**APPENDIX 1**

**List of adverse events related to sexual dysfunction based on MedDRA v14.1 preferred term**

Anorgasmia

Disturbance in sexual arousal

Dyspareunia

Ejaculation delayed

Ejaculation disorder

Ejaculation failure

Erectile dysfunction

Female orgasmic disorder

Female sexual arousal disorder

Female sexual dysfunction

Inadequate lubrication

Libido decreased

Libido disorder

Loss of libido

Male orgasmic disorder

Male sexual dysfunction

Organic erectile dysfunction

Orgasm abnormal

Orgasmic sensation decreased

Premature ejaculation

Psychogenic erectile dysfunction

Sexual aversion disorder

Sexual dysfunction

Sexual inhibition

Vaginismus

Vulvovaginal dryness

**APPENDIX 2**

**Short-term (6–8 weeks in duration) clinical trials of vortioxetine in patients with major depressive disorder or generalized anxiety disorder**

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| --- | --- | --- | --- | --- |
| **Completed Phase 2 and 3 Major Depressive Disorder Studies** | | | | |
| **Study No./**  **Region** | **Study Design/**  **Duration** | **Diagnosis and Main Inclusion Criteria** | **Study Drug Doses (mg)** (a) | **No. of Subjects Treated** |
| NCT00839423  Europe, Australia, Canada, Asia | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (venlafaxine), fixed-dose /  6 weeks + 2 weeks taper-down/ discontinuation period | MDD, 18–65 years, MADRS ≥30, men and women | Vortioxetine:  5 or 10  Venlafaxine: 225  placebo | Vortioxetine 5 mg: 108  Vortioxetine 10 mg: 100  Venlafaxine 225 mg: 113  Placebo: 105 |
| NCT00635219  Europe, Canada, Asia, Australia, | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (duloxetine), fixed-dose /  8 weeks + 1 week taper-down (only duloxetine) | MDD, 18–75 years, MADRS ≥26, men and women | Vortioxetine: 2.5, 5 or 10  Duloxetine: 60  Placebo | Vortioxetine 2.5 mg: 155  Vortioxetine 5 mg: 157  Vortioxetine 10 mg: 151  Duloxetine 60 mg: 155  Placebo: 148 |
| NCT00735709  Europe, Asia, Australia, South Africa | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | MDD, 18–75 years, MADRS ≥26, men and women | Vortioxetine:  1, 5, or 10  Placebo | Vortioxetine 1 mg: 140  Vortioxetine 5 mg: 140  Vortioxetine 10 mg: 139  Placebo: 140 |
| NCT01140906  Europe, South Africa | Randomized, double-blind, placebo-controlled, active-referenced (duloxetine), parallel-group, fixed-dose /  8 weeks + 2 weeks discontinuation period | MDD, 18–75 years, MADRS ≥26 and  CGI-S ≥4, men and women | Vortioxetine:  15 or 20  Duloxetine: 60  Placebo | Vortioxetine 15 mg: 152  Vortioxetine 20 mg: 151  Duloxetine 60 mg: 147  Placebo: 157 |
| NCT01153009  United States | Randomized, double-blind, placebo-controlled, active-referenced (duloxetine), parallel-group, fixed-dose /  8 weeks + 2 weeks discontinuation period | MDD, 18–75 years, MADRS ≥26 and  CGI-S ≥4, men and women | Vortioxetine:  15 or 20  Duloxetine: 60  Placebo | Vortioxetine 15 mg: 147  Vortioxetine 20 mg: 154  Duloxetine 60 mg : 152  Placebo: 161 |
| NCT01163266  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks +  2 weeks discontinuation period | MDD, 18–75 years, MADRS ≥26 and  CGI-S ≥4, men and women | Vortioxetine:  10 or 20  Placebo | Vortioxetine 10 mg: 154  Vortioxetine 20 mg: 148  Placebo: 155 |
| NCT01179516  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | MDD, 18–75 years, MADRS ≥26 and  CGI-S ≥4, men and women | Vortioxetine:  10 or 15  Placebo | Vortioxetine 10 mg: 143  Vortioxetine 15 mg: 142  Placebo: 149 |
| NCT00672958  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 6 weeks + 2 weeks discontinuation period | MDD, 18–75 years, MADRS ≥30, men and women | Vortioxetine: 5  Placebo | Vortioxetine 5 mg: 299  Placebo: 298 |
| NCT00672620  United States | Randomized, double-blind, placebo-controlled, parallel-group, active-referenced (duloxetine), fixed-dose /  8 weeks + 1 week taper-down (only duloxetine) | MDD, 18–75 years, MADRS ≥22, men and women | Vortioxetine:  2.5 or 5  Duloxetine: 60  Placebo | Vortioxetine 2.5 mg: 153  Vortioxetine 5 mg: 153  Duloxetine 60 mg: 152  Placebo: 153 |
| NCT00811252  Europe, Canada, United States | Randomized, double-blind, parallel-group, placebo-controlled, active-referenced (duloxetine), fixed dose, in elderly subjects / 8 weeks +  1 week taper-down (only duloxetine) | MDD, ≥65 years, MADRS ≥26, men and women | Vortioxetine: 5  Duloxetine: 60  Placebo | Vortioxetine 5 mg: 156  Duloxetine 60 mg: 151 |
| **Completed Phase 3 Generalized Anxiety Disorder Studies** | | | | |
| NCT00730691  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose, active-reference (duloxetine) /  8 weeks + 2 weeks taper-down discontinuation period | GAD, 18–65 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine:  2.5, 5, or 10  Duloxetine: 60  Placebo | Vortioxetine 2.5 mg: 156  Vortioxetine 5 mg: 155  Vortioxetine 10 mg: 156  Duloxetine 60 mg: 154  Placebo: 155 |
| NCT00731120  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine:  2.5 or 10  Placebo | Vortioxetine 2.5 mg: 151  Vortioxetine 10 mg: 152  Placebo: 153 |
| NCT00734071  United States | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 5  Placebo | Vortioxetine 5 mg: 148  Placebo: 151 |
| NCT00744627  Europe | Randomized, double-blind, placebo-controlled, parallel-group, fixed-dose / 8 weeks | GAD, ≥18 years, HAM-A ≥20, HAM-A ≥2 on item 1 (anxious mood) and item 2 (tension), men and women | Vortioxetine: 5  Placebo | Vortioxetine 5 mg: 150  Placebo: 150 |
| CGI-S=Clinical Global Impression-Severity of Illness, GAD=generalized anxiety disorder, HAM-A=Hamilton Anxiety Scale, MADRS=Montgomery-Åsberg Depression Rating Scale, MDD=major depressive disorder.  (a) Route of administration was oral. | | | | |