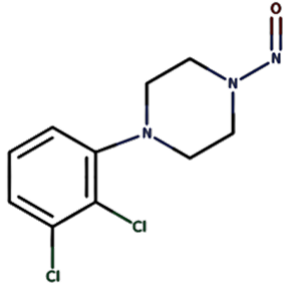
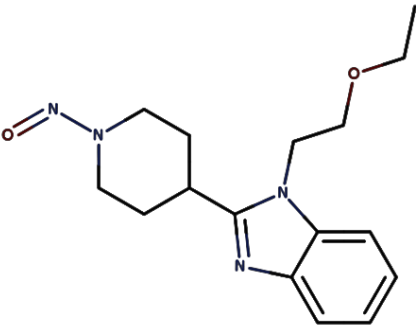
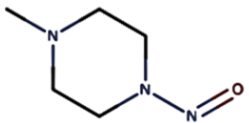
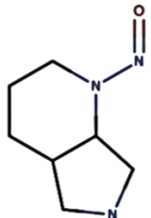
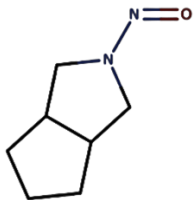
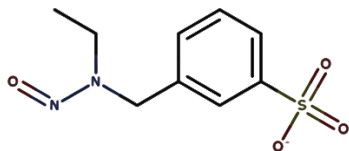
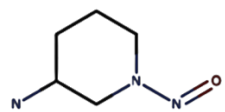
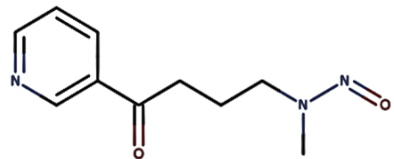
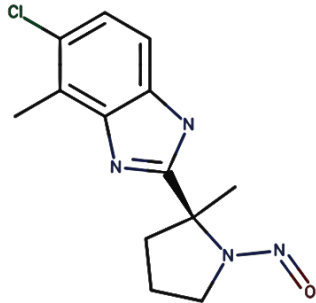
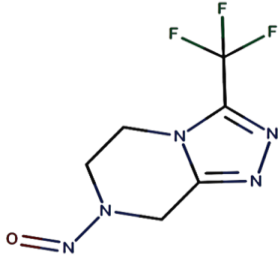
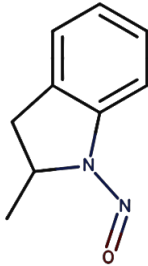
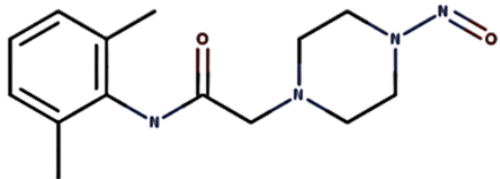
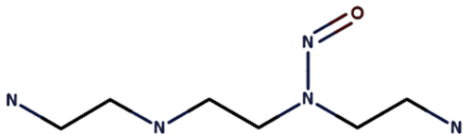
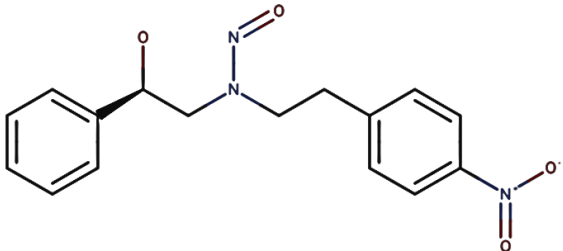
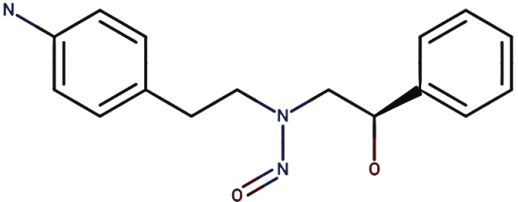


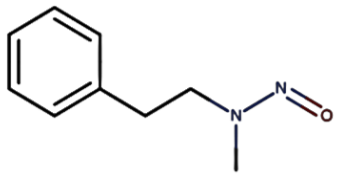
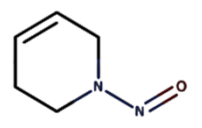
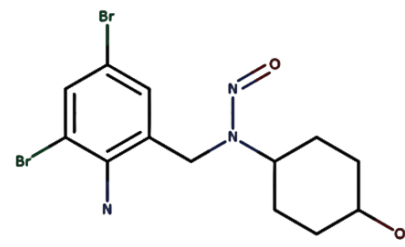
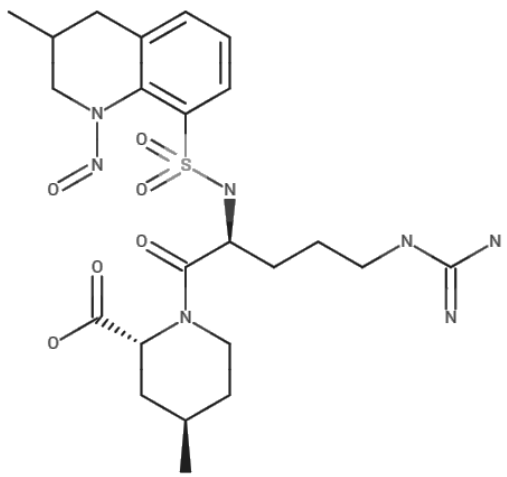
The acceptable intakes (AI) below are recommended by the Health Sciences Authority and are determined using the Carcinogenic Potency Categorisation Approach (CPCA) where applicable. The source refers to drug substances that may potentially contain the nitrosamine impurity. However, this does not mean that the impurity will be found in all products or pharmaceutical forms containing the named drug substance. This list and the source examples provided are not exhaustive and will be updated as more information becomes available.

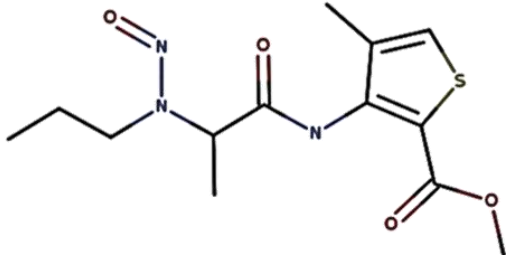
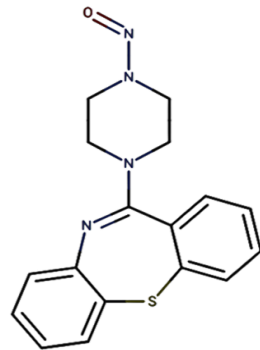
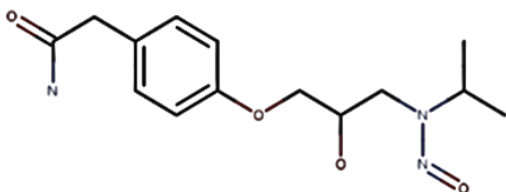
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	1-(2,3-dichlorophenyl)-4-nitrosopiperazine	Aripiprazole	3	400
	1-(2-ethoxyethyl)-2-(1-nitrosopiperidin-4-yl)-1H-benzo[d]imidazole	Bilastine	3	400
	1-methyl-4-nitrosopiperazine	Multiple sources	3	400

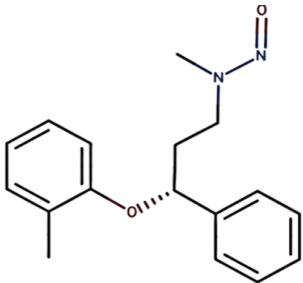
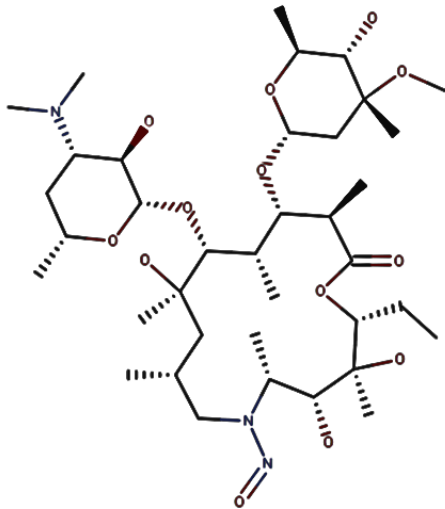
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	1-nitroso-pyrroloperidine	Multiple sources	4	1500
	2-nitroso-octahydrocyclopenta(c)pyrrole	Gliclazide	-	1700
	3-((ethyl(nitroso)amino)methyl) benzenesulfonate	Multiple sources	1	18
	3-amino-N-nitrosopiperidine	Alogliptin	3	400
	4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone	Multiple sources	-	100

