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Illinois Department of Healthcare and Family Services (HFS)
University of Illinois at Chicago – College of Pharmacy

Prior Authorization Criteria

Long-Acting Injectable (LAI) Atypical Antipsychotics

Program Rationale

This program is designed to promote appropriate utilization of LAI Atypical Antipsychotics in patients with repeated nonadherence to oral pharmacological treatment. Guidelines published by the American Psychiatric Association state that most patients with schizophrenia are at a very high risk for relapse in the absence of treatment.[1] Patients with recurrent relapses related to partial or full nonadherence to oral treatment are candidates for LAI Atypical Antipsychotic medications.

See LAI Atypical Antipsychotics Dosing Guide for information on individual agents.

Approval Criteria

Initial Requests

A preferred LAI Atypical Antipsychotic may be approved when ALL the following criteria are met:

1. Patient is ≥ 18 years old.
2. Diagnosis is schizophrenia, schizoaffective disorder, or bipolar 1 in accordance with the medication's specific FDA labeling.
3. Prescriber is a board-certified psychiatrist.
4. Patient has documented:
    a. history of nonadherence to oral antipsychotics OR
    b. stabilization on a LAI Atypical Antipsychotic while in a mental health facility
5. Patient has documented oral tolerability of the active ingredient in accordance with the medication's specific FDA labeling.
    c. Request for Invega Trinza requires documented trial of Invega Sustenna of at least 4 months.
6. The treatment regimen prescribed is not outside the medication's FDA labeling, and no contraindications or significant drug interactions to treatment exist as specified in accordance with the medication's specific FDA labeling.
7. If the request is for a non-preferred LAI Atypical Antipsychotic, there must be documented clinically significant treatment failure, intolerance, or contraindication to preferred LAI Atypical Antipsychotic agents.
8. Evidence of outpatient follow up appointment or if not available the prescriber agrees to coordinate follow up appointment and administration of the next dose of LAI Atypical Antipsychotic in accordance with the medication's specific FDA labeling.
9. Request for medically necessary exceptions to these criteria will be handled on a case-by-case basis.

Initial requests will be approved for 3 months.

References

1. American Psychiatric Association. Practice guidelines for the treatment of patients with schizophrenia – Third Edition. September 2020. Available at: https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890424841. Accessed October 22, 2021.
2. Abilify Maintena. Package insert. Otsuka Pharmaceutical Co., Ltd.; 2020.
3. Aristada. Package insert. Alkermes, Inc.; 2020.
4. Aristada Initio. Package insert. Alkermes, Inc.; 2020.
5. Invega Sustenna. Package insert. Janssen Pharmaceuticals, Inc.; 2021.
6. Invega Trinza. Package insert. Janssen Pharmaceuticals, Inc.; 2021.
7. Invega Hafyera. Package insert. Janssen Pharmaceuticals, Inc.; 2021.
8. Risperdal Consta. Package insert. Janssen Pharmaceuticals, Inc.; 2021.
9. Perseris. Package insert. Indivior, Inc.; 2019.
10. Zyprexa Relprevv. Package insert. Eli Lilly; 2019.

Long-Acting Injectable (LAI) Atypical Antipsychotics Dosing Guide – 10.21.21

<table>
<tr><th>Medication and Dosage Form</th><th>FDA Indication / Minimum Patient age</th><th>Initial Dose</th><th>Maintenance Dose</th><th>Clinical Pearls</th></tr>
<tr><td colspan="5">Preferred (with prior approval) Agents</td></tr>
<tr>
<td>Abilify Maintena
(aripiprazole monohydrate)

ER powder for suspension in
single-dose vial or
pre-filled single-dose dual chamber syringes

300 mg
400 mg

IM injection: deltoid or gluteal</td>
<td>Schizophrenia in adults (≥ 18 years)

Maintenance monotherapy for bipolar I in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td>
<td>400 mg IM

Dose adjustments required for CYP2D6 poor metabolizers and those taking CYP3A4 inhibitors/inducers or CYP2D6 inhibitors</td>
<td>400 mg IM once monthly

Can be reduced to 300 mg IM for tolerability

Give no sooner than 26 days after previous injection.</td>
<td>• Establish tolerability with aripiprazole tablets before initiating ER IM injection. It may take up to 2 weeks to fully assess tolerability.
• Oral aripiprazole (10 – 20 mg) or current antipsychotic medication should be given concurrently with the initial injection and should be continued for 14 consecutive days.
• Do not confuse with short-acting aripiprazole injection (9.75mg/vial)
• Missed Doses of Abilify Maintena
  • Give the next dose of Abilify Maintena as soon as possible if:
  • >4 and <5 weeks since dose 2 or 3
  • >4 and <6 weeks since dose ≥4
  • Restart Abilify Maintena AND bridge with 14 days of aripiprazole tablets if:
  • >5 weeks since dose 2 or 3
  • >6 weeks since dose ≥4</td>
</tr>
<tr>
<td>Aristada
(aripiprazole lauroxil)

ER suspension, single-dose prefilled syringe

441 mg
662 mg
882 mg
1064 mg

IM injection: 441mg is deltoid or gluteal, other strengths gluteal only</td>
<td>Schizophrenia in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td>
<td>Dosing based on total daily dose of oral aripiprazole.
May start in 2 ways:
1. Initio 675mg loading dose + one dose of 30mg aripiprazole PO + Aristada IM
2. Aristada IM + 21 days of aripiprazole PO

Conversion Table
<table>
<tr><th>aripiprazole PO</th><th>Aristada IM</th></tr>
<tr><td>10 mg/day</td><td>441 mg monthly</td></tr>
<tr><td>15 mg/day</td><td>662 mg monthly
882 mg every 6 weeks
1064 mg every 2 months</td></tr>
<tr><td>≥20 mg/ day</td><td>882 mg monthly</td></tr>
</table>
</td>
<td>441 mg IM once monthly

662 mg IM once monthly

882 mg IM once monthly or every 6 weeks

1064 mg every 2 months

Dose adjustments required by for CYP2D6 poor metabolizers or those taking CYP3A4 inhibitors/inducers or CYP2D6 inhibitors</td>
<td>• Establish tolerability with aripiprazole tablets before initiating ER IM injection. It may take up to 2 weeks to fully assess tolerability.
• Aristada should not be given earlier than 14 days after previous injection.
• Missed Doses of Aristada
  • Restart Aristada therapy with Aristada Initio OR bridge with 7 days of aripiprazole PO:
  • >6 and ≤7 weeks since 441 mg IM doses
  • >8 and ≤12 weeks since 662 mg or 882 mg IM doses
  • >10 and ≤12 weeks since 106 mg IM dose
  • Restart Aristada therapy with Aristada Initio + one dose of 30mg aripiprazole PO OR bridge with 21 days of aripiprazole PO if:
  • >7 weeks since 441 mg IM dose
  • >12 weeks since 662 mg, 882 mg, or 1064 mg IM doses</td>
</tr>
</table>

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Aristada Initio *(aripiprazole lauroxil)* ER suspension, single-dose prefilled syringe 675 mg IM injection: deltoid or gluteal	**Schizophrenia** in adults (≥ 18 years) BBW: increased mortality in elderly patients with dementia-related psychosis	Used only as loading dose in combination with aripiprazole tablets and Aristada IM, not for repeat dosing. To intiate Aristada therapy: Give 675mg Aristada Initio IM + one 30mg aripiprazole tablet + first dose of Aristada IM To restart Aristada IM therapy after missed doses, Aristada Initio may be used. See above entry for Aristada.	Not applicable	• Establish tolerability with aripiprazole tablets before initiating ER IM injection. It may take up to 2 weeks to fully assess tolerability. • Give Aristada injection on same day as Aristada Initio or up to 10 days later. • Do not inject Aristada Initio and Aristada into the same muscle. • Avoid use in CYP2D6 poor metabolizers or those taking strong CYP3A4 inhibitors/inducers or strong CYP2D6 inhibitors. • Using Aristada Initio + 30mg aripiprazole + first dose Aristada will reach relevant aripiprazole concentrations within 4 days. • Aristada Initio is not interchangeable with Aristada.

