**Supplemental Digital Content 5, Supplementary Table 5:** Frequency of abuse-related treatment emergent adverse events (category euphoria-related adverse events) by Preferred Term - Safety Set

|  | **Cebranopadol N (%)** | | | | **Comparator N (%)** | | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **200 µg** | **400 µg** | **800 µg** | **Overall** | **Hydromorphone IR** | | | **Placebo** |
| **8 mg** | **16 mg** | **Overall** | **Overall** |
| Total number of subjects | 45 (100.0) | 46 (100.0) | 46 (100.0) | 47 (100.0) | 44 (100.0) | 45 (100.0) | 46 (100.0) | 46 (100.0) |
| Any event | 3 (6.7) | 8 (17.4) | 22 (47.8) | 26 (55.3) | 20 (45.5) | 32 (71.1) | 36 (78.3) | 5 (10.9) |
| Euphoric mood | 1 (2.2) | 5 (10.9) | 17 (37.0) | 21 (44.7) | 16 (36.4) | 28 (62.2) | 33 (71.7) | 4 (8.7) |
| Elevated mood | 0 (0.0) | 0 (0.0) | 1 (2.2) | 1 (2.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Feeling abnormal | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.2) | 1 (2.2) | 0 (0.0) |
| Dizziness | 1 (2.2) | 4 (8.7) | 5 (10.9) | 8 (17.0) | 4 (9.1) | 8 (17.8) | 11 (23.9) | 1 (2.2) |
| Feeling of relaxation | 1 (2.2) | 0 (0.0) | 0 (0.0) | 1 (2.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

Treatment emergent adverse events (TEAEs) were selected based on the *Adverse Event Working Group of the Cross Company Abuse Liability Council (CCALC).* Adverse events were coded with Medical Dictionary for Regulatory Activities version 17.0.  
IR = immediate release, N (%) = number (percentage) of subjects in dose group/comparator group; Placebo – Overall (fully randomized and fixed)