**Supplemental Table 1. Dose adjustments for LAI antipsychotics when co-prescribed with potent or mild inducers1,2 (no dose adjustments are recommended if CYP450 modulators are added for <2 weeks)**

|  |  |
| --- | --- |
| **Second-generation LAI antipsychotic** | **Adjusted dose** |
| **Aripiprazole monohydrate (Abilify Maintena®)** | |
| Aripiprazole monohydrate |  |
| Known CYP2D6 poor metabolizers | 300 mg |
| Known CYP2D6 poor metabolizers taking concomitant CYP3A4 inhibitors | 200 mg**a** |
| Aripiprazole monohydrate 400 mg |  |
| Strong CYP2D6 or CYP3A4 inhibitors | 300 mg |
| CYP2D6 and CYP3A4 inhibitors | 200 mg**a** |
| CYP3A4 inducers | Avoid use |
| Aripiprazole monohydrate 300 mg |  |
| Strong CYP2D6 **or** CYP3A4 inhibitors | 200 mg**a** |
| CYP2D6 **and** CYP3A4 inhibitors | 160 mg**a** |
| CYP3A4 inducers | Avoid use |
| **Aripiprazole lauroxil (Aristada®)** | |
| Aripiprazole lauroxil 441 mg |  |
| Strong CYP2D6 **or** CYP3A4 inhibitors | No adjustment necessary, if tolerated |
| CYP2D6 **and** CYP3A4 inhibitors | No adjustment necessary, if tolerated |
| CYP3A4 inducers | 662 mg |
| Aripiprazole lauroxil 662 mg |  |
| Strong CYP2D6 **or** CYP3A4 inhibitors | 441 mg |
| CYP2D6 **and** CYP3A4 inhibitors | Avoid use |
| CYP3A4 inducers | No dose adjustment necessary |
| Aripiprazole lauroxil 882 mgb |  |
| Strong CYP2D6 **or** CYP3A4 inhibitors | 662 mg |
| CYP2D6 **and** CYP3A4 inhibitors | Avoid use |
| CYP3A4 inducers | No dose adjustment necessary |
| Aripiprazole lauroxil 1064 mg |  |
| Strong CYP2D6 **or** CYP3A4 inhibitors | 441 mg |
| CYP2D6 **and** CYP3A4 inhibitors | Avoid use |
| CYP3A4 inducers | No dose adjustment necessary |
| **Paliperidone palmitate (Invega Sustenna® and Invega Trinza®)** | |
| Paliperidone palmitate (all doses)c |  |
| Strong CYP3A4 inducers | Avoid use |
| **Olanzapine pamoate (Zyprexa Relprevv®)** | |
| Olanzapine pamoate (all doses) |  |
| CYP2D6 inhibitors | No dose adjustment necessary |

LAI=long-acting injectable.

**a**200-mg and 160-mg dose adjustments are obtained only by using the 300-mg- or 400-mg-strength vials.

**b**For the 882-mg dose administered every 6 weeks and the 1064-mg dose administered every 2 months, the next lower strength should be 441 mg administered monthly.

**c**If a strong inducer is necessary, consider managing the patient using paliperidone extended-release tablets.

**Supplemental Table 2. Overview of LAI drug interactions from other drugs that could impact optimal response or contribute to breakthrough symptoms1-13**

