

TABLE 1. Comparison of information on the FDA table of pharmacogenetic associations focusing on antidepressants and antipsychotics, compared with the DPWG and CPIC recommendations for antidepressant and antipsychotic drugs.

| CYP2C19        | FDA             | PharmGKB - drug label annotation                    | PharmGKB - Clinical annotation        | DPWG   | CPIC  |
|----------------|-----------------|---|---------------------------------------|--|---|
| Amitriptyline  | -               | -   | Efficacy                              | PK effects; no action  | PM, PM and LM; alternative drug; IM; no action ** |
| Citalopram     | Therapeutic     | Actionable (FDA/Can/Swiss)                          | Level 1A<br>Efficacy/toxicity         | PM 50%; IM 75%; LM PK effects; no action                       | PM 50%; PM, LM; consider alternative drug         |
| Clomipramine   | -               | Actionable (FDA)                                    | Level 2A<br>Efficacy                  | PM and IM; PK effects; no action; LM; alternative drug         | PM, PM, LM; alternative drug **                   |
| Doxepin        | Pharmacokinetic | Actionable (FDA)                                    | Level 3<br>Other                      | PK effects; no action  | PM, PM, LM; alternative drug **                   |
| Escitalopram   | Pharmacokinetic | Actionable (FDA/Japan/Swiss)                        | Level 1A<br>Efficacy/toxicity         | PM 50%; IM 75%; LM alternative drug                            | PM 50%; PM, LM; alternative drug                  |
| Imipramine     | -               | -   | Level 2A<br>Doseage/Other             | PM 70%; IM and LM; PK effects; no action                       | PM 50%; PM and LM; alternative drug **            |
| Moclobemide    | -               | Actionable (Swiss)                                  | -                                     | PK effects; no action  | -   |
| Sevraline      | -               | -   | Level 1A<br>Metabolism/PK             | PM max; 75 mg/day; IM and LM; PK effects; no action            | PM 50%  |
| Timipramine    | -               | Actionable (FDA)                                    | Level 2A<br>Metabolism/PK             | -  | PM 50%; PM, LM; alternative drug **               |
| <b>CYP2D6</b>  |                 |   |                                       |  |   |
| Amitriptyline  | Pharmacokinetic | Actionable (FDA)                                    | PharmGKB - Clinical annotation        | DPWG   | CPIC  |
| Atomoxetine    | Pharmacokinetic | Actionable (FDA/Japan/Can/Swiss)                    | Level 1A<br>Doseage/Efficacy          | PM 70%; IM 75%; LM 140%  | PM and LM; alternative drug; IM 75%               |
| Aripiprazole   | Therapeutic     | Actionable (FDA/EMA/Can/Swiss)                      | Level 1A<br>Efficacy/toxicity         | -  | -   |
| Bupropion      | Therapeutic     | Actionable (FDA/EMA/Swiss)                          | Level 3<br>Other                      | PM max; 10 mg/day; IM and LM; PK effects; no action            | -   |
| Citalopram     | -               | -   | Level 3<br>Efficacy/toxicity          | PM 50%; IM and LM; PK effects; no action                       | -   |
| Clomipramine   | Pharmacokinetic | Actionable (FDA/Swiss)                              | Level 1A<br>Doseage/Toxicity/Efficacy | No effect  | PM, LM; alternative drug; IM 75%; **              |
| Clozapine      | Therapeutic     | Actionable (FDA)                                    | -                                     | No effect  | -   |
| Desipramine    | Pharmacokinetic | Actionable (FDA)                                    | Level 1A<br>Doseage/Toxicity          | PM 40%; IM 80%; LM 200%  | PM, LM; alternative drug; IM 75%; **              |
| Doxepin        | Pharmacokinetic | Actionable (FDA/Swiss)                              | Level 1A<br>Doseage/Toxicity/Efficacy | PK effects; no action  | PM, LM; alternative drug; IM 75%; **              |
