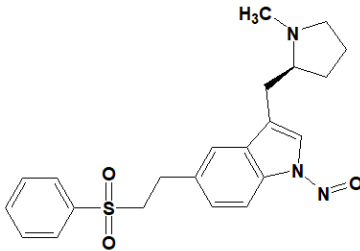
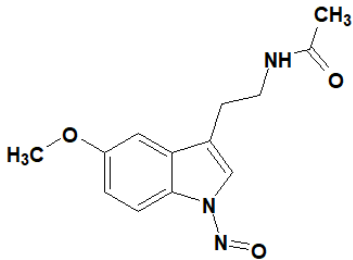
Below is a list of established AI limits for some other *N*-nitroso-structures. *N*-Nitroso-structures include *N*-nitrosoguanidines, *N*-nitroso-indoles and *N*-nitrosoureas. These apply for all routes of administration.

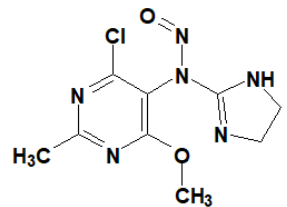
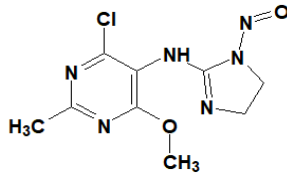
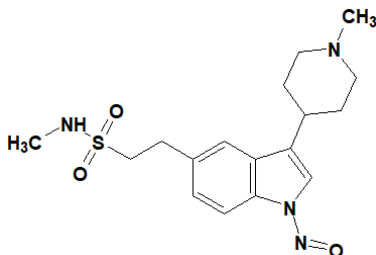
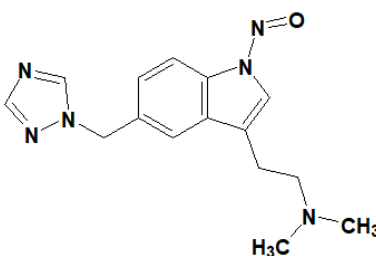
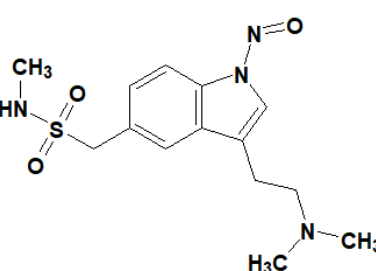
Established AI limits for some nitrosamine impurities are listed [separately](#).

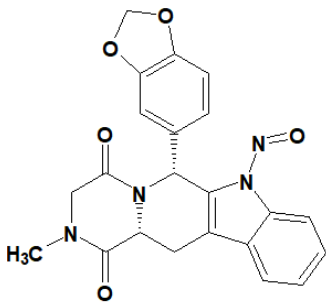
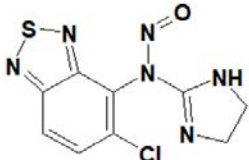
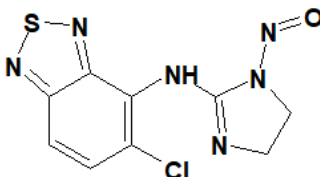
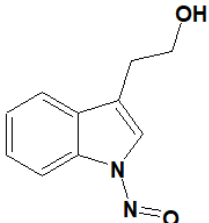
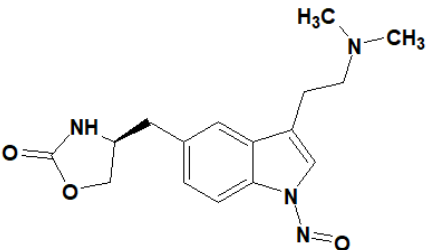
A revision table listing updates to the AI limit information for nitrosamines and other *N*-nitroso-structures is available [separately](#).

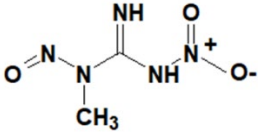
Established acceptable intake for other *N*-nitroso-structures in medicines

<i>N</i> -Nitroso-structure (CAS number, Abbreviation)	Source ²	<i>N</i> -Nitroso-structure molecular structure	AI limit (ng/day) ¹	First published
<i>N</i> -Nitroso-biotin / 5-((3a <i>S</i> ,4 <i>S</i> ,6a <i>R</i>)-1-nitroso-2- oxohexahydro-1 <i>H</i> -thieno[3,4- <i>d</i>]imidazol- 4-yl)pentanoic acid (56859-26-8)	Biotin		1500	24 January 2025

<i>N</i> -Nitroso-cimetidine / 3-cyano-1-methyl-2-[2-[(5-methyl-1 <i>H</i> -imidazol-4-yl)methylsulfanyl]ethyl]-1-nitrosoguanidine (73785-40-7)	Cimetidine		553	24 January 2025
<i>N</i> -Nitroso-clonidine / <i>N</i> -(2,6-dichlorophenyl)-1-nitroso-4,5-dihydroimidazol-2-amine (148950-49-6)	Clonidine		553	24 January 2025
<i>N</i> -Nitroso-clonidine-2 / <i>N</i> -(2,6-dichlorophenyl)- <i>N</i> -(4,5-dihydro-1 <i>H</i> -imidazol-2-yl)nitrous amide	Clonidine		553	24 January 2025
<i>N</i> -Nitroso-eletriptan / (<i>S</i>)-3-((1-methylpyrrolidin-2-yl)methyl)-1-nitroso-5-(2-(phenylsulfonyl)ethyl)-1 <i>H</i> -indole	Eletriptan		1500	24 January 2025
<i>N</i> -Nitroso-melatonin / <i>N</i> -(2-(5-methoxy-1-nitroso-1 <i>H</i> -indol-3-yl)ethyl)acetamide (278783-22-5)	Melatonin		1500	24 January 2025

1-Nitroso-moxonidine / <i>N</i> -(4-chloro-6-methoxy-2-methylpyrimidin-5-yl)- <i>N</i> -(4,5-dihydro-1 <i>H</i> -imidazol-2-yl)nitrous amide	Moxonidine		553	24 January 2025
1-Nitroso-moxonidine Impurity 3 / 4-chloro-6-methoxy-2-methyl- <i>N</i> -(1-nitroso-4,5-dihydro-1 <i>H</i> -imidazol-2-yl)pyrimidin-5-amine	Moxonidine		553	24 January 2025
<i>N</i> -Nitroso-naratriptan / <i>N</i> -methyl-2-[3-(1-methylpiperidin-4-yl)-1-nitrosoindol-5-yl]ethanesulfonamide (1216880-64-6)	Naratriptan		1500	24 January 2025
<i>N</i> -Nitroso-rizatriptan / 2-(5-((1 <i>H</i> -1,2,4-triazol-1-yl)methyl)-1-nitroso-1 <i>H</i> -indol-3-yl)- <i>N,N</i> -dimethylethan-1-amine	Rizatriptan		1500	24 January 2025
<i>N</i> -Nitroso-sumatriptan / 1-(3-(2-(dimethylamino)ethyl)-1-nitroso-1 <i>H</i> -indol-5-yl)- <i>N</i> -methylmethanesulfonamide	Sumatriptan		1500	24 January 2025

<i>N</i> -Nitroso-tadalafil / (2 <i>R</i> ,8 <i>R</i>)-2-(1,3-benzodioxol-5-yl)-6-methyl-17-nitroso-3,6,17-triazatetracyclo[8.7.0.03,8.011,16]heptadeca-1(10),11,13,15-tetraene-4,7-dione	Tadalafil		1500	24 January 2025
<i>N</i> -Nitroso-tizanidine / <i>N</i> -(5-chlorobenzo[<i>c</i>][1,2,5]thiadiazol-4-yl)- <i>N</i> -(4,5-dihydro-1 <i>H</i> -imidazol-2-yl)nitrous amide	Tizanidine		553	24 January 2025
<i>N</i> -Nitroso-tizanidine Impurity 3 / <i>N</i> -(5-chlorobenzo[<i>c</i>][1,2,5]thiadiazol-4-yl)- <i>N</i> -(4,5-dihydro-1 <i>H</i> -imidazol-2-yl)nitrous amide	Tizanidine		553	24 January 2025
<i>N</i> -Nitroso-tryptophol / 2-(1-nitrosoindol-3-yl)ethanol (120314-14-9)	Tryptophol		1500	24 January 2025
<i>N</i> -Nitroso-zolmitriptan / (4 <i>S</i>)-4-[[3-[2-(dimethylamino)ethyl]-1-nitrosoindol-5-yl]methyl]-1,3-oxazolidin-2-one	Zolmitriptan		1500	24 January 2025

<i>N</i> -Methyl- <i>N'</i> -nitro- <i>N</i> -nitrosoguanidine / 1-methyl-3-nitro-1-nitrosoguanidine (70-25-7, MNNG)			553	24 January 2025
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NMI: Non mutagenic impurity should be controlled to [ICH Q3A](#) and [ICH Q3B](#) guideline limits

¹ Acceptable Intake (AI) Limit to be applied to maximum daily dose (MDD) of the drug product.

² Potential presence of nitroso-structure impurities with structures derived from drug substances or their related impurities. This does not mean that the impurity will be found in all products or pharmaceutical forms containing the drug substance. Please refer to [EMA's Q&A](#) for details.