

Determination of N-Nitrosamine

As reported in the latest revision EMA/409815/2020 Rev. 17 of 28 July 2023, the regulatory authority has updated the list of Nitrosamines to be monitored by also introducing Nitroso APIs and the relative limit for this molecule.

We therefore report below the new table of reference nitrosamines and the relative limits:

N-Nitrosamine (CAS number)	ng/day	Source
1-cyclopropylmethyl-4-nitrosopiperazine	400	
1-methyl-4-nitrosopiperazine, MeNP ⁵ (16339-07-4)	400	Rifampicin
1-nitroso-pyrroloperidine	1500	
2-nitroso-octahydrocyclopenta(c)pyrrole ¹⁷	1700	
4-(methylnitrosoamino)-1-(3-pyridinyl)-1-butanone (NNK) ⁷	100	
7-nitroso-3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3- a]pyrazine ¹¹	37	Sitagliptin
nitroso impurity C [N-(2,6-dimethylphenyl)-2-(4-nitrosopiperazin-1-yl)acetamide]	18	Orphenadrine
nitroso-praziquanamine [2-nitroso-3,6,7,11b-tetrahydro-1H-pyrazino[2,1-a]isoquinolin-4-one]	1500	Arpraziquantel
N-methyl-N-nitrosophenethylamine, NMPEA ^{3,7} (13256-11-6)	8	
N-nitroso-1,2,3,6-tetrahydropyridine, NTHP ³ (55556-92-8)	37	
N-nitroso-2,6-pipecoloxilidide	1500	Ropivacaine
N-nitroso-ambroxol	400	Ambroxol
N-nitroso-aryl piperazine/N-nitroso-desalkylquetiapine (NDAQ)	400	Quetiapine
N-nitroso-Atomoxetine ¹³	100	Atomoxetine
N-nitroso-atenolol	1500	Atenolol
N-nitroso-azaerythromycin	NMI ¹⁶	Azithromycin
N-nitroso-benazepril	1500	Benazepril
N-nitroso-betahistine	18	Betahistine
N-nitroso-bisoprolol (NBP)	1500	Bisoprolol
N-nitroso-bumetanide (NNB)	1500	Bumetanide
N-nitroso-bupropion	1500	Bupropion
N-nitroso-cilazapril	1500	Cilazapril
N-nitroso-ciprofloxacin	1500	Ciprofloxacin
N-nitroso-dabigatran ¹⁰	400	Dabigatran
N-nitroso-desloratadine	400	Desloratadine
N-nitroso-desmethyl trimebutine	1500	Trimebutine

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N-Nitrosamine (CAS number)	ng/day	Source
N-nitroso-desmethylazithromycin	NMI ¹⁶	Azithromycin
N-nitroso-desmethyl-chloropyramine (N-DMCP)	18	Chloropyramine
N-nitroso-desmethyl-tripelennamine	18	Tripelennamine
N-nitroso-diclofenac	1500	Diclofenac
N-nitroso-diethanolamine NDELA ^{3,7} (1116-54-7)	1900	
N-nitroso-diethylamine, NDEA ^{3,4} (55-18-5)	26.5	
N-nitroso-diisopropylamine, DIPNA ^{3,5} (601-77-4)	26.5	
N-nitroso-dimethylamine, NDMA ^{3,4} (62-75-9)	96.0	
N-nitroso-di-n-butylamine, NDBA ^{3,5} (924-16-3)	26.5	
N-nitroso-diphenylamine NDPh ¹⁴ (86-30-6)	78000	
N-nitroso-dipropylamine, NDPA (621-64-7) ^{3,5}	26.5	
N-nitroso-duloxetine ¹³	100	Duloxetine
N-nitroso-enalapril	1500	Enalapril
N-nitroso-ethylisopropylamine, EIPNA ^{3,5} (16339-04-1)	26.5	
N-nitroso-fluoxetine ¹³	100	Fluoxetine
N-nitroso-folic acid (NFA)	1500	
N-nitroso-hydrochlorothiazide	NMI ¹⁶	Hydrochlorothiazide
N-nitroso-ketamine	1500	Ketamine
N-nitroso-labetalol	1500	Labetalol
N-nitroso-landiolol	400	Landiolol
N-nitroso-levofloxacin	1500	Levofloxacin
N-nitroso-lisinopril	1500	Lisinopril
N-nitroso-mefenamic acid 15	78000	Mefenamic acid
N-nitroso-methylphenidate ⁹ , NMPH, (55557-03-4)	1300	Methylphenidate
N-nitroso-metoprolol	1500	Metoprolol
N-nitroso-mirabegron	400	Mirabegron
N-nitroso-morpholine, NMOR ^{3,7} (59-89-2)	127	
N-nitroso-moxifloxacin	1500	Moxifloxacin
N-nitroso-nebivolol (NNEB)	1500	Nebivolol
N-nitroso-N-ethyl-valacyclovir	400	Valacyclovir
N-nitroso-N-methyl-4-aminobutyric acid, NMBA ^{3,6} (61445-55-4)	96.0	
N-nitroso-N-methylaniline, NMPA ^{3,7} (614-00-6)	34.3	
N-nitroso-N-methyl-valacyclovir	400	Valacyclovir

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N-Nitrosamine (CAS number)	ng/day	Source
N-nitroso-nortriptyline ¹²	8	Amitriptyline, Nortriptyline
N-nitroso-paroxetine ⁹	1300	Paroxetine
N-nitroso-p-chloro-benzylamino-pyridine (N-CBAP)	100	
N-nitroso-perindopril	1500	Perindopril
N-nitroso-phenylephrine	100	Phenylephrine
N-nitroso-piperazine (NPZ)	400	
N-nitroso-piperidine ^{3,7} (100-75-4)	1300	
N-nitroso-pramipexole	400	Pramipexole
N-nitroso-propranolol	1500	Propranolol
N-nitroso-pseudoephedrine	1500	Pseudoephedrine
N-nitroso-pyrrolidine NPYR ^{3,7} (930-55-2)	1700	
N-nitroso-quinapril	NMI ¹⁶	Quinapril
N-nitroso-ramipril	1500	Ramipril
N-nitroso-rasagiline ¹⁰	100	Rasagiline
N-nitroso-reboxetine	127	Reboxetine
N-nitroso-salbutamol	1500	Salbutamol
N-nitroso-sertraline	100	Sertraline
N-nitroso-sotalol	1500	Sotalol
N-nitroso-tamsulosin	1500	Tamsulosin
N-nitroso-trimetazidine (NTMZ)	400	Trimetazidine
N-nitroso-varenicline, NNV ⁸	37	Varenicline
N-nitroso-vildagliptin	1500	Vildagliptin
N-nitroso-vortioxetine	400	Vortioxetine

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