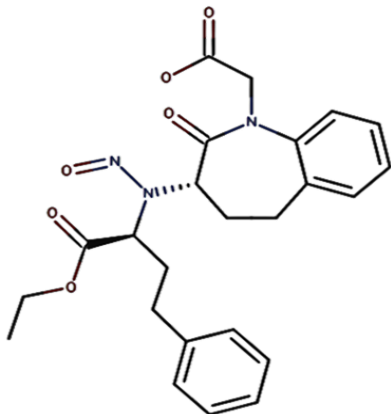
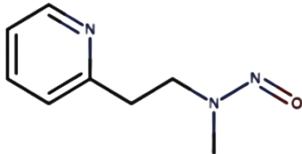
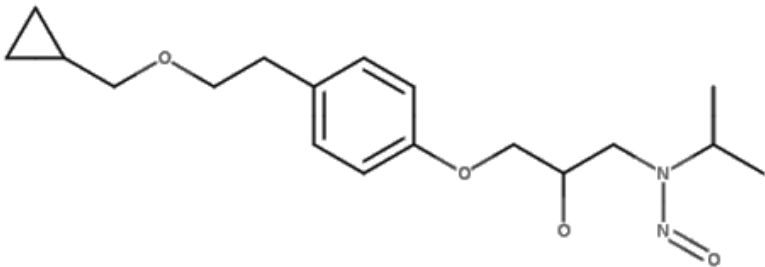
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	5-chloro-4-methyl-2-[(2S)-2-methyl-1-nitrosopyrrolidin-2-yl]-1H-benzimidazole	Daridorexant	5	1500
	7-Nitroso-3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo-[4,3-a]pyrazine	Sitagliptin	2	100
	Indapamide EP Impurity A / (2RS)-2-methyl-1-nitroso-2,3-dihydro-1H-indole	Indapamide	5	1500

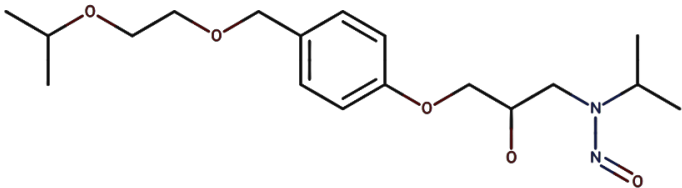
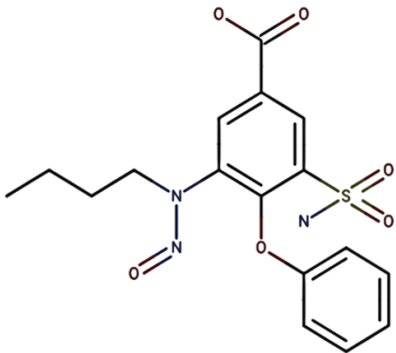
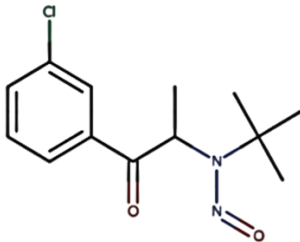
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-(2,6-dimethylphenyl)-2-(4-nitrosopiperazin-1-yl)acetamide	Ranolazine	3	400
	N-(2-aminoethyl)-N-(2-((2-aminoethyl)amino)ethyl)nitrous amide / N-nitroso-trientine	Trientine	1	18
	N-(2-hydroxy-2-phenylethyl)-N-(4-nitrophenethyl)nitrous amide	Mirabegron	3	400
	N-(4-aminophenethyl)-N-(2-hydroxy-2-phenylethyl)nitrous amide	Mirabegron	3	400

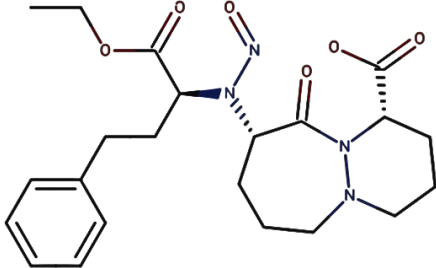
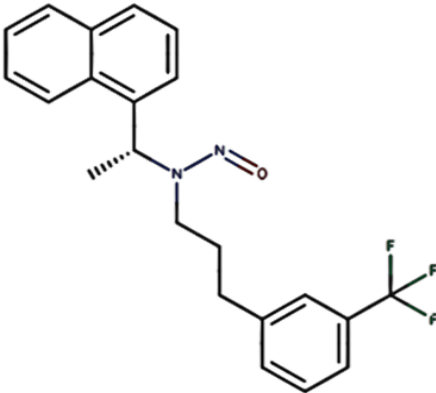
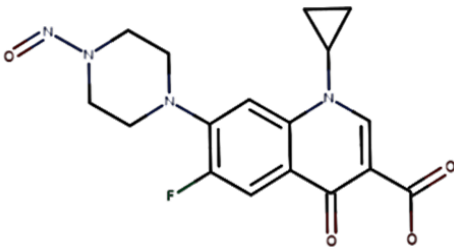
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-methyl-N-nitroso-phenethylamine	Multiple sources	-	8
	N-nitroso-1,2,3,6-tetrahydropyridine	Multiple sources	-	37
	N-nitroso-ambroxol	Ambroxol	-	1500
	N-nitroso-argatroban	Argatroban	4	1500

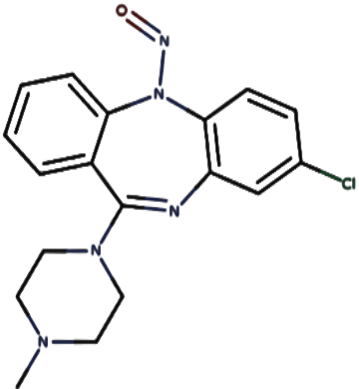
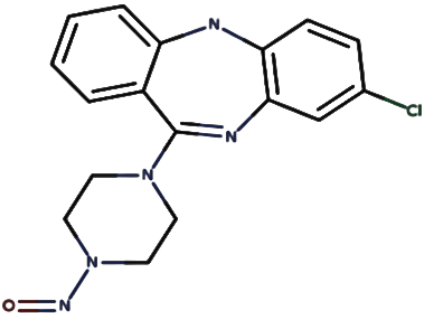
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-articaine	Articaine	4	1500
	N-nitroso-aryl piperazine / N-nitroso-desalkylquetiapine / N-nitroso-norquetiapine	Quetiapine	3	400
	N-nitroso-atenolol	Atenolol	4	1500

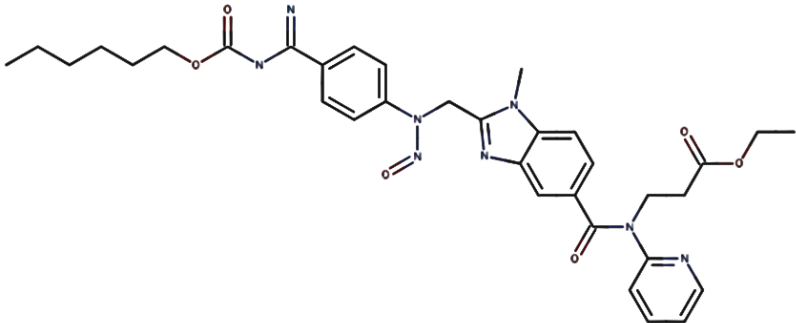
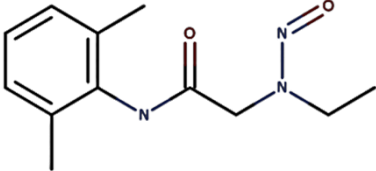
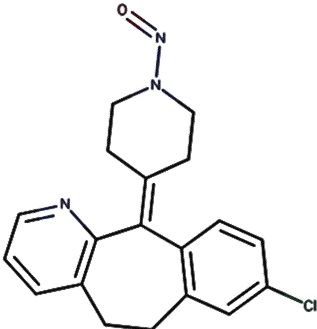
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-atomoxetine	Atomoxetine	-	100
	N-nitroso-azaerythromycin	Azithromycin	-	Can be controlled according to ICH Q3A/B

