



Therapeutic Class ReviewSM

Mental Health – Paliperidone (InvegaTM Extended-Release Tablets)

April 2007

New Product for Review:

Paliperidone (InvegaTM) [Ortho-McNeil Janssen]

Dossier Provided by Manufacturer:

Dossier Evaluation: 3

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

Available Therapeutic Alternatives:

| Preferred/Formulary | Non-Preferred/Non-Formulary |
|---|--|
| <i>Atypical Anti-psychotics</i> | |
| clozapine (Clozaril [®] , generic) | ziprasidone (Geodon [®]) [Pfizer-Roerig] |
| risperidone (Risperdal [®]) [Janssen Pharmaceuticals] | aripiprazole (Abilify [®]) [Otsuka Pharmaceutical] |
| olanzapine (Zyprexa [®]) [Eli Lilly] | paliperidone (Invega TM) [Ortho-McNeil Janssen] |
| quetiapine (Seroquel [®]) [AstraZeneca] | |

Executive Summary

- Schizophrenia is a debilitating mental illness that affects about one percent of the population.
 - Antipsychotic medication is the mainstay of treatment for this condition.
 - Adverse events and/or loss of efficacy related to individual agents often results in frequent therapy changes.
 - There is an unmet need for reliably effective antipsychotic medications with low incidence of troublesome side effects.
- Paliperidone (Invega) is a psychotropic agent classified as an atypical antipsychotic.
 - Paliperidone (Invega) is indicated for the treatment of schizophrenia based on trials of up to 6 weeks in duration.
 - Paliperidone is the major active metabolite of risperidone (Risperdal).
- Paliperidone (Invega) is dosed as 6 mg each morning without the need for dose titration.
 - The dose must be individualized for renal impairment.
 - No dose adjustment is needed for liver impairment.

Evidence

- None of the trials evaluating the efficacy of paliperidone (Invega) in the management of patients with schizophrenia were useful or possibly useful.
- There are no head-to-head trials comparing either the safety or efficacy of paliperidone (Invega) to other typical or atypical antipsychