

Listing 16.2.7: Individual Subject Adverse Events

Subject No.	Cohort	Treatment	AE No.	AE Description	Preferred Term ¹	Start Date/Time (YYYYMMDD THHMM)	Study Day ²	Stop Date/Time (YYYYMMDD THHMM)	AE Duration	Severity ³	Action Taken ⁴	Rel ⁵	Serious AE	Serious Criteria ⁶	Outcome ⁷	Additional Information
004	1a	ESB1609 300 mg	1	NOSE CONGESTION	Nasal congestion	2019-09-23T06:00	Day 7	2019-09-23T12:30	6H30M	1	5	1	No	No	1	
007	1b	-	1	VASOVAGAL REACTION	Presyncope	2019-09-17T11:10	Prior	2019-09-17T11:17	7M	1	1	1	No	No	1	
007	1b	ESB1609 300 mg	2	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-09-17T15:30	Day 1	2019-09-23T20:00	6D4H30M	1	5	1	No	No	1	
007	1b	ESB1609 300 mg	3	VASOVAGAL REACTION	Presyncope	2019-09-18T12:06	Day 2	2019-09-18T12:09	3M	1	5	1	No	No	1	
007	1b	ESB1609 300 mg	4	FORGETFULNESS	Memory impairment	2019-09-18T16:00	Day 2	2019-09-23T12:00	4D20H	1	5	3	No	No	1	
007	1b	ESB1609 300 mg	5	LIGHT SENSITIVITY	Photophobia	2019-09-17T14:00	Day 1	2019-09-20T16:00	3D2H	1	5	3	No	No	1	
007	1b	ESB1609 300 mg	6	NAUSEA	Nausea	2019-09-18T23:21	Day 2	2019-09-18T23:31	10M	1	5	3	No	No	1	
007	1b	ESB1609 300 mg	7	CONCENTRATION IMPAIRED	Disturbance in attention	2019-09-17T15:30	Day 1	2019-09-24T09:00	6D17H30M	1	5	3	No	No	1	

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007	1b	ESB1609 300 mg	8	TENDERNESS TESTIS	Testis discomfort	2019-09-19T15:15	Day 3	2019-09-24T20:00	5D4H45M	1	5	1	No	No	1	
007	1b	ESB1609 300 mg	9	BACK PAIN	Back pain	2019-09-17T15:00	Day 1	2019-09-23T15:00	6D	1	5	1	No	No	1	
008	1b	ESB1609 300 mg	1	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-10-08T19:30	Day 1	2019-10-09T04:10	8H40M	1	5	1	No	No	1	
008	1b	ESB1609 300 mg	2	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-10-09T09:30	Day 2	2019-11-05T10:00	27D30M	2	5	1	No	No	1	
008	1b	ESB1609 300 mg	3	HYPERVENTILATION HEADACHE	Hyperventilation	2019-10-10T10:18	Day 3	2019-10-10T14:00	3H42M	1	5	1	No	No	1	
008	1b	ESB1609 300 mg	4	MUSCLE PAIN NECK INTERMITTENT	Neck pain	2019-10-10T10:20	Day 3	2019-11-05T10:00	0025D23H40M	1	5	1	No	No	1	
008	1b	ESB1609 300 mg	5	NAUSEA	Nausea	2019-10-10T23:31	Day 3	2019-10-10T23:37	6M	1	5	2	No	No	1	

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008	1b	ESB1609 300 mg	6	VOMITING	Vomiting	2019-10-10T23:31	Day 3	2019-10-10T23:37	6M	1	5	2	No		1	
008	1b	ESB1609 300 mg	7	EMOTIONAL DISTRESS	Emotional distress	2019-10-09T13:00	Day 2	2019-11-05T10:00	26D21H	1	5	2	No		1	
008	1b	ESB1609 300 mg	8	DECREASED APPETITE	Decreased appetite	2019-10-09T13:00	Day 2	2019-10-14T07:00	4D18H	1	5	2	No		1	
008	1b	ESB1609 300 mg	9	LIGHT SENSITIVITY	Photophobia	2019-10-09T13:00	Day 2	2019-10-15T20:30	6D7H30M	1	5	3	No		1	
008	1b	ESB1609 300 mg	10	VOMITING	Vomiting	2019-10-11T21:55	Day 4	2019-10-11T22:00	5M	1	5	2	No		1	
008	1b	ESB1609 300 mg	11	IMPAIRED HEARING RIGHT EAR	Hypoacusis	2019-10-11T15:00	Day 4	2019-10-14T10:00	2D19H	1	5	2	No		1	
008	1b	ESB1609 300 mg	12	TINNITUS	Tinnitus	2019-10-12T09:15	Day 5	Ongoing		2	5	2	No		5	
008	1b	ESB1609 300 mg	13	IMPAIRED HEARING LEFT EAR	Hypoacusis	2019-10-11T15:05	Day 4	2019-10-23T13:00	11D21H55M	1	5	2	No		1	

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008	1b	ESB1609	14	LOWER BACK PAIN	Back pain	2019-10-17T07:00	Day 10	2019-10-17T12:30	5H30M	1	5	1	No	No	1	
008	1b	ESB1609	15	SUICIDAL IDEATION	Suicidal ideation	2019-10-13T16:13	Day 6	2019-10-17T13:13	3D21H	1	5	1	No	No	1	
016	2b	ESB1609	1	PAIN RIGHT HIP	Arthralgia	2019-10-08T12:48	Day 1	2019-10-09T04:41	15H53M	1	5	1	No	No	1	
016	2b	ESB1609	2	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-10-08T14:40	Day 1	2019-10-21T10:00	12D19H20M	2	5	1	No	No	1	
016	2b	ESB1609	3	NECK STIFFNESS	Musculoskeletal stiffness	2019-10-10T17:30	Day 3	2019-10-21T10:00	10D16H30M	1	5	1	No	No	1	
016	2b	ESB1609	4	NAUSEA	Nausea	2019-10-10T22:00	Day 3	2019-10-10T22:05	5M	1	5	2	No	No	1	
016	2b	ESB1609	5	VOMITING	Vomiting	2019-10-10T22:00	Day 3	2019-10-10T22:05	5M	1	5	2	No	No	1	
016	2b	ESB1609	6	HIP PRESSURE INTERMITTENT	Musculoskeletal discomfort	2019-10-10T22:00	Day 3	2019-10-14T08:00	3D10H	1	5	2	No	No	1	

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016	2b	ESB1609 450 mg	7	DECREASED APPETITE	Decreased appetite	2019-10-10T22:00	Day 3	2019-10-15T13:00	4D15H	1	5	2	No		1	
016	2b	ESB1609 450 mg	8	COLD FEELING	Feeling cold	2019-10-14T22:10	Day 7	2019-10-14T23:00	50M	1	5	2	No		1	
016	2b	ESB1609 450 mg	9	HYPOTENSION	Hypotension	2019-10-09T22:39	Day 2	2019-10-09T22:47	8M	1	5	3	No		1	
017	2b	-	1	HEADACHE	Headache	2019-10-08T10:30	Prior	2019-10-08T17:00	6H30M	1	5	1	No		1	
017	2b	ESB1609 450 mg	2	LOWER BACK STIFFNESS	Musculoskeletal stiffness	2019-10-08T14:00	Day 1	2019-10-09T17:38	1D3H38M	1	5	1	No		1	
017	2b	ESB1609 450 mg	3	HIP STIFFNESS	Joint stiffness	2019-10-09T23:00	Day 2	2019-10-10T17:00	18H	1	5	2	No		1	
018	2b	ESB1609 450 mg	1	EPIDURAL CATHETER INSERTION SITE PAIN	Catheter site pain	2019-10-08T12:30	Day 1	2019-10-16T13:00	8D30M	2	5	1	No		1	
018	2b	ESB1609 450 mg	2	VASOVAGAL REACTION	Presyncope	2019-10-08T15:28	Day 1	2019-10-08T15:32	4M	1	5	1	No		1	