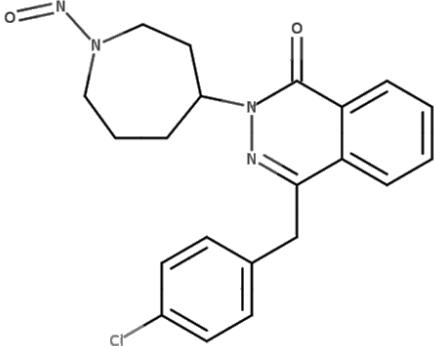
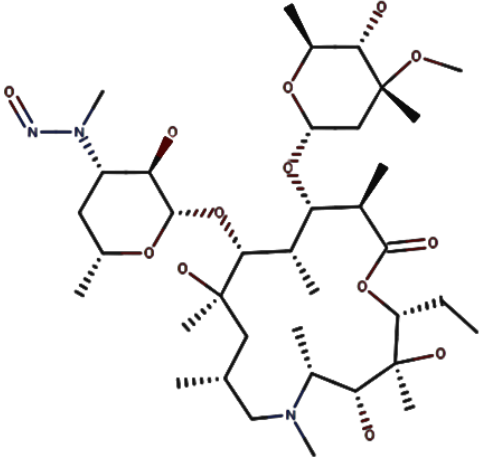
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-benazepril	Benazepril	5	1500
	N-nitroso-betahistine	Betahistine	1	18
	N-nitroso-betaxolol	Betaxolol	4	1500

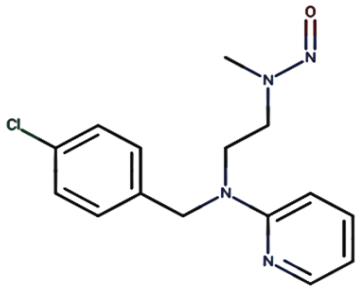
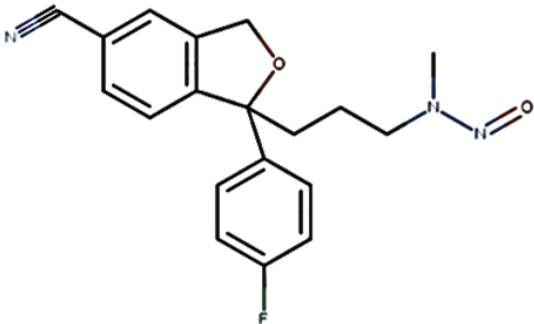
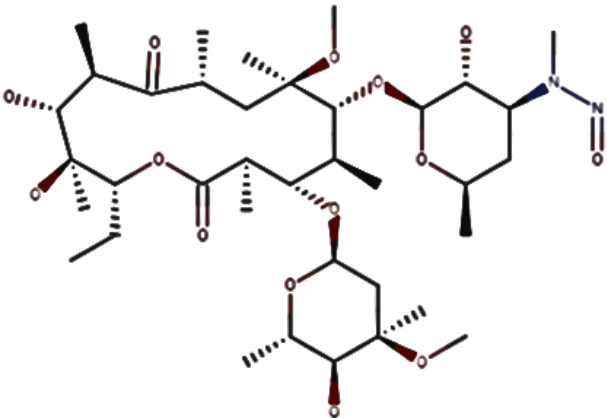
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-bisoprolol	Bisoprolol	4	1500
	N-nitroso-bumetanide	Bumetanide	4	1500
	N-nitroso-bupropion	Bupropion	5	1500

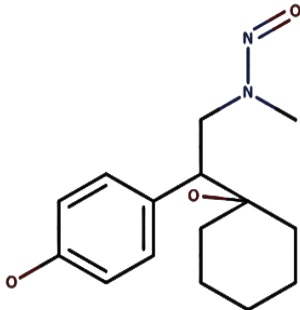
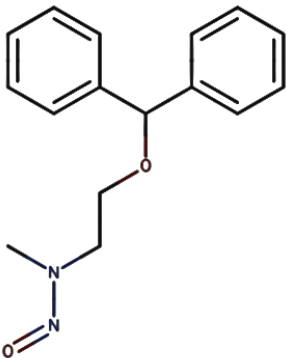
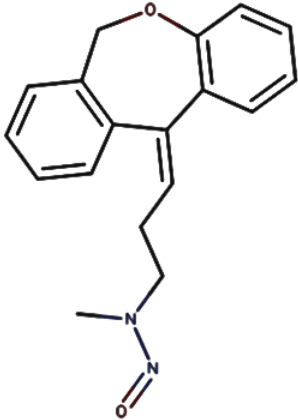
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-cilazapril	Cilazapril	5	1500
	N-nitroso-cinacalcet	Cinacalcet	3	400
	N-nitroso-ciprofloxacin	Ciprofloxacin	-	Can be controlled according to ICH Q3A/B

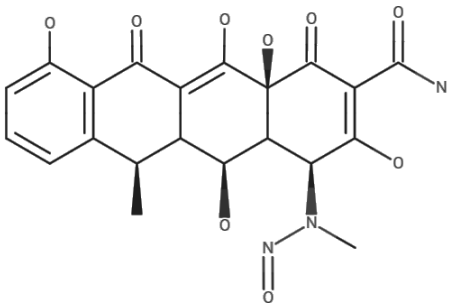
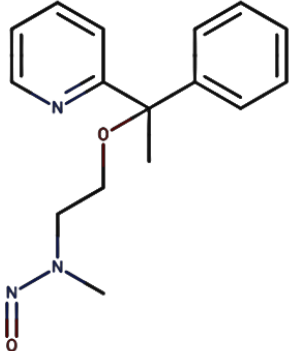
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-clozapine	Clozapine	5	1500
	N-nitroso-clozapine EP Impurity C	Clozapine	3	400

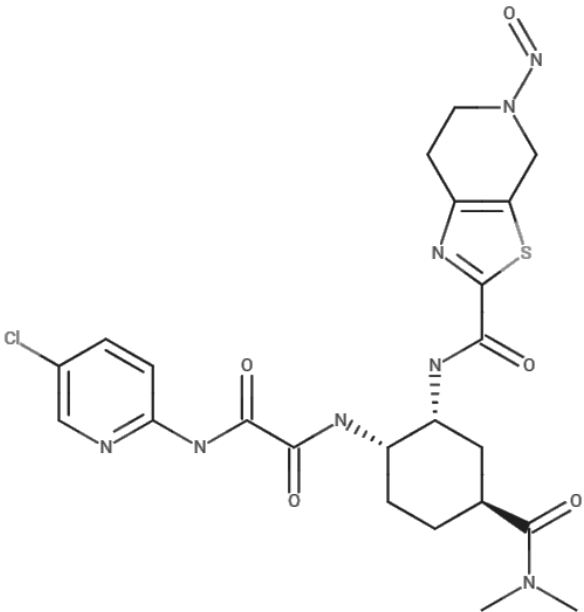
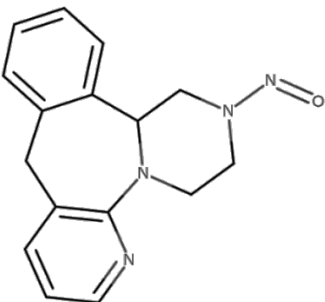
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-dabigatran etexilate	Dabigatran etexilate	-	1500
	N-nitroso-desethyl-lidocaine	Lidocaine	2	100
	N-nitroso-desloratadine	Desloratadine	3	400

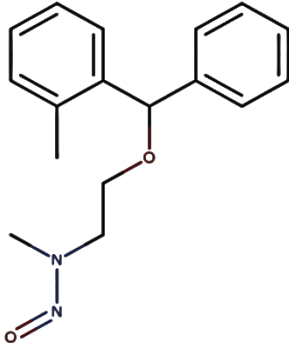
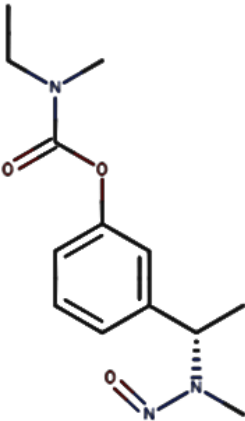
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
 The structure shows a benzimidazole ring system. One nitrogen of the imidazole ring is substituted with a 7-chlorophenylmethyl group. The other nitrogen is substituted with a 7-nitrosomethylheptyl group. The benzimidazole has a carbonyl group at the 2-position.	N-nitroso-desmethyl-azelastine	Azelastine	2	100
 The structure is a complex macrolide antibiotic. It features a 14-membered macrolide ring with multiple stereocenters indicated by wedges and dashes. A side chain contains a nitrosamine group (N-nitroso-N-methyl). Another side chain is a tetrahydropyran ring with a methoxy group and a methyl group.	N-nitroso-desmethyl-azithromycin	Azithromycin	-	Can be controlled according to ICH Q3A/B