| Duloxetine     | -               | Actionable (FDA/EMA/Swiss)                          | -                                     | PK effects; no action  | -   |
| Escitalopram   | -               | Actionable (FDA/Japan)                              | Level 3<br>Doseage/Toxicity/Efficacy  | No effect  | -   |
| Flupenthixol   | -               | -   | Level 3<br>Doseage/Toxicity/Efficacy  | No effect  | -   |
| Fluoxetine     | Pharmacokinetic | Actionable (FDA/Swiss)                              | Level 1A<br>Efficacy/toxicity         | No effect  | PM 50-75%   |
| Haloperidol    | -               | -   | Level 1A<br>Efficacy/toxicity         | PM, IM and LM; PK effects; no action                           | PM, IM and LM; PK effects; no action              |
| Imipramine     | Pharmacokinetic | Actionable (FDA)                                    | Level 1A<br>Doseage/Toxicity          | PM 50%; IM PK effect; no action; LM; alternative drug          | PM 50%; IM 75%; LM; alternative drug **           |
| lloperidone    | Therapeutic     | Actionable (FDA)                                    | Level 3<br>Toxicity/ADR               | PM 30%; IM 70%; LM 170%  | PM 50%; IM 75%; LM; alternative drug **           |
| Mirtazapine    | -               | -   | Level 2A<br>Efficacy/toxicity         | PM, IM and LM; PK effects; no action                           | -   |
| Nortriptyline  | Pharmacokinetic | Actionable (FDA/Can)                                | Level 1A<br>Doseage/Toxicity/Efficacy | PM 40%; IM 80%; LM 170%  | PM 50%; IM 75%; LM; alternative drug              |
| Clanzapine     | -               | Actionable (FDA)                                    | Level 1A<br>Efficacy/toxicity         | No effect  | -   |
| Paroxetine     | Pharmacokinetic | Informative (FDA)                                   | Level 1A<br>Efficacy/toxicity         | PM and IM; PK effects; no action; LM alternative drug          | -   |
| Perphenazine   | Safety/Response | Actionable (FDA/Japan)                              | Level 4<br>Other                      | PM max; 10 mg/day; IM max; 16 mg/day; LM PK effects; no action | -   |
| Pimozide       | Therapeutic     | <b>Testing required (FDA)</b>                       | Level 4<br>Toxicity/ADR               | No effect  | -   |
| Quetiapine     | -               | -   | Level 4<br>Toxicity/ADR               | No effect  | -   |
| Protriptyline  | Pharmacokinetic | Actionable (FDA)                                    | Level 2A<br>Efficacy/toxicity/Other   | PM 50-57%; IM PK effects; no action; LM; alternative drug      | -   |
| Risperidone    | Pharmacokinetic | Informative (FDA/Can/Swiss)                         | Level 3<br>Doseage                    | -  | -   |
| Sevraline      | -               | -   | Level 3<br>Doseage                    | -  | -   |
| Teubenzamide   | Therapeutic     | <b>mg required (FDA/Swiss) / Actionable (Japan)</b> | Level 3<br>Other                      | -  | -   |
| Thioridazole   | Therapeutic     | Actionable (FDA)                                    | Level 3<br>Other                      | -  | -   |
| Timipramine    | Pharmacokinetic | Actionable (FDA)                                    | Level 1A<br>Doseage/Toxicity/Other    | -  | PM 50%; IM 75%; LM; alternative drug **           |
| Verapamil      | Therapeutic     | Actionable (FDA/Swiss)                              | Level 2A<br>Efficacy/toxicity         | PM and IM; PK effects; alternative drug; LM 150%               | -   |
| Zuclopenthixol | -               | Informative (Swiss)                                 | Level 3<br>Other                      | PM 50%; IM 75%; LM; alternative drug                           | -   |

*†† CYP2C9\*17 is added to a rapid metabolizer (RM) in US. For DPWG, CYP2C9\*17 is reported as a normal metabolizer (NM).*

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*\*\* CPIC also has combined advice based on both CYP2D6 and CYP2C19 genotype*

*Note: sometimes both an alternative dose as well as the option for an alternative drug is recommended. In that case, only the dose reduction is mentioned in this table*