

DRUG SHORTAGES

Depot Antipsychotic Shortages – 2016 Update

Considerations when switching depot antipsychotics:

1. To select an alternative agent consider:
 - a. Availability (see Table 1 and check local wholesaler)
 - b. Dosing frequency
 - i. Frequency of the previous antipsychotic may have been determined for a variety of reasons including convenience and/or necessity. (For instance, some patients will be on an every 4 week regimen because of a Community Treatment Order.) Try to determine how important the dosing frequency is *now* for the patient.
 - c. Previous medication and psychiatric history including success / challenges of previous (and present) trials of antipsychotics – both oral and injectable
 - i. If previous trials were not tolerated due to side effects, if possible, choose an injectable that does not carry a high frequency of such side effect. (see Table 3).
 - ii. This provides an opportunity to assess the need for an injectable antipsychotic. Give consideration to the possibility of switching to an oral. (Especially if, for example, the patient was placed on fluphenazine years ago and there was never a need to change therapy; an oral second antipsychotic may be appropriate.)
 - d. Concomitant medications and comorbidities
 - e. Patient's present psychiatric state
 - f. Allergies (for instance to the vehicle – see Table 2)
 - g. Cost (See Table 1)

2. There are no guidelines as to how to switch depot antipsychotics.
 - a. If possible, have the patient re-assessed by a psychiatrist.
 - b. An estimated target dose can be determined using the Approximate Equivalent Dose from Table 3. However, it is prudent to start with a lower dose (than the estimated target dose) of the new injectable and titrate up. By using a lower than equivalent dose, chances of additive adverse effects are reduced. However, this strategy will likely leave some patients with a gap in antipsychotic requirements; oral antipsychotics can be used during the titration phase to supplement any such gap.
 - c. In most cases, start the new injectable on the same day as the next scheduled dose of the unavailable injectable.
 - d. Use the target dose as a guide, but titrate up to the final dose based on clinical response.
 - e. Monitor adverse effects and therapeutic effect on a weekly basis until stable; then resume the dosage frequency of the new antipsychotic and adjust as required.

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Table 1: Depot Injectable Antipsychotics: Availability and Coverage in Canada **Check your wholesaler as availability is variable**				
DPD ¹	Listed at McKesson ²	SDPEBB ³	NIHB ⁴	Relative Price*/Month ^{3,5}
FIRST GENERATION ANTIPSYCHOTICS				
Flupentixol				
Fluanxol	√	√	√	\$
Sandoz	X	X	X	
Fluphenazine				
Modecate	√-no stock	√	√	\$
Omega	X	√	X	\$
PMS	X	X	√	\$
Haloperidol LA				
Omega	X	√	√	\$
PMS	X	X	√	\$
Sandoz	√	√	√	\$
Zuclopenthixol				
Clopixol	√	√	√	\$
SECOND GENERATION ANTIPSYCHOTICS				
Paliperidone				
Invega Sustenna	√	√ EDS	√	\$\$\$\$\$\$
Risperidone				
Risperdal	√	√ EDS	√	\$\$\$\$\$
Aripiprazole				
Abilify Maintena	√	√ EDS	X	\$\$\$\$\$\$\$\$\$
DPD = Drug Product Database; SDPEBB=Saskatchewan Drug Plan and Extended Benefits Branch; NIHB= Included on Non-Insured Health Benefits Formulary *Each \$ represents \$50 range: example \$= <\$50; \$\$ = \$51-100; cost per month				

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Table 2: Select Dose, Kinetic and Formulation Parameters of Depot Antipsychotics^{5-7,9}

	Approx. Equiv. Dose	Usual Starting Dose (mg)	Usual Dose Range (mg)	Max Dose (mg)	Usual Frequency of Dose (weeks)	Time to Maximum Concentration	Half-Life	Vehicle
Flupentixol	24 mg q4 week	20-40 [^]	20-40	80; some have been given more	2-3	4-7 days	8 days (SD) 17 days (MD)	Sesame oil
Fluphenazine	15 mg q4 week	12.5 - 25	12.5-50	50; up to 100 been used	2-4*	1 st : 8-10 h 2 nd : 8-12 days	7-10 days	Sesame oil
Haloperidol	40 mg q4 week	25 [†]	50-200	450	2-4	3-9 days	18-21 days	Sesame oil
Zuclopenthixol	120mg q4week	50-100	100-300	400	2-4	3- 7 days	19 days	Coconut oil
Paliperidone	20 mg q4 week? [†]	25-50 [‡]	25-150	150	4	13 days	25-49 days	Sesame oil
Risperidone	5 mg q2 week	12.5-25	25-50	50	2	4-6 weeks after 1 st dose	7-8 weeks	Micro-spheres in diluent
Aripiprazole	Not Established	400	300-400	400	4	5-7 days	30-46 days	Low solubility particles in aqueous susp

[^]Assuming patient is being switched from long acting IM antipsychotic. If patient is long acting IM antipsychotic naïve, start with 5-20mg

*Duration of action is generally 2-3 weeks but lasts up to 4 weeks in some patients; monitor

[‡]Can also start with 10-15x the previous oral dose to a max of 100 mg

[‡]The loading dose of 150 mg day 1, then 100 mg day 8 mentioned in the monograph is not appropriate when switching from another antipsychotic

[†]Indirectly estimated⁸

Approx. = approximate; Equiv. = equivalent; q4=every 4; q2 = every 2; SD= single dose; MD= multiple dose

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Table 3: Frequency (%) of Select Adverse Reactions^{6,7,9}

	Flupen	Fluphen	Haloper	Zuclo	Paliper	Risper	Aripip
Drowsiness/ Sedation	>2	>2	>2	>30	>2	>10	>10
Insomnia/ Agitation	<2	>2	>10	>10	>10	>10	>10
Parkinsonism	>30	>30	>30	>30	>2	>10	>2
Akathisia	>30	>30	>30	>10	>2	>10	>10
Dystonic reactions	>10	>10	>30	>10	<2	>2	>2
Anticholinergic Effects	>10	>2	>2	>10	>2	>10	<2
Orthostatic Hypotension	>2	>2	>2	>2	>2	>10	<2
Tachycardia	>2	>10	<2	>2	>2	>10	<2
ECG Abnormalities	<2	<2	<2	<2	<2	>2	<2
QTc prolongation (>450 millisecond)	<2	>2	>2	<2	>2	<2	<2
Weight gain	>10	>30	>10	>10	>10	>30	>10
Hyperglycemia	>10	>10	>10	>2	?	>10	>10
Hyperlipidemia	?	?	>2	>30	?	>10	>10

Flupen = Flupentixol ; Fluphen = Fluphenazine; Haloper= Haloperidol; Zuclo = Zuclopenthixol
Paliper = Paliperidone; Risper=Risperidone; Aripip - Aripiprazole

Adapted from Virani AS, Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Clinical handbook of psychotropic drugs. 20th ed. Toronto: Hogrefe & Huber Publishers; 2014.

Written by Carmen Bell, Drug Information Consultant | 30 Mar 2012 | Thank you to Drs. Alfred J. Remillard and Melanie McLeod for reviewing and suggestions. Updated by Dorothy Sanderson, Drug Information Consultant | 27 Jun 2016

References: 1. Health Canada. Drug Product Database Online Query. Ottawa, ON: Health Canada; [updated 2015 Jun 18; cited 2016 Jun 10]. Available from: <http://webprod.hc-sc.gc.ca/dpd-bdpp/dispatch-repartition.do?lang=eng> 2. McKesson Canada; c2016 [cited 2016 Jun 10] PharmaClik; Available from <http://clients.mckesson.ca>. Account required. 3. Saskatchewan Formulary. Drug Plan and Extended Benefits Branch [homepage on the Internet]. Government of Saskatchewan; [updated 2016 May 1; cited 2016 Jun 10]. Available from: <http://formulary.drugplan.health.gov.sk.ca/> 4. Non-Insured Health Benefits - Drug Benefit List 2015. Government of Canada; Date modified: 2016-04-11; cited 2016 Jun 10. Available from: <http://www.healthycanadians.gc.ca/publications/health-system-systeme-sante/nihb-drug-list-liste-medicaments-sna/index-eng.php> 5. Jensen B. Antipsychotic comparison chart. RxFiles drug comparison charts. 10th ed. Saskatoon, SK: Saskatoon Health Region; May 2016 Available from: www.RxFiles.ca. Accessed 2016 Jun 10. Subscription required. 6. Clinical handbook of psychotropic drugs. Eds: Virani AS, Bezchlibnyk-Butler KZ, Jeffries JJ. 20th ed. Toronto: Hogrefe & Huber Publishers; 2014. 7. RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2015 [cited 2016 Jun 14]. Available from: <http://www.e-therapeutics.ca>. Subscription required. 8. Invega Sustenna (paliperidone prolonged-release injection). Pharmacist's Letter/Prescriber's Letter 2010;26(10):261020. 9. Micromedex® 2.0. (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/> (cited: 14 Jun 2016). Subscription required

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