**Supplement 2**: CYP2D6 activity composed of the genotype-predicted phenotype and CYP2D6 saturation by substrate exposure.

|  |  |  |  |
| --- | --- | --- | --- |
| **Genotype-predicted CYP2D6 phenotype** | **No CYP2D6 saturation** | **Moderate CYP2D6 saturation** | **Strong CYP2D6 saturation** |
| **Poor metabolizer** | poor activity | poor activity | poor activity |
| **Intermediate metabolizer** | intermediate activity | poor activity | poor activity |
| **Normal metabolizer** | normal activity | intermediate activity | poor activity |
| **Ultra-rapid metabolizer** | ultra-rapid activity | normal activity | intermediate activity |

No CYP2D6 saturation: no CYP2D6 substrate was taken

Moderate CYP2D6 saturation: one or two CYP2D6 substrates were taken

Strong CYP2D6 saturation: three or more CYP2D6 substrates were taken.