Depot Antipsychotic Shortages – 2019 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, necessity, efficacy, and tolerance. (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 adverse effects, if possible, choose an injectable that does not carry a high frequency of such adverse effect (see Table 3).
    d. Concomitant medications and comorbidities
        i. Review drug interactions
        ii. Renal function, hepatic function
    e. Patient's present psychiatric state
    f. Allergies (for instance to the depot vehicle – see Table 2)
    g. Cost/coverage (See Table 1)

2. *To switch:*
    a. If possible, have the patient re-assessed by a psychiatrist.
    b. switchrx.ca is an excellent Canadian-based tool to aid the switching process. Be aware this website does not include first generation antipsychotics in its selection of "switch to" agents.
    c. If switching to another first generation antipsychotic, determine an **estimated** target dose using the Approximate Equivalent Dose from Table 2 and take into account necessary dosage adjustments for organ impairment, frailty, drug interactions, etc. Keep in mind these doses are only estimates that have been calculated by a variety of methods and are intended as guidance only. It is prudent to start with a lower dose (than the estimated target dose) of the new injectable and titrate up at subsequent injections, as required. Using a lower dose reduces the risk of additive adverse effects and allows for assessment of response to the new medication. However, this strategy may leave some patients with a gap in antipsychotic requirements and oral antipsychotics could be used during the titration phase to supplement any such gap. If concerned about tolerability of the new antipsychotic depot, patients can be given a trial of the oral formulation of the new antipsychotic to assess tolerability before giving the depot.
    d. In most cases, start the new injectable on the same day as the next scheduled dose of the former injectable.
    c. Use the target dose as a guide, but titrate up to the final dose based on clinical response.
    d. Monitor adverse effects and therapeutic effect on a weekly basis until stable. Follow the usual dosing and dosing frequency of the new antipsychotic depot and assess each dose change at steady state (after 5 half-lives). Adjust dose/dosing frequency based on tolerability/efficacy.

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Table 1: Available Depot Injectable Antipsychotics: Coverage and Costs in Saskatchewan **Check your wholesaler as availability is variable**			
Generic Name/ Trade Name	**SDP[1]**	**NIHB[2]**	**Approximate Cost in SK per Month ($)[¥ 3]**
First Generation			
Flupentixol			
Fluanxol Depot 2%	√	√	22-90
Fluanxol Depot 10%	√	√	60-110
Fluphenazine			
Modecate 100 mg/ml	Discontinued		
Haloperidol LA			
Sandoz 100 mg/ml	√	√	125-240
Omega 100 mg/ml*	√	√	-
Pipotiazine			
Piportil L4	Discontinued		
Zuclopenthixol			
Clopixol Depot 200 mg/ml	√	√	30-90
Second Generation			
Paliperidone			
Invega Sustenna 100 mg/ml	√ EDS	√ LUB	400-750
Invega Trinza 200 mg/ml	√ EDS	√ LUB	360-685
Risperidone			
Risperdal Consta	√ EDS	√ LUB	225-830
Third Generation			
Aripiprazole			
Abilify Maintena 300 mg	√ EDS	√ LUB	570
Abilify Maintena 400 mg	√ EDS	√ LUB	570

EDS= Exceptional Drug Status; LUB= Limited Use Benefit; NIHB = Non-Insured Health Benefits; SDP = Saskatchewan Drug Plan; SK = Saskatchewan

[¥] Includes wholesaler & pharmacy markups and professional fee

*Currently not listed at McKesson

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Table 2: Select Dose, Kinetic and Formulation Parameters of Depot Antipsychotics[4,5]								
Generic Name/ Trade Name	**Approx Equiv Clinical Dose[Δ]**	**Usual Start Dose (mg)**	**Usual Dose Range (mg)**	**Max Dose (mg)**	**Usual Dose Frequency (weeks)**	**Time to Peak Plasma Level**	**Half-Life (days)**	**Vehicle**
First Generation								
Flupentixol Fluanxol®	40 mg q2w	20-40^	20-80	80	2-3	4-7d	SD: 8 MD: 17	Vegetable Oil
Fluphenazine Modecate®	25 mg q2w	2.5-12.5	12.5-50	50	2-4*	8-12d	7-10	Sesame oil
Haloperidol	150 mg q4w	25-50[‡]	50-200	450	2-4	3-9d	18-21	Sesame Oil
Zuclopenthixol Clopixol® Depot	200 mg q2w	50-100	150-300	400	2-4	3-7d	19	Coconut Oil
Second Generation								
Paliperidone Invega Sustenna®	100mg q4w[¥]	50[¥¥]	75 (50-150)	150	4	13d	25-49	Aqueous Suspension
Paliperidone Invega Trinza®	350 mg q12w[†]	††	175-525	525	12	SD: 24-34d	Delt: 52-74 Glut: 69-82	Aqueous Suspension
Risperidone Risperdal Consta®	50 mg q2w	12.5-25	25-50	50	2	30d	3-6[€]	Aqueous Suspension
Third Generation								
Aripiprazole Abilify Maintena®	Not Established	400	300-400	400	4	5-7d	30-47	Aqueous Suspension

[Δ] Approximate dose equivalent to oral olanzapine 20 mg once daily with respect to clinical efficacy.[5]
^Assuming patient is being switched from long acting IM antipsychotic. If patient is long acting IM antipsychotic naïve, start with 5-20 mg
* Duration of action is generally 2-3 weeks but lasts up to 4 weeks in some patients.
[‡] Can also start with 10-15x the previous oral dose to a max of 100 mg
[¥] Indirectly estimated based on conversion from Risperdal Consta[6]
[¥¥] The loading dose of 150 mg day 1, then 100 mg day 8 mentioned in the monograph is not required when switching from another antipsychotic depot
[†] Indirectly estimated based on conversion rate of 3.5x Invega Sustenna dose
†† Start only after stable on Invega Sustenna for at least 4 months. Start Trinza at a dose 3.5x that of stable Sustenna dose.
[€] At 3-6 days, the microspheres have eroded with subsequent risperidone absorption. Complete elimination in approx. 7-8 weeks.
approx = approximate; d=days; delt= following deltoid administration; equiv = equivalent; glut= following gluteal administration; MD= multiple dose; q=every; SD= single dose; w=weeks

Table 3: Frequency(%) of Select Adverse Reactions							
Reaction	**Flupentixol**	**Fluphenazine**	**Haloperidol**	**Zuclopenthixol**	**Paliperidone**	**Risperidone**	**Aripiprazole**
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	>2	<2
Orthostatic Hypotension	>2	>2	>2	>2	>2	>10	>2
Tachycardia	>2	>10	<2	>2	>2	<2	>2
QTc prolongation (>450 ms)	<2	>2	>2	<2	>2	<2	-
Weight gain	>10	>30	>10	>10	>10	>10	>2
Hyperglycemia	>10	>10	>10	>2	?	>10	<2
Hyperlipidemia	?	?	>2	?	?	>10	<2

^Lower incidence as depot formulation

ms=millisecond; QTc = QT interval corrected for heartrate

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