| **LAI antipsychotic** | **Drugs that could increase LAI AUC or Cp** | **Drugs that could decrease LAI AUC or Cp** | **Prescribing information/monograph URLa** | | **Date** | |
| --- | --- | --- | --- | --- | --- | --- |
| **First generation** | | | |  | |
| Flupenthixol decanoate | Tricyclic antidepressant drugs | N/A | <https://www.lundbeck.com/upload/ca/en/files/pdf/pm/Fluanxol.pdf> | | July 2016 | |
| Fluphenazine decanoate | CYP2D6 inhibitors, tricyclic antidepressant drugs, beta blockers | Clonidine, cimetidine | <http://www.bmscanada.ca/static/products/en/pm_pdf/MODECATE_en_PM.pdf>  <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b580471f-44a1-4da0-96ad-2f537eabec3e> | | August 2017  October 2017 | |
| Haloperidol decanoateb | Substrates or inhibitors of CYP2D6  *Inhibitors*: **fluvoxamine**, **quinidine**, **fluoxetine**, sertraline  *Substrates*: venlafaxine, chlorpromazine, promethazine  Substrates or inhibitors of CYP3A4  *Inhibitors*: **itraconazole, nefadozone**  *Substrates*: buspirone, alprazolam | CYP3A4 inducers, **rifampin**, **carbamazepine**, oxcarbazepine, topiramate, eslicarbazepine | <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/HALDOL+Decanoate-pi.pdf> | | February 2017 | |
| Zuclopenthixol decanoate | CYP2D6 inhibitors, tricyclic antidepressant drugs | N/A | [https://www.lundbeck.com/upload/ca/en/files/pdf/pm/Clopixol.pdf](https://www.lundbeck.com/upload/ca/en/files/pdf/pm/Clopixol.pdf\) | | July 2016 | |
| Second generation | | | |  | |
| Aripiprazole lauroxil (Aristada®)b | CYP2D6 inhibitors: **quinidine**, **fluoxetine**, **paroxetine**  CYP3A4 inhibitors: **ketoconazole**, **itraconazole**, **clarithromycin** | CYP3A4 inducers: **carbamazepine**, **rifampin,** oxcarbazepine, topiramate, eslicarbazepine | <https://www.aristadahcp.com/downloadables/ARISTADA-PI.pdf> | | Sept 2017 | |
| Aripiprazole monohydrate (Abilify Maintena®)b | CYP2D6 inhibitors: **quinidine**, **fluoxetine**, **paroxetine**  CYP3A4 inhibitors: **ketoconazole** | CYP3A4 inducers: **carbamazepine, rifampin**, oxcarbazepine, topiramate, eslicarbazepine | <https://www.otsuka-us.com/media/static/Abilify-M-PI.pdf?_ga=2.159922100.847483391.1508178291-26936955.1508178291> | | July 2017 | |
| Olanzapine pamoate (Zyprexa Relprevv®)b | CYP1A2 inhibitors: **fluvoxamine** | Inducers of CYP1A2 or glucuronyl transferase enzymes: **carbamazepine**, omeprazole, **rifampin**, oxcarbazepine, topiramate, eslicarbazepine | <http://pi.lilly.com/us/zyprexa_relprevv.pdf> | | January 2017 | |
| PP1M (Invega Sustenna®)b | CYP2D6 inhibitors: **paroxetine** | CYP3A4/P-gp inducers: **carbamazepine**, **rifampin**, St. John’s wort, oxcarbazepine, topiramate, eslicarbazepine | <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA+SUSTENNA-pi.pdf> | | June 2017 | |
| PP3M (Invega Trinza®)b | CYP2D6 inhibitors: **paroxetine** | CYP3A4/P-gp inducers: **carbamazepine**, **rifampin**, St. John’s wort, oxcarbazepine, topiramate, eslicarbazepine | <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA+TRINZA-pi.pdf> | | February 2017 | |
| Risperidone LAI (Risperidal Consta®)b | CYP1A2 substrate: clozapine  CYP2D6 inhibitors **fluoxetine**, **paroxetine**, **quinidine** | CYP3A4 inducers: **carbamazepine**, **phenytoin**, **rifampin**, **phenobarbital**, oxcarbazepine, eslicarbazepine | <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/RISPERDAL+CONSTA-pi.pdf> | | February 2017 | |

Agents presented in **bold** are strong inhibitors/inducers; those in plain text are moderate or mild inhibitors/inducers.

AUC=area under the concentration-time curve; Cp=concentration in plasma; LAI=long-acting injectable; N/A= not applicable; PP1M=paliperidone palmitate once monthly; PP3M=paliperidone palmitate once-every-3-months.

**a**Drug interaction information is subject to change. Please check the latest prescribing information or product monograph for the most up-to-date information.

bNo specific drug interaction studies were performed with the LAI formulation; drug interaction data are based on the corresponding oral formulation.

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