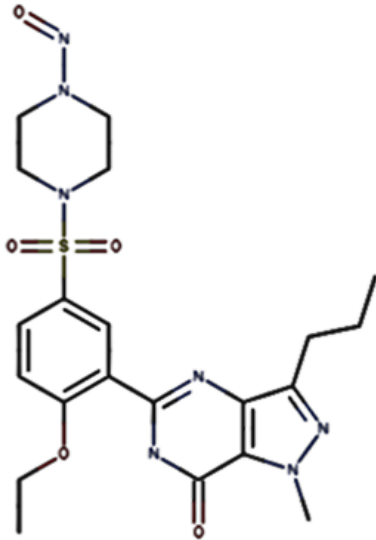
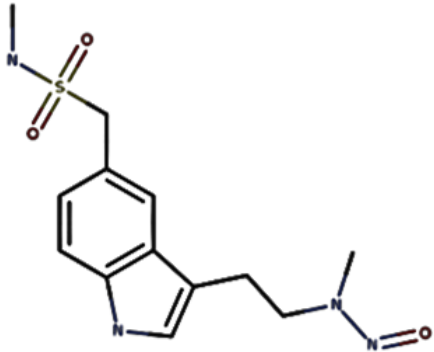
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-chloropyramine	Chloropyramine	1	18
	N-nitroso-desmethyl-citalopram	Citalopram	-	100
	N-nitroso-desmethyl-clarithromycin	Clarithromycin	-	Can be controlled according to ICH Q3A/B

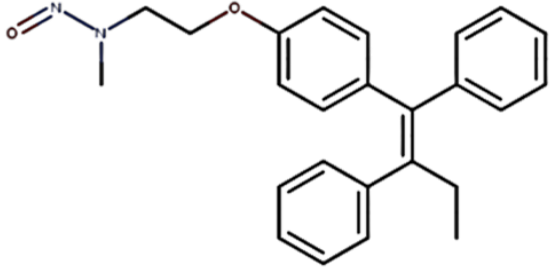
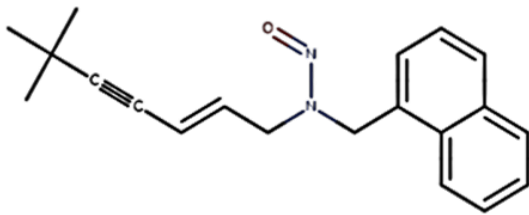
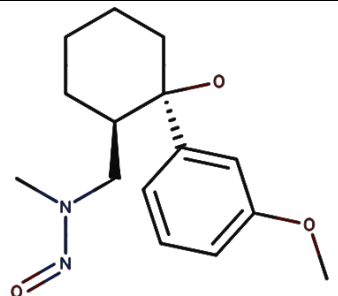
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-desvenlafaxine	Desvenlafaxine	1	18
	N-nitroso-desmethyl-diphenhydramine	Diphenhydramine	1	18
	N-nitroso-desmethyl-doxepin	Doxepin	1	18

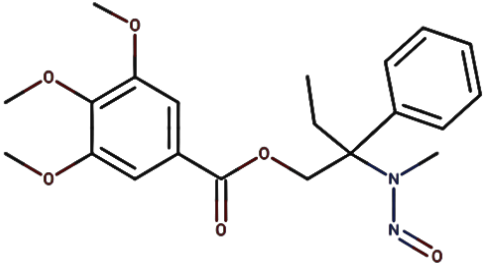
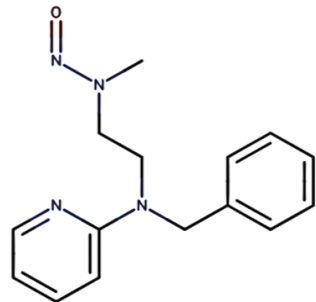
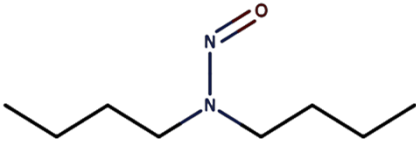
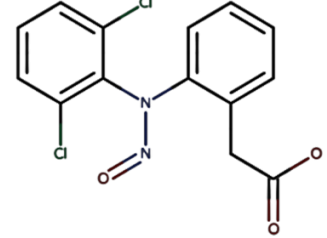
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-doxycycline	Doxycycline	3	400
	N-nitroso-desmethyl-doxylamine	Doxylamine	1	18

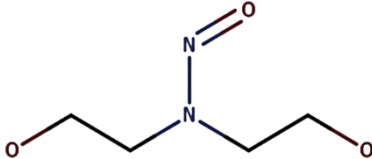
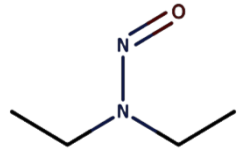
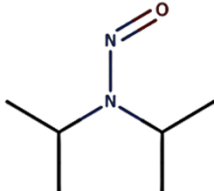
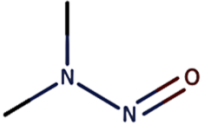
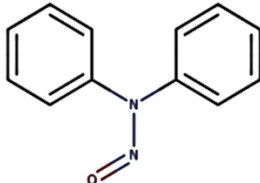
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
 The chemical structure of N-nitroso-desmethyl-edoxaban features a central cyclohexane ring. On the left, it is connected via a dashed bond to a carbonyl group, which is part of a chain including a pyridine ring with a chlorine substituent. On the right, it is connected via a solid wedge bond to another carbonyl group, which is linked to a thiazole ring. The thiazole ring is further connected to a piperidine ring that has an N-nitroso group.	N-nitroso-desmethyl-edoxaban	Edoxaban	2	100
 The chemical structure of N-nitroso-desmethyl-mirtazapine consists of a tricyclic system. It includes a benzene ring fused to a seven-membered ring, which is in turn fused to a pyridine ring. A piperidine ring is attached to the seven-membered ring, and this piperidine ring has an N-nitroso group.	N-nitroso-desmethyl-mirtazapine	Mirtazapine	3	400

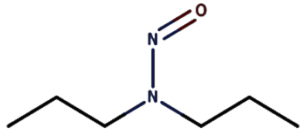
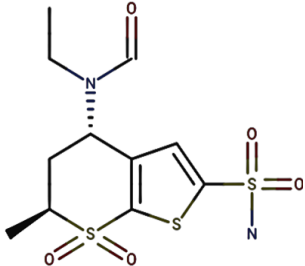
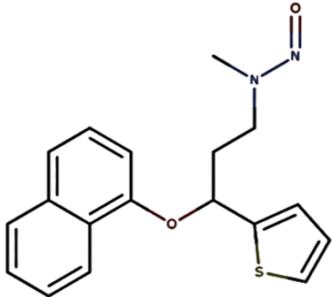
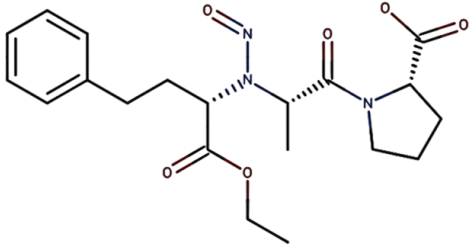
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-orphenadrine	Orphenadrine	1	18
	N-nitroso-desmethyl-rivastigmine	Rivastigmine	2	100

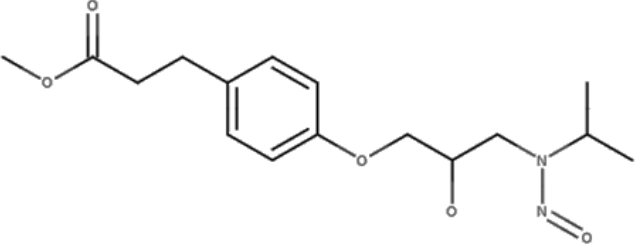
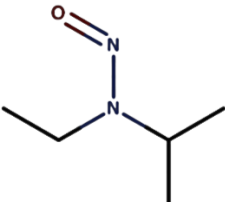
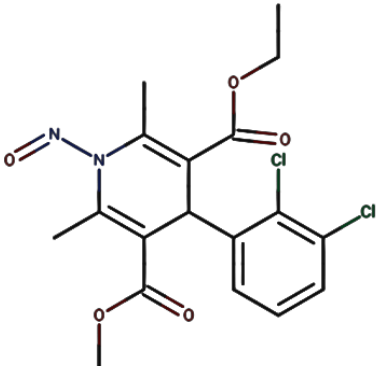
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-sildenafil	Sildenafil	3	400
	N-nitroso-desmethyl-sumatriptan	Sumatriptan	1	18

