

Supplementary Material

Safety of Memantine in Combination with Potentially Interactive Drugs in the Real World: A Pharmacovigilance Study Using the Japanese Adverse Drug Event Report (JADER) Database

Supplementary Table 1. Definition of adverse events categories

MedDRA term	term	defined categories				
	level	AMS	Fall	Seizure	LOC	Dizziness
Altered state of consciousness	PT	×				
Somnolence	PT	×				
Depressed level of consciousness	PT	×				
Coma	PT	×				
Stupor	PT	×				
Consciousness fluctuating	PT	×				
Delirium	PT	×				
Disorientation	PT	×				
Confusional state	PT	×				
Delusion	PT	×				
Abnormal behavior	PT	×				
Anger	PT	×				
Agitation	PT	×				
Hallucination	PT	×				
Hallucination, visual	PT	×				
Fall	PT		×			
Seizure	PT			×		
Loss of consciousness	PT				×	
Syncope	PT				×	
Dizziness	PT					×
Dizziness postural	PT					×

LOC, loss of consciousness; AMS, altered mental status; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term

Supplementary Table 2. A) Contingency table of combinations.

		with AE of interest	without AE of interest
combination 1	those with amantadine and memantine	a1	b1
	those with amantadine and any ChEi	c1	d1
combination 2	those with dextromethorphan and amantadine	a2	b2
	those with dextromethorphan and any ChEi	c2	d2
combination 3	those with cimetidine and memantine	a3	b3
	those with cimetidine and any ChEi	c3	d3
combination 4	those with ranitidine and memantine	a4	b4
	those with ranitidine and any ChEi	c4	d4
combination 5	those with sodium bicarbonate and memantine	a5	b5
	those with sodium bicarbonate and any ChEi	c5	d5

Supplementary Table 2. B) Results p-value of Fisher's exact test on tables in (A)

		p-values				
		combination 1	combination 2	combination 3	combination 4	combination 5
Defined categories	AMS	1.000	1.000	0.266	1.000	1.000
	Fall	0.538	1.000	0.308	1.000	1.000
	Seizure	0.098	0.468	1.000	1.000	0.275
	LOC	1.000	1.000	0.308	1.000	1.000
	Dizziness	1.000	1.000	1.000	0.284	1.000
MedDRA terms	Altered state of consciousness	0.349	1.000	0.530	1.000	1.000
	Somnolence	0.318	1.000	1.000	1.000	1.000
	Depressed level of consciousness	1.000	0.468	0.308	0.398	1.000
	Coma	1.000	1.000	1.000	1.000	1.000
	Stupor	1.000	1.000	1.000	1.000	1.000
	Consciousness fluctuating	1.000	1.000	1.000	1.000	1.000
	Delirium	0.586	1.000	1.000	1.000	1.000
	Disorientation	0.318	1.000	1.000	1.000	1.000
	Confusional state	1.000	1.000	1.000	1.000	1.000
	Delusion	1.000	1.000	1.000	1.000	1.000
	Abnormal behavior	1.000	1.000	1.000	1.000	1.000
	Anger	1.000	1.000	1.000	1.000	1.000
	Agitation	0.173	1.000	1.000	1.000	1.000
	Hallucination	0.589	1.000	1.000	1.000	1.000
	Hallucination, visual	0.438	1.000	1.000	1.000	1.000
	Fall	0.538	1.000	0.308	1.000	1.000
	Seizure	0.098	0.468	1.000	1.000	0.275

Loss of consciousness	0.438	1.000	0.308	1.000	1.000
Syncope	1.000	1.000	1.000	1.000	1.000
Dizziness	1.000	1.000	1.000	0.284	1.000
Dizziness postural	1.000	1.000	1.000	1.000	1.000

AE, adverse event; ChEi, acetylcholinesterase inhibitors; LOC, loss of consciousness; AMS, altered mental status; MedDRA, Medical Dictionary for Regulatory Activities.