Invega Sustenna
(paliperidone palmitate)
 	
ER suspension, single-dose pre-filled syringe
 	
39 mg
78 mg
117 mg
156 mg
234 mg
 	
IM injection: deltoid or gluteal
	Schizophrenia in adults (≥ 18 years)
	
	Schizoaffective disorder in adults (≥ 18 years)
	
	BBW: increased mortality in elderly patients with dementia-related psychosis
		Day 1: 234 mg IM
		Day 8: 156 mg IM (+/- 4 days)
		
		Doses on day 1 and day 8 are given in the deltoid, subsequent doses can be given in deltoid or glute)
		
		Missed 2nd dose
		• < 4 weeks since day 1, give 156mg IM ASAP, resume regular maintence at 5 weeks from Day 1.
		• 4 -7 weeks since day 1, give 156 mg IM ASAP, 156 mg IM dose 7 days later, wait 28 days and give 117 mg monthly.
		• > 7 weeks since day 1, restart for treatment naïve patient (i.e. Day 1 234 mg IM, Day 8 156 mg IM, week 5 117 mg IM.)
			Starting 5 weeks after first injection, given monthly (+/- 7 days).
			
			Monthly dose is based on diagnosis, tolerability, and efficacy.
			
			Schizophrenia: range is 39 mg to 234 mg, but recommended dose is 117 mg
			
			Schizoaffective disorder: range is 78 mg to 234 mg
			
			Conversion table
			Paliperidone PO / **Sustenna IM**
			12 mg/day / 234 mg/month
			9 mg/day / 156 mg/month
			6 mg/day / 117 mg/month
			3 mg/day / 39-78 mg/month
				• Establish tolerability with oral paliperidone or risperidone before initiating Invega Sustenna. Options per clinical trials:
				  • Paliperidone ER 3 mg/day for ≥2 consecutive days
				  • Paliperidone ER 3 mg/day or risperidone 1 mg/day for at least 28 or 3 days
				  • Paliperidone ER for 4 days at a dose of 3 mg/day
				  • Paliperidone ER 6 mg/day for 4-6 days
				• Oral AAP should be discontinued with initiation of IM formulation.
				• Alternate deltoid injections.
				• Renal Impairment
				  • CrCl 50 to 80 mL/min dose adjust to Day 1: 156 mg, Day 89 117 mg, and 78 mg for maintenance
				  • Not recommended if CrCl < 50 ml/min
				• Avoid use of Invega Sustenna with strong CYP3A4/P-glycoprotein (P-gp) inducers.
				• Missed maintenance doses of Invega Sustenna
				  • 4 - 6 weeks since last dose, resume ASAP
				  • >6 weeks to < 6 months since last dose resume previous dose ASAP (except 234 mg)
				  • If stable on 234mg, give 156 mg IM ASAP followed by 156 mg 7 days later, wait 28 days and resume 234 mg IM
				  • >6 months since last dose, restart therapy as treatment naïve patient.
				• Higher Cmax attained following deltoid injection versus gluteal injection. Longer half-life following gluteal injection versus deltoid injection. Recommend gluteal injection for providers requesting q 3 week administration.

Long-Acting Injectable (LAI) Atypical Antipsychotics Dosing Guide – 10.21.21

<table>
<tr>
<td>Invega Trinza
(paliperidone palmitate)

ER Suspension, single-dose pre-filled syringe
273 mg
410 mg
546 mg
819 mg

IM injection: deltoid or gluteal</td>
<td>Schizophrenia in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td>
<td>Start Invega Trinza only after ≥4 months of adequate treatment on Invega Sustenna.

PI recommends that the last 2 doses of Invega Sustenna be the same strength before starting Trinza.

Give the first dose of Trinza in place of the next scheduled dose of Invega Sustenna (+/- 7 days).

Dosing based on equivalent 3.5x higher dose.

Conversion Table
<table><tr><th>Sustenna</th><th>Trinza</th></tr><tr><td>78 mg</td><td>273 mg</td></tr><tr><td>117 mg</td><td>410 mg</td></tr><tr><td>156 mg</td><td>546 mg</td></tr><tr><td>234 mg</td><td>819 mg</td></tr></table></td>
<td>IM dosing every 3 months (+/- 14 days)

Dose adjustments made based on efficacy and tolerability.

Due to long half-life response to dose adjustment may not be apparent for several months.</td>
<td>Missed doses of Invega Trinza
3.5-4 months since last dose, give Trinza ASAP, then resume 3-month dosing schedule.
4-9 months since last dose, re-initiate equivalent Invega Sustenna dose on Day 1 and Day 8, then wait 28 days and resume Trinza.
>9 months since last dose, re-initiate as treatment naïve for Invega Sustenna. See instructions above. Patient must have ≥4 months of adequate treatment with Sustenna before resuming Trinza.
Renal Impairment
CrCl 50 to 80 mL/min dose adjust Invega Sustenna and transition to equivalent dose of Trinza.
Not recommended if CrCl < 50 ml/min
Avoid use of Invega Trinza with strong CYP3A4/P-glycoprotein (P-gp) inducers.
Oral AAP should be discontinued with initiation of all IM paliperidone formulations.
Longer half-life following gluteal injection versus deltoid injection. Recommend gluteal injection for providers requesting administration < every 3 months.</td>
</tr>
<tr><td colspan="5">Non-Preferred Agents</td></tr>
<tr>
<td>Invega Hafyera
(paliperidone palmitate)

ER Suspension, single-dose pre-filled syringe

1092 mg
1560 mg

IM injection: gluteal</td>
<td>Schizophrenia in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td>
<td>Start Hafyera only after:
1) trial of Sustenna ≥4 months
2) trial of Trinza for ≥1 3-month cycle

<table><tr><td>Conversion Table</td><td></td></tr><tr><td>Sustenna*</td><td>Hafyera</td></tr><tr><td>156 mg</td><td>1092 mg</td></tr><tr><td>234 mg</td><td>1560 mg</td></tr><tr><td>Trinza*</td><td>Hafyera</td></tr><tr><td>564 mg</td><td>1092 mg</td></tr><tr><td>819 mg</td><td>1560 mg</td></tr></table>*other doses not studied for switching.</td>
<td>IM dosing to gluteal muscle every 6 months (-14 days to +21 days)

Dose adjustments made based on efficacy and tolerability.

Due to long half-life response to dose adjustment may not be apparent for several months.</td>
<td>Invega Hafyera can only be administered to the gluteal muscle.
Give the first dose of Hafyera in place of the next scheduled dose of Invega Sustenna (+/- 7 days); the previous 2 doses of Sustenna be the same strength before starting Hafyera.
Give the first dose of Hafyera in place of the next scheduled dose of Invega Trinza (+/-14 days)
Avoid use of Invega Hafyera with strong CYP3A4/P-glycoprotein (P-gp) inducers.
Renal Impairment
CrCl 50 to 80 mL/min dose adjust Invega Sustenna and transition to equivalent dose of Trinza.
Not recommended if CrCl < 50 ml/min
Missed doses of Invega Hafyera
6.75-8 months since last dose give Sustenna Day 1 and Invega Hafyera Day 29. Dosing is Sustenna 156 mg for Hafyera 1092 mg or Sustenna 234mg for Hafyear 1560 mg.
8-11 months since last dose. Give Sustenna 156mg on Day 1 and Day 8, wait 28 days and give Hafyera 1092 mg or 1560 mg.</td>
</tr>
</table>

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<table>
<tr><td></td><td></td><td></td><td></td><td>• >11 months since last dose, do not give Hafyera. Restart as if treatment naïve with Invega Sustenna.</td></tr>
<tr><td>Risperdal Consta
(risperidone)

ER powder for suspension, vial kits
12.5 mg
25 mg
37.5 mg
50 mg

IM injection: deltoid or gluteal</td><td>Schizophrenia in adults (≥ 18 years)

Maintenance monotherapy or as adjunct to lithium or valproate for bipolar I in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td><td>Use 25mg dose for most patients

Use 12.5 mg for geriatric patients or those with poor renal/hepatic function, but efficacy has not been studied at this dose.</td><td>IM dosing every 2 weeks.

No recommendations on earliest time to next dose.

Dose adjustments made based on efficacy and tolerability.

Wait 4 weeks between each dose escalation.</td><td>• Establish tolerability to oral risperidone before initiating with long-acting IM injection.
• Oral risperidone or another AAP should be given with the first Consta injection and should be continued for 3 weeks of therapy and then discontinued.
• Clinical effects of dose adjustment should not be expected earlier than 3 weeks after the injection of the higher dose
• No data for missed doses. Restart Consta with oral rispidone for 3 weeks.
• Use of concurrent CYP3A4 inducers and CYP2D6 inhibitors will result in altered concentrations of risperidone.</td></tr>
<tr><td>Perseris
(risperidone)

ER powder for suspension, syringe kits

90 mg
120 mg

Subcutaneous: abdomen</td><td>Schizophrenia in adults (≥ 18 years)

BBW: increased mortality in elderly patients with dementia-related psychosis</td><td>May start either dose. See table below for equivalency.

Equivalent Plasma Concentrations
Risperidone PO | Perseris
3 mg/day | 90 mg/month
4 mg/day | 120 mg/month</td><td>Monthly subcutaneous injection into abdomen.

No recommendations on earliest time to next dose.</td><td>• Establish tolerability to oral risperidone. Patients stable on < 3mg/day or higher than 4 mg/day may not be good candidates for Perseris.
• Do not supplement Perseris with oral risperidone or another AAP.
• Use of concurrent CYP3A4 inducers and CYP2D6 inhibitors will result in altered concentrations of risperidone.
• For missed doses of Perseris. give next dose ASAP.
• Patients with hepatic or renal impairment, must be safely titrated to ≥3 mg/day of risperidone PO before considering Perseris 90 mg.</td></tr>
<tr><td>Zyprexa Relprevv
(olanzapine pamoate)

ER powder for suspension
210 mg
300 mg
405 mg

IM injection: gluteal</td><td>Schizophrenia in adults (≥ 18 years)

BBW: Post-injections delirium/sedation syndrome, increased mortality in elderly patients with dementia-related psychosis</td><td>Dosing for weeks 1 to 8 based on conversion table below.
No recommendations on earliest time to next dose.

Conversion Table Week 1 - 8 | Maintenance after week 8
Olanzapine PO | IM | IM
10 mg/day | 210 mg/2 weeks or 405 mg/4 weeks | 150 mg/ 2 weeks or 300 mg/4 weeks
15 mg/day | 300 mg/2 weeks | 210 mg/2 weeks or 405 mg/4 weeks
20 mg/day | 300 mg/2 weeks | 300 mg/2 weeks</td><td>Maintenance dosing after week 8.
No recommendations for missed doses.</td><td>• Establish tolerability with oral olanzapine before initiating ER IM injection. No Data for switching from other AAP available.
• Plasma concentrations after switch to Zyprexa Relprev may require treatment of 3 months to reestablish steady-state conditions.
• For deep IM gluteal injection only.
• For debilitated patients, those with predisposition to hypotensive reactions, slow metabolizers of olanzapine, or those pharmacodynamically sensitive to olanzapine the recommended starting dose is 150 mg/4 weeks.
• Do not confuse the short-acting formulation (Zyprexa IM 10 mg/vial) with the ER suspension Zyprex Relprevv (olanzapine pamoate)
• REMS enrollment required due risk of post-injection</td></tr>
</table>

					delirium/sedation syndrome; patient must be observed for ≥3 hours post-injection with Relprevv.

AAP atypical antipsychotics, *ER* extended-release, *FDA* United States Food and Drug Administration, *IM* intramuscular, *PO* by mouth

1. Abilify Maintena. Package insert. Otsuka Pharmaceutical Co., Ltd.; 2020.
2. Aristada. Package insert. Alkermes, Inc.; 2020.
3. Aristada Initio. Package insert. Alkermes, Inc.; 2020.
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5. Dosing of Invega Sustenna - Tolerability Testing. Updated May 5, 2021. https://www.janssenmd.com/invega-sustenna/dosage-administration/tolerability/dosing-of-invega-sustenna-tolerability-testing. Accessed October 27, 2021.
6. Invega Trinza. Package insert. Janssen Pharmaceuticals, Inc.; 2021
7. Invega Hafyera. Package insert. Janssen Pharmaceuticals, Inc.; 2021
8. Risperdal Consta. Package insert. Janssen Pharmaceuticals, Inc.; 2021
9. Perseris. Package insert. Indivior, Inc.; 2019.
10. Zyprexa Relprevv. Package insert. Eli Lilly; 2019.