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018	2b	ESB1609 450 mg	3	PAIN RIGHT LEG	Pain in extremity	2019-10-08T16:00	Day 1	2019-10-09T23:00	1D7H	1	5	1	No	No	1	
018	2b	ESB1609 450 mg	4	HEADACHE	Headache	2019-10-10T09:30	Day 3	2019-10-13T19:00	3D9H30M	1	5	3	No	No	1	
018	2b	ESB1609 450 mg	5	MUSCLE PAIN NECK	Neck pain	2019-10-10T11:15	Day 3	2019-10-21T08:00	10D20H45M	2	5	1	No	No	1	
018	2b	ESB1609 450 mg	6	PRESSURE EARS	Ear discomfort	2019-10-10T11:15	Day 3	2019-10-16T20:00	6D8H45M	1	5	2	No	No	1	
018	2b	ESB1609 450 mg	7	HEADACHE	Headache	2019-10-13T19:00	Day 6	2019-10-15T09:00	1D14H	2	5	2	No	No	1	
018	2b	ESB1609 450 mg	8	TINNITUS	Tinnitus	2019-10-10T10:15	Day 3	2019-10-21T08:00	10D21H45M	1	5	2	No	No	1	
018	2b	ESB1609 450 mg	9	FEVER	Pyrexia	2019-10-08T19:13	Day 1	2019-10-08	1D	1	5	3	No	No	1	STOP TIME NOT RECORDED
018	2b	ESB1609 450 mg	10	ALT INCREASED	Alanine aminotransferase increased	2019-10-12T11:11	Day 5	2019-10-17T14:22	5D3H11M	1	5	3	No	No	1	

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020	3a	Placebo	1	RASH/ECG STICKERS	Application site rash	2019-10-29T09:30	Day 2	2019-11-21T12:28	23D2H58M	1	5	1	No		1	
020	3a	Placebo	2	CANNULA SITE REACTION (BRUISE)	Application site bruise	2019-10-29T08:00	Day 2	2019-11-03T10:00	5D2H	1	5	1	No		1	
020	3a	Placebo	3	GENERALIZED MUSCLE PAIN	Myalgia	2019-11-02T20:00	Day 6	2019-11-03T22:02	1D2H2M	1	1	3	No		1	
020	3a	Placebo	4	SHIVERING	Chills	2019-11-02T23:00	Day 6	2019-11-03T03:45	4H45M	1	1	3	No		1	
020	3a	Placebo	5	DECREASED APPETITE	Decreased appetite	2019-11-03T14:00	Day 7	2019-11-03T21:00	7H	1	1	3	No		1	
026	3b	ESB1609 1350 mg	1	NON-SUSTAINED VENTRICULAR TACHYCARDIA	Ventricular tachycardia	2019-10-28T13:23	Day 1	2019-10-28T13:23	0M	1	5	3	No		1	
027	3b	ESB1609 1350 mg	1	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-10-29T13:10	Day 2	2019-11-05T17:00	7D3H50M	2	5	1	No		1	
027	3b	ESB1609 1350 mg	2	DECREASED APPETITE	Decreased appetite	2019-10-31T12:40	Day 4	2019-11-05T17:00	5D4H20M	1	5	2	No		1	

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029	4a	ESB1609 2700 mg	1	ACID REFLUX	Gastroesophageal reflux disease	2019-11-18T10:05	Day 1	2019-11-18T23:00	12H55M	1	5	1	No		1	
029	4a	ESB1609 2700 mg	2	COMMON COLD	Nasopharyngitis	2019-11-18T22:00	Day 1	2019-11-26T15:00	7D17H	1	5	1	No		1	
029	4a	ESB1609 2700 mg	3	EPISTAXIS	Epistaxis	2020-01-27T21:55	Day 71	2020-01-27T21:58	3M	1	1	1	No		1	
029	4a	ESB1609 2700 mg	4	ACID REFLUX	Gastroesophageal reflux disease	2020-01-28T10:30	Day 72	2020-01-29T18:00	1D7H30M	1	5	2	No		1	
030	4a	ESB1609 2700 mg	1	ABDOMINAL PAIN	Abdominal pain	2019-11-18T10:40	Day 1	2019-11-18T16:00	5H20M	1	5	3	No		1	
030	4a	ESB1609 2700 mg	2	DIARRHEA	Diarrhoea	2019-11-18T12:24	Day 1	2019-11-20T06:30	1D18H6M	1	5	3	No		1	
030	4a	ESB1609 2700 mg	3	INCREASED ALT	Alanine aminotransferase increased	2019-11-24T10:10	Day 7	2019-12-24T12:14	1MON2H4M	1	5	3	No		1	