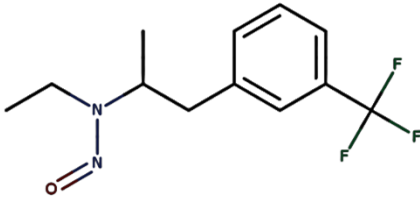
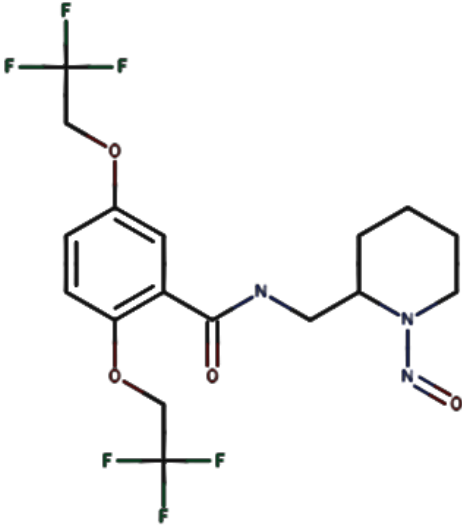
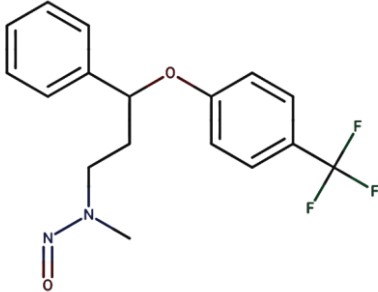
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-tamoxifen	Tamoxifen	1	18
	N-nitroso-desmethyl-terbinafine	Terbinafine	1	18
	N-nitroso-desmethyl-tramadol	Tramadol	1	18

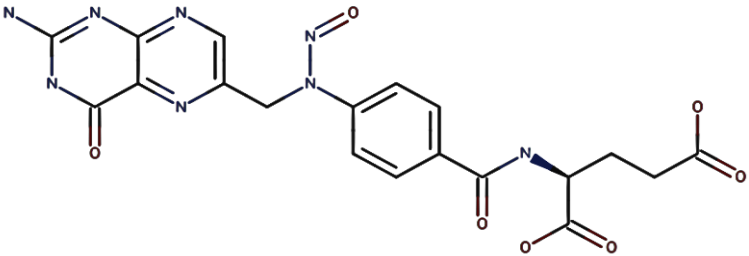
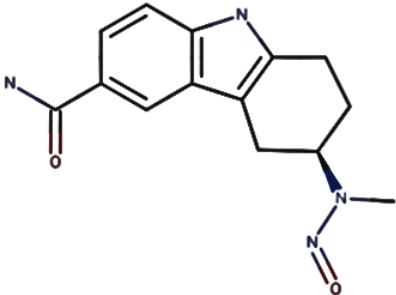
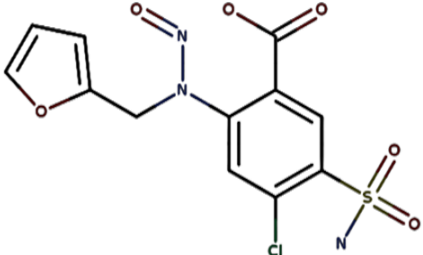
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-desmethyl-trimebutine	Trimebutine	5	1500
	N-nitroso-desmethyl-tripelennamine	Tripelennamine	1	18
	N-nitroso-di-butylamine	Multiple sources	-	26.5
	N-nitroso-diclofenac	Diclofenac	-	78000

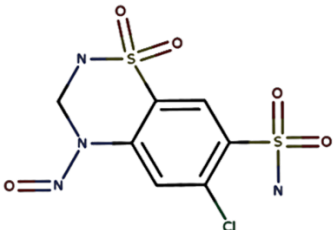
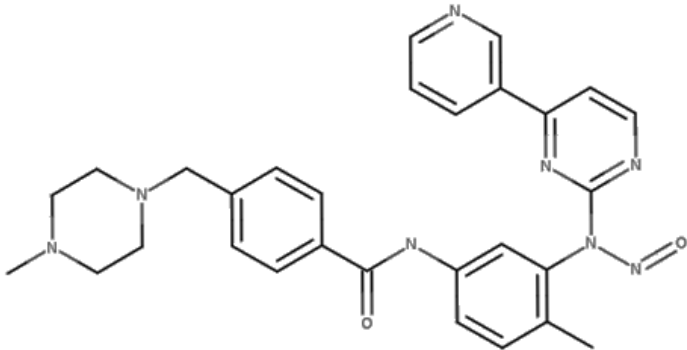
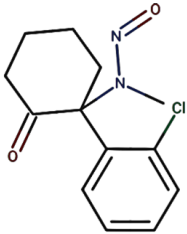
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-diethanolamine	Multiple sources	-	1900
	N-nitroso-diethylamine	Multiple sources	-	26.5
	N-nitroso-diisopropylamine	Multiple sources	5	1500
	N-nitroso-dimethylamine	Multiple sources	-	96
	N-nitroso-diphenylamine	Multiple sources	-	78000

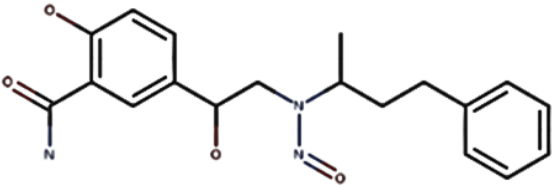
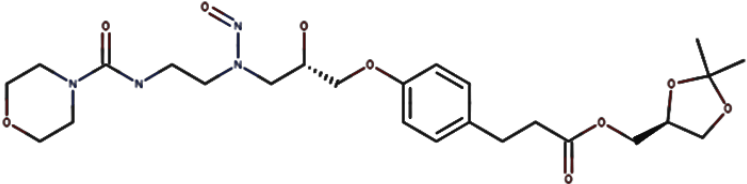
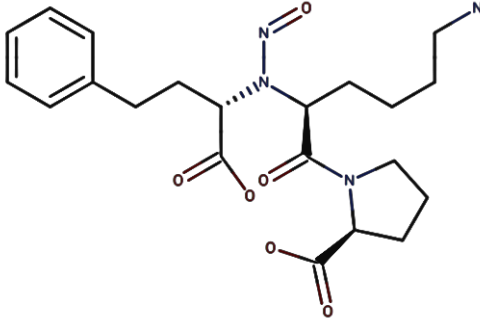
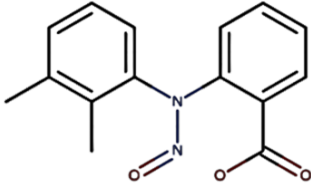
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-dipropylamine	Multiple sources	-	26.5
	N-nitroso-dorzolamide	Dorzolamide	-	1500
	N-nitroso-duloxetine	Duloxetine	-	100
	N-nitroso-enalapril	Enalapril	5	1500

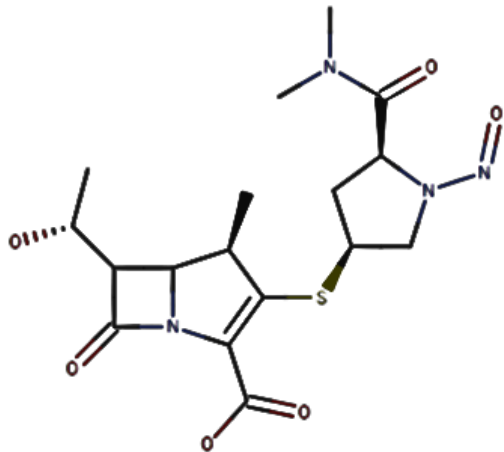
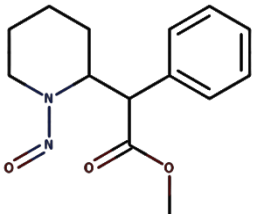
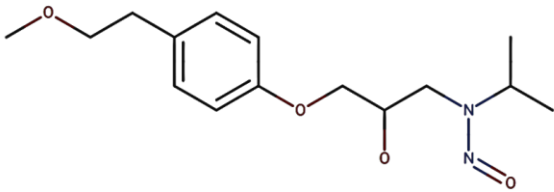
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-esmolol	Esmolol	4	1500
	N-nitroso-ethylisopropylamine	Multiple sources	3	400
	N-nitroso-felodipine	Felodipine	5	1500

