

**S3 Table: Nesting of Outcomes**

Primary outcomes	Secondary outcomes	
	Aggregated ADRs*	Individual ADR*
ADRs indicative of anti-cholinergic activity (ACH-ADRs)	Dry mouth-related ADRs (15)	<b>Dry mouth</b> (14) <b>Dry mucous membrane</b> (1)
	Digestion-related ADRs (13)	Constipation (13)
	Genitourinary-related ADRs (5)	Urinary retention (2) Difficulty urinating (1) Micturition disorder (1) Urogenital (1)
	Vision-related ADRs (8)	Blurred vision (4) Amblyopia (2) Vision abnormalities (2)
	Thermoregulation-related ADRs (1)	Sweat discoloration (1)
	Cardiovascular-related ADRs (7)	Tachycardia (3) Palpitation (3) Postural Hypotension (1) Standing heartrate (1) Supine heartrate (1) Increased standing and supine pulse (2)
	Fatigue-related ADRs (20)	<b>Fatigue</b> (6) Asthenia (2) <b>Drowsiness</b> (8) Dizziness (19) Depression (2) <b>Somnolence</b> (8) <b>Sedation</b> (4) Sedative effects (drowsiness, sedation, excessive sleep) (1) <b>Constitutional symptoms (primarily fatigue, malaise)</b> (1)
	Attention-related ADRs (1)	Confusion (1)
	Memory-related ADRs (1)	Amnesia (1)
	Restlessness-related ADRs (13)	Restlessness (1) Agitation (3) Nervousness (3) Tingling (1) Sensory system (1) Anxiety (1) Panic attack (1) Insomnia (11)
	Coordination-related ADRs (8)	Tremor (8) Hyperkinesia (1) Hypokinesia (1) Slurred speech (1) Paresthesia (1)
	Unspecifically reported ACH-ADRs (1)	<b>Anticholinergic effects (dry mouth, constipation, visual disturbances)</b> (1)
	ADRs not indicative of anticholinergic activity (NACH-ADRs)	<b>Nausea</b> (6) Vomiting (1) <b>Dyspepsia</b> (4) Bloating (1) Diarrhea (3) Hemorrhoids (1) Intestinal fluid (1) Metabolic nutritional (1)

	Anorexia (1) Abdominal pain (2) <b>Epigastralgia</b> (1) Taste perversion (1)
<i>ADRs related to hypersensitivity</i> (6)	Pruritus (2) Rash (2) <b>Allergic</b> (1) Liver function abnormality (1)
ADRs related to the endocrine system (3)	Impotence (1) <b>Sexual</b> (2) Change in appetite (1) <b>Increased appetite</b> (3)
<i>Unspecifically reported NACH-ADRs</i> (12)	Reduced appetite (1) Sweat (3) <i>Weight gain</i> (5) <b>Headache</b> (9)
<i>General unspecific ADRs (G-ADRs)</i>	<i>Unspecifically reported G-ADRs</i> (5)
	<b>Chest pain</b> (2) Heartburn (1) Infection/fever (1) Musculoskeletal (2) <b>Nasal congestion</b> (1) Otolaryngologic (1) Pain (primarily headache) (1) Respiratory (1) Pulmonary (2) Endocrine (1) Hematologic (1) Clostridium difficile infection (1) <b>Neurological</b> (2) Psychiatric (1) Cardiovascular (1) Dermatology/skin (2) Renal/genitourinary (1) Gynecologic (1) Gastrointestinal (2) Dreams (1)
	<b>ADRs overall</b> (No specific ADRs reported) (11)
	<b>Discontinued due to ADRs</b> (No specific ADRs reported) (13)

bold = ADR included in primary outcome; italic = meta-analysis conducted (at least 5 studies); \* = in brackets: number of included studies.