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030	4a	ESB1609 2700 mg	4	FREQUENT PREMATURE VENTRICULAR CONTRACTIONS (INTERMITTENT)	Ventricular extrasystoles	2020-01-27T12:29Day 71	2020-01-31T10:00	3D21H31M	1	1	1	1	No	No	1	
030	4a	ESB1609 2700 mg	5	ORTHOSTATIC DIZZINESS	Dizziness postural	2020-01-30T07:10Day 74	2020-01-30T19:00	11H50M	1	5	3	3	No	No	1	
030	4a	ESB1609 2700 mg	6	FATIGUE	Fatigue	2020-01-30T07:10Day 74	2020-01-31T08:00	1D50M	1	5	3	3	No	No	1	
030	4a	ESB1609 2700 mg	7	PALPITATIONS	Palpitations	2020-01-30T07:00Day 74	2020-02-01T22:00	2D15H	1	5	3	3	No	No	1	
030	4a	ESB1609 2700 mg	8	INCREASED ALT	Alanine aminotransferase increased	2020-02-03T09:31Day 78	Ongoing		1	5	3	3	No	No	3	
031	4a	ESB1609 2700 mg	1	DIARRHEA	Diarrhoea	2019-11-18T15:00	Day 1	2019-11-18T16:00	1H	1	5	3	No	No	1	
032	4a	Placebo	1	RASH ECG STICKERS	Application site rash	2019-11-19T11:00	Day 2	2019-11-21T17:00	2D6H	1	5	1	No	No	1	

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032	4a	Placebo	2	EYE IRRITATION	Eye irritation	2019-11-25T11:15	Day 8	2019-11-26T15:00	1D3H45M	1	5	1	No		1	
034	4b	-	1	VASOVAGAL REACTION	Presyncope	2019-11-18T08:44	Prior	2019-11-18T08:51	7M	2	1	1	No		1	
035	4b	ESB1609 2700 mg	1	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-11-18T14:50	Day 1	2019-11-20T09:00	1D18H10M	1	5	1	No		1	
035	4b	ESB1609 2700 mg	2	POST LUMBAR PUNCTURE HEADACHE	Post lumbar puncture syndrome	2019-11-20T09:00	Day 3	2019-11-27T13:10	7D4H10M	2	5	1	No		1	
035	4b	ESB1609 2700 mg	3	NECK MUSCLE PAIN	Neck pain	2019-11-19T13:15	Day 2	2019-11-26T10:20	6D21H5M	2	5	1	No		1	
035	4b	ESB1609 2700 mg	4	DECREASED APPETITE	Decreased appetite	2019-11-20T09:00	Day 3	2019-11-25T20:00	5D11H	1	5	2	No		1	
035	4b	ESB1609 2700 mg	5	NAUSEA	Nausea	2019-11-20T11:30	Day 3	2019-11-20T15:00	3H30M	1	5	2	No		1	

Note:

[MON: Month; D: Day; H: Hour; M: Minute; For subjects not listed, no adverse Event was recorded]

¹ Medical Dictionary for Regulatory Activities (MedDRA)² Study Day: AE onset date - Date of prior administration + 1.³ 1=Mild (Grade 1), 2=Moderate (Grade 2), 3=Severe (Grade 3), 4=Life-threatening (Grade 4), 5=Death (Grade 5)⁴ 1=Dose Not changed, 2=Dose Reduced, 3=Drug Permanently Withdrawn, 4=Drug Temporarily Withdrawn, 5=Not Applicable⁵ Relationship to Study Drug: 1=Not Related, 2=Unlikely, 3=Possible, 4=Probable, 5=Definite⁶ 1=Death, 2=Life threatening, 3=In-patient hospitalization or prolongation of existing hospitalization, 4=Persistent or significant disability/incapacity, 5=A congenital anomaly/birth defect⁷ 1=Recovered/Resolved, 2=Recovered/Resolved with Sequelae, 3=Not Recovered/Not Resolved, 4=Fatal, 5=Recovering/Resolving, 6=Unknown

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035	4b	ESB1609 2700 mg	6	SHOULDER PAIN	Musculoskeletal pain	2019-11-21T09:00	Day 4	2019-11-24T09:40	3D40M	1	5	1	No	No	1	
036	4b	-	1	VASOVAGAL REACTION	Presyncope	2019-12-11T08:45	Prior	2019-12-11T08:47	2M	2	1	1	No	No	1	
036	4b	ESB1609 2700 mg	2	ABDOMINAL PAIN	Abdominal pain	2019-12-12T01:00	Day 2	2019-12-12T09:45	8H45M	1	1	3	No	No	1	

Note:

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