**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 2017October 2017 |
| Haloperidol decanoateb | Substrates or inhibitors of CYP2D6*Inhibitors*: **fluvoxamine**, **quinidine**, **fluoxetine**, sertraline*Substrates*: venlafaxine, chlorpromazine, promethazineSubstrates 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](http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/HALDOL%2BDecanoate-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%5C) | 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](http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA%2BSUSTENNA-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](http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA%2BTRINZA-pi.pdf) | February 2017 |
| Risperidone LAI (Risperidal Consta®)b | CYP1A2 substrate: clozapineCYP2D6 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](http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/RISPERDAL%2BCONSTA-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.

**REFERENCES**

1. Otsuka Pharmaceutical Co. Ltd. *ABILIFY MAINTENA® (aripiprazole) for extended-release injectable suspension, for intramuscular use.* Otsuka Pharmaceutical Co. Ltd., Tokyo, Japan 03/2018.

2. Alkermes Inc. *ARISTADA® (aripiprazole lauroxil) extended-release injectable suspension, for intramuscular use.* Alkermes Inc., Waltham, MA, USA 01/2018.

3. Eli Lilly and Co. *ZYPREXA RELPREVV® (olanzapine) for extended release injectable suspension.* Eli Lilly and Co., Indianapolis, IN, USA 01/2018.

4. Janssen Pharmaceuticals Inc. *HALDOL® Decanoate 50 (haloperidol), HALDOL® Decanoate 100 (haloperidol) for IM injection only.* Janssen Pharmaceuticals Inc., Titusville, NJ, USA 12/2017.

5. Janssen Pharmaceuticals Inc. *INVEGA SUSTENNA® (paliperidone palmitate) extended-release injectable suspension, for intramuscular use.* Janssen Pharmaceuticals Inc., Titusville, NJ, USA 12/2017.

6. Bristol-Myers Squibb. *PrMODECATE® CONCENTRATE Fluphenazine Decanoate Injection, B.P. 100 mg/ml.* Bristol-Myers Squibb Canada, Montreal, Canada 08/2017.

7. Par Pharmaceuticals Inc. *FLUPHENAZINE DECANOATE - fluphenazine decanoate injection, solution.* Par Pharmaceuticals Inc., Chestnut Ridge, NY, USA 10/2017.

8. Janssen Pharmaceuticals Inc. *INVEGA TRINZA® (paliperidone palmitate) extended-release injectable suspension, for intramuscular use.* Janssen Pharmaceuticals Inc., Titusville, NJ, USA 02/2017.

9. Janssen Pharmaceuticals Inc. *RISPERDAL CONSTA® (risperidone) long-acting injection.* Janssen Pharmaceuticals Inc.,Titusville, NJ, USA 06/2012.

10. Lundbeck Canada Inc. *FLUANXOL® Flupentixol Tablets (as flupentixol dihydrochloride) 0.5 mg, 3 mg, and 5 mg; FLUANXOL® DEPOT (Flupentixol decanoate) intramuscular injection 2% and 10% flupentixol decanoate.* Lundbeck Canada Inc., St. Laurent, Quebec, Canada 08/2016.

11. Lundbeck Canada Inc. *CLOPIXOL® (Zuclopenthixol) Tablets (10 and 25 mg), intramuscular injection (50 mg/mL), depot intramuscular injection (200 mg/mL).* Lundbeck Canada Inc., St. Laurent, Quebec, Canada 08/2016.

12. McGrane IR, Loveland JG, de Leon J. Possible oxcarbazepine inductive effects on aripiprazole metabolism: a case report. *J Pharm Pract.* 2017:897190017710523. [Epub ahead of print].

13. de Leon J. The effects of antiepileptic inducers in neuropsychopharmacology, a neglected issue. Part I: A summary of the current state for clinicians. *Revista de Psiquiatria y Salud Mental.* 2015;8(2):97-115.