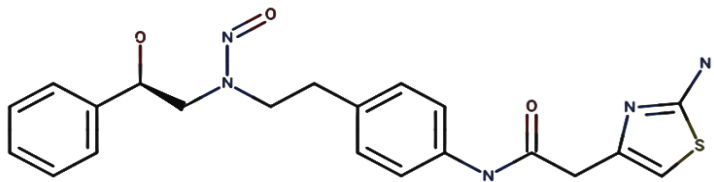
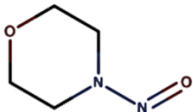
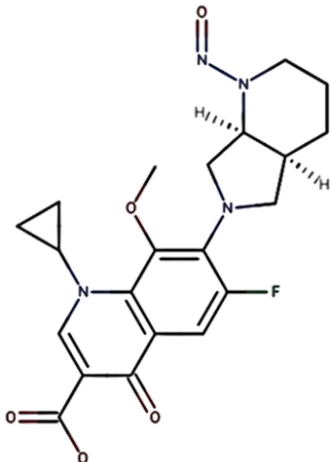
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-fenfluramine	Fenfluramine	3	400
	N-nitroso-flecainide	Flecainide	4	1500
	N-nitroso-fluoxetine	Fluoxetine	-	100

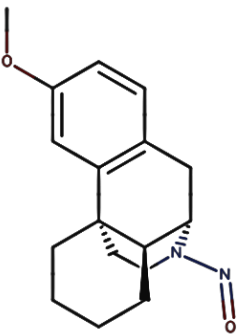
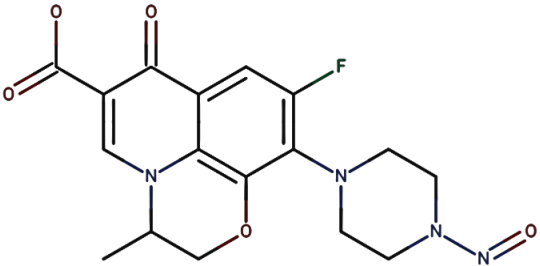
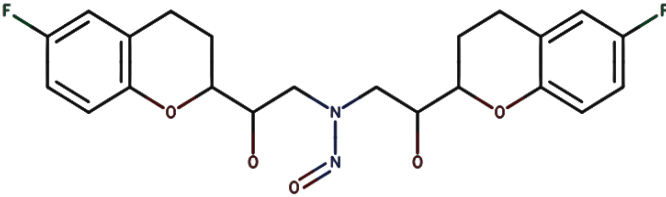
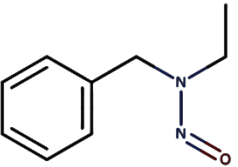
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-folic acid	Folic acid	4	1500
	N-nitroso-frovatriptan	Frovatriptan	3	400
	N-nitroso-furosemide	Furosemide	4	1500

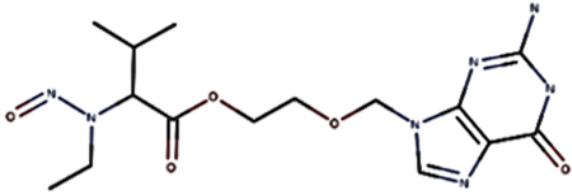
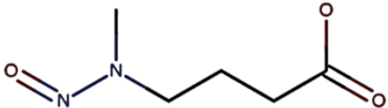
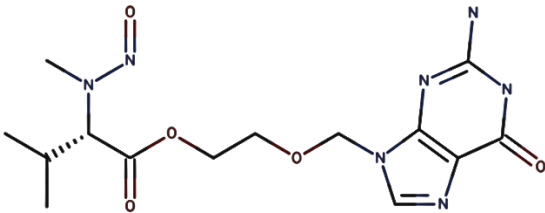
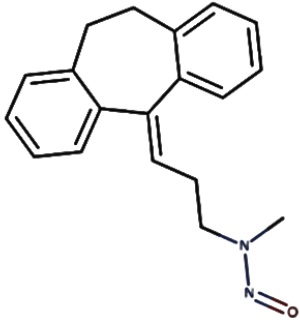
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-hydrochlorothiazide	Hydrochlorothiazide	-	Can be controlled according to ICH Q3A/B
	N-nitroso-imatinib	Imatinib	5	1500
	N-nitroso-ketamine	Ketamine	5	1500

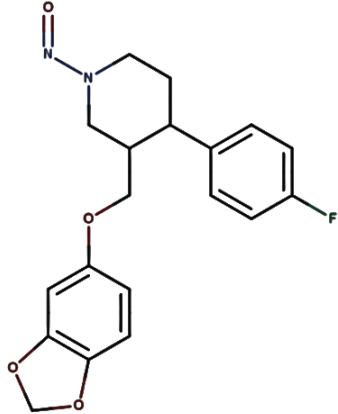
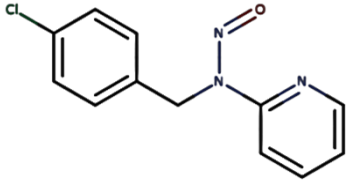
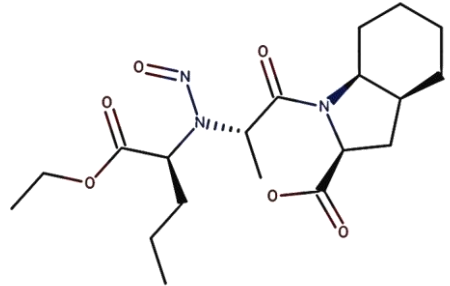
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-labetalol	Labetalol	4	1500
	N-nitroso-landiolol	Landiolol	3	400
	N-nitroso-lisinopril	Lisinopril	-	Can be controlled according to ICH Q3A/B
	N-nitroso-mefenamic acid	Mefenamic acid	-	78000

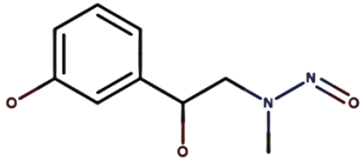
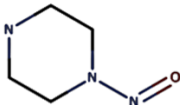
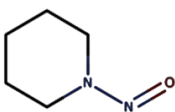
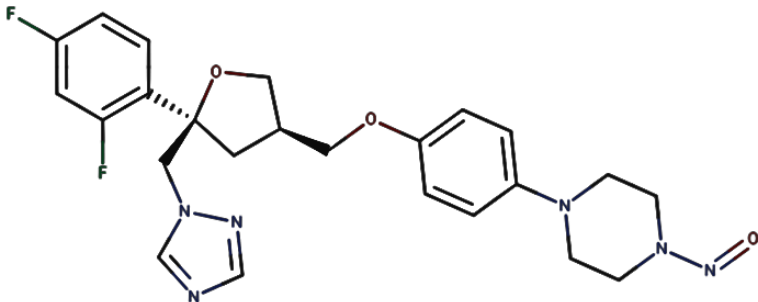
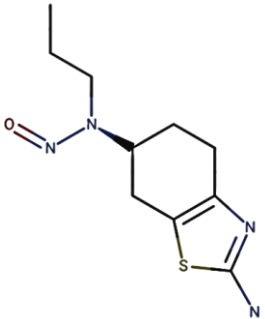
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-meropenem	Meropenem	4	1500
	N-nitroso-methylphenidate	Methylphenidate	-	1300
	N-nitroso-metoprolol	Metoprolol	4	1500

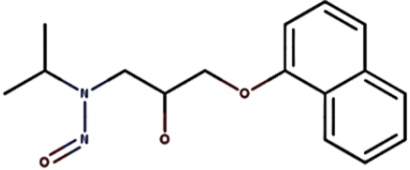
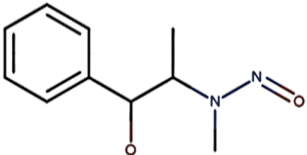
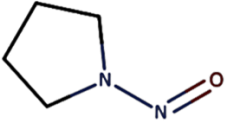
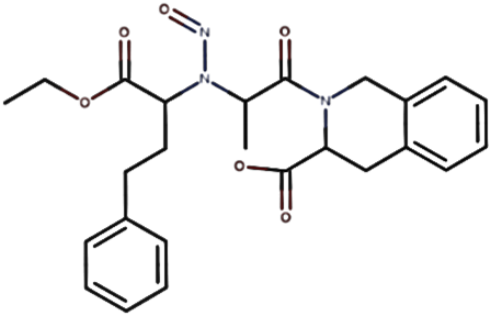
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-mirabegron	Mirabegron	3	400
	N-nitroso-morpholine	Multiple sources	-	127
	N-nitroso-moxifloxacin	Moxifloxacin	4	1500

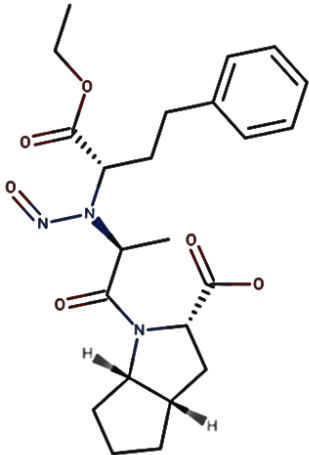
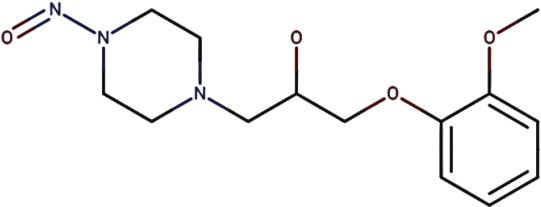
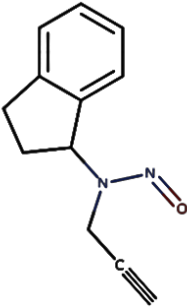
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-N-desmethyl-dextromethorphan	Dextromethorphan	4	1500
	N-nitroso-N-desmethyl-levofloxacin	Levofloxacin	4	1500
	N-nitroso-nebivolol	Nebivolol	4	1500
	N-nitroso-N-ethyl-benzylamine	Multiple sources	1	18

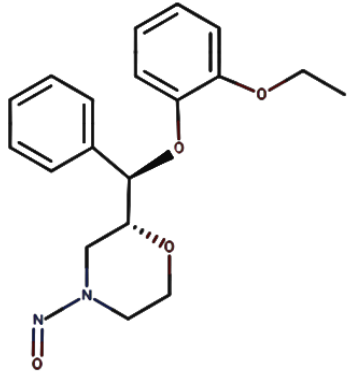
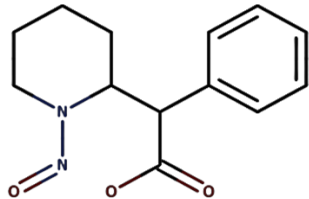
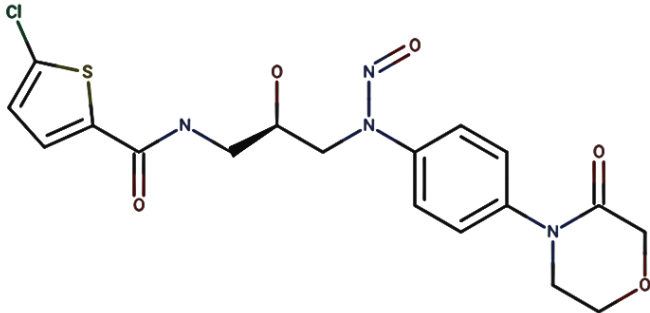
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-N-ethyl-valaciclovir	Valaciclovir	3	400
	N-nitroso-N-methyl-4-aminobutyric acid	Multiple sources	4	1500
	N-nitroso-N-methyl-valaciclovir	Valaciclovir	3	400
	N-nitroso-nortriptyline	Amitriptyline, Nortriptyline	1	18

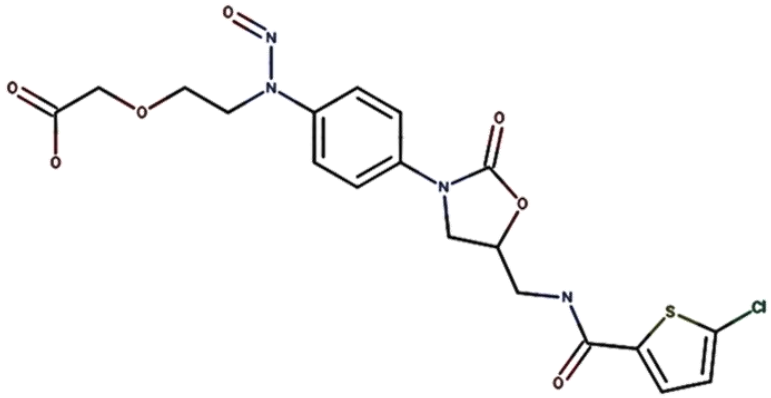
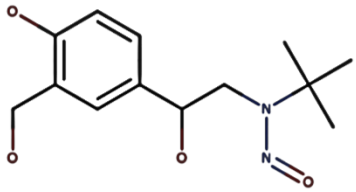
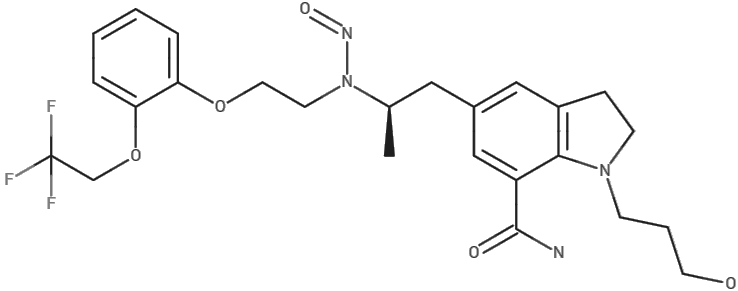
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-paroxetine	Paroxetine	-	1300
	N-nitroso-p-chloro-benzylamino-pyridine	Chloropyramine	2	100
	N-nitroso-perindopril	Perindopril	5	1500

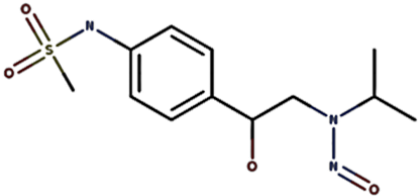
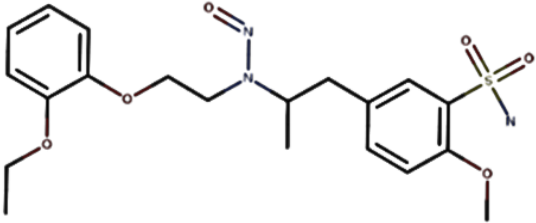
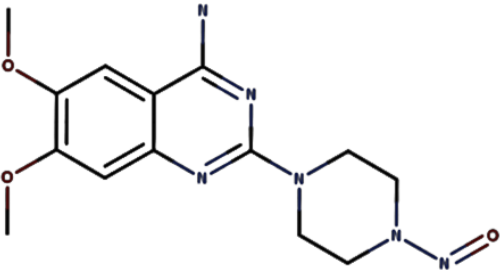
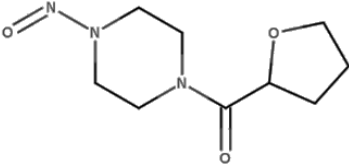
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-phenylephrine	Phenylephrine	2	100
	N-nitroso-piperazine	Multiple sources	3	400
	N-nitroso-piperidine	Multiple sources	-	1300
	N-nitroso-positaconazole Impurity 1 / 1-(4-(((3R,5R)-5-((1H-1,2,4-triazol-1-yl)methyl)-5-(2,4-difluorophenyl)tetrahydrofuran-3-yl)methoxy)phenyl)-4-nitrosopiperazine	Posaconazole	3	400
	N-nitroso-pramipexole	Pramipexole	3	400

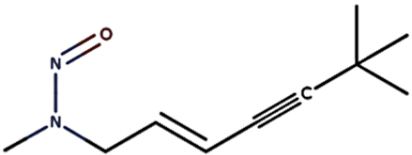
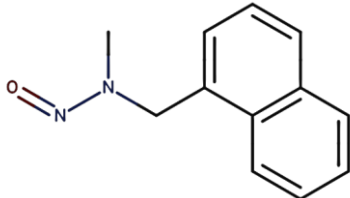
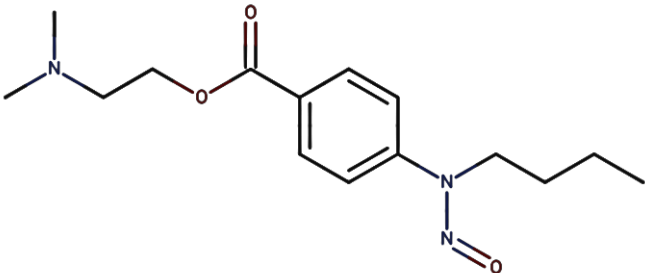
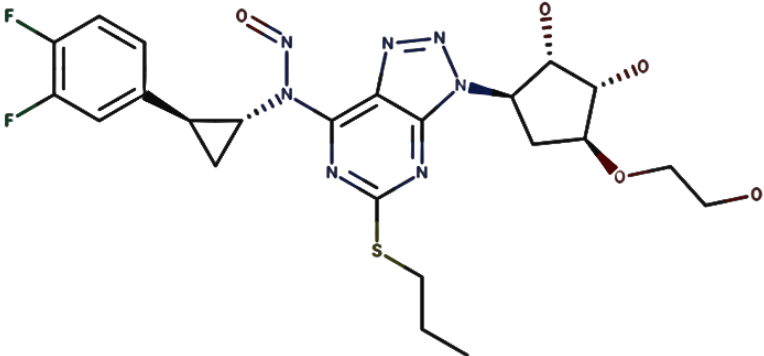
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-propranolol	Propranolol	4	1500
	N-nitroso-pseudoephedrine	Pseudoephedrine	4	1500
	N-nitroso-pyrrolidine	Multiple sources	-	1700
	N-nitroso-quinapril	Quinapril	-	Can be controlled according to ICH Q3A/B

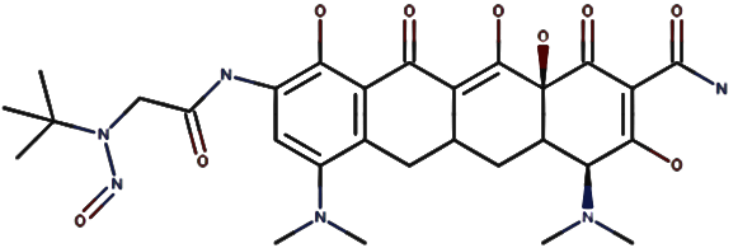
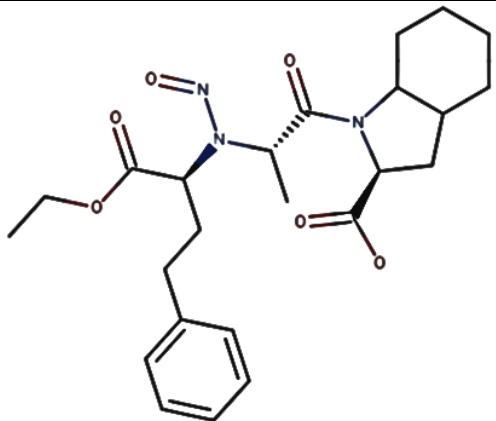
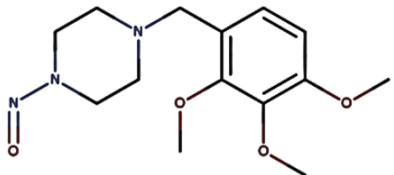
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-ramipril	Ramipril	5	1500
	N-nitroso-ranolazine impurity 1 / 1-(2-methoxyphenoxy)- 3-(4-nitrosopiperazin-1-yl) propan-2-ol	Ranolazine	3	400
	N-nitroso-rasagiline	Rasagiline	2	100

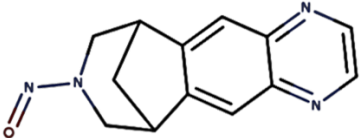
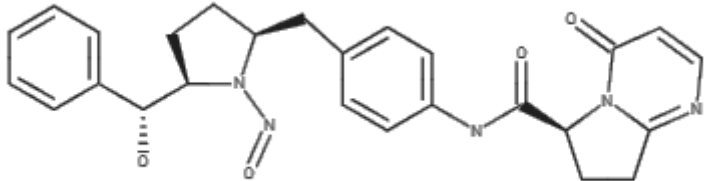
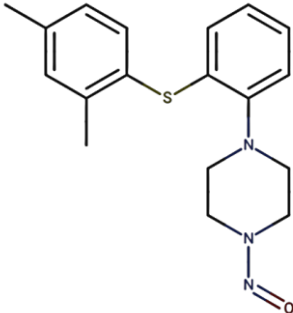
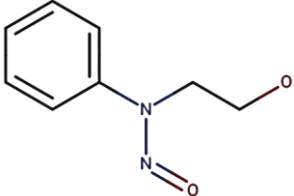
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-reboxetine	Reboxetine	-	127
	N-nitroso-ritalinic acid	Methylphenidate	4	1500
	N-nitroso-rivaroxaban amide / (S)-5-chloro-N-(2-hydroxy-3-(nitroso(4-(3-oxomorpholino)phenyl)amino)propyl)thiophene-2-carboxamide	Rivaroxaban	4	1500

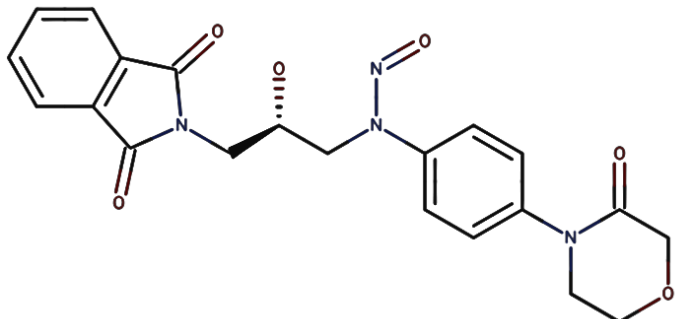
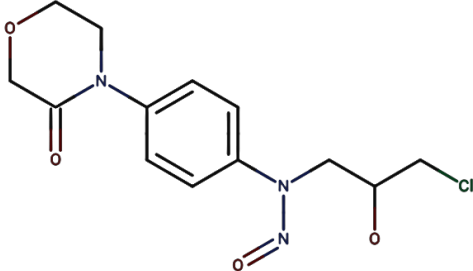
Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-rivaroxaban open-ring acid / (S)-2-(2-((4-(5-(5-chlorothiophene-2-carboxamido)methyl)-2-oxooxazolidin-3-yl)phenyl)(nitroso)amino)ethoxy)acetic acid	Rivaroxaban	4	1500
	N-nitroso-salbutamol	Salbutamol	5	1500
	N-nitroso-silodosin	Silodosin	4	1500

Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-sotalol	Sotalol	4	1500
	N-nitroso-tamsulosin	Tamsulosin	4	1500
	N-nitroso-terazosin EP Impurity C	Terazosin	3	400
	N-nitroso terazosin Impurity N / (4-nitrosopiperazin-1-yl) (tetrahydrofuran-2-yl)methanone	Terazosin	3	400

Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-terbinafine degradant / N-[(2E)-6,6-dimethyl-2-hepten-4-yn-1-yl]-N-nitrosomethanamine	Terbinafine	1	18
	N-nitroso-terbinafine Impurity A / N-nitroso-N-methyl-1-naphthylmethanamine	Terbinafine	1	18
	N-nitroso-tetracaine	Tetracaine	3	400
	N-nitroso-ticagrelor	Ticagrelor	5	1500

Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-tigecycline	Tigecycline	-	Can be controlled according to ICH Q3A/B
	N-nitroso-trandolapril	Trandolapril	5	1500
	N-nitroso-trimetazidine	Trimetazidine	3	400

Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	N-nitroso-varenicline	Varenicline	3	400
	N-nitroso-vibegron	Vibegron	5	1500
	N-nitroso-vortioxetine	Vortioxetine	3	400
	Rivaroxaban Nitroso Impurity 1 / N-(2-hydroxyethyl)-N-phenylnitrous amide	Rivaroxaban	4	1500

Structure	Name	Source (non-exhaustive)	CPCA Category (if applicable)	Recommended AI (ng/day)
	Rivaroxaban Nitroso Impurity 2 / (S)-N-(3-(1,3-dioxoisindolin-2-yl)-2-hydroxypropyl)-N-(4-(3-oxomorpholino)phenyl)nitrous amide	Rivaroxaban	4	1500
	Rivaroxaban Nitroso Impurity 5 / (R)-N-(3-chloro-2-hydroxypropyl)-N-(4-(3-oxomorpholino)phenyl)nitrous amide	Rivaroxaban	4	1500