## Supplementary appendix

Table S1. Dose-titration schedule for antidepressant therapies (ADTs)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Day** | **Duloxetine** | **Escitalopram** | **Fluoxetine** | **Paroxetine IR** | **Sertraline** | **Venlafaxine XR** |
| Day 1 to 7 | 60mg | 10mg | 20 mg | 20mg | 50mg | 75mg |
| Day 8 to 14 | 60 mg | 20 mg | 40 mg | 40 mg | 100 mg | 75 or 150 mg |
| Day 15 to 21 | 60 mg | 10 or 20 mg | 20 or 40 mg | 20, 30, or | 100 or 150 mg | 75, 150, or |
|  |  |  |  | 40 mg |  | 225 mg |
| Day 22 to 28 | 60 mg | 10 or 20 mg | 20 or 40 mg | 20, 30, or | 100, 150, or | 75, 150, or |
|  |  |  |  | 40 mg | 200 mg | 225 mg |
| Day 29 onwardsa | 60 mg | 10 or 20 mg | 20 or 40 mg | 20, 30, or40 mg | 100, 150, or200 mg | 75, 150, or225 mg |

a Fixed dose; during the first 4 weeks, the dose could be decreased to the minimum dose indicated in case of tolerability issues.

Table S2. Dose-titration schedule for study medication

|  |  |  |
| --- | --- | --- |
| **Treatment****Group** | **Day 1 to Week 8****Prospective treatment period****Period A** | **Week 1 Week 2 Week 3 to 7 Week 7 to 24****Randomized treatment period** |
| Brexpiprazole | placebo | 1 mg 2 mg 1, 2, or 3 mg 1, 2, or 3 mg(flexible dose) (fixed dose) |
| Placebo | placebo | placebo placebo placebo placebo |

The investigator could indicate a need for dose adjustments (increase or decrease) for brexpiprazole/placebo at scheduled or unscheduled visits between Week 2 in the prospective treatment period and Week 7 in the randomized treatment period to keep the masking. Requested dose adjustments were only implemented via the IVRS/IWRS in the brexpiprazole group after the patient had reached the 2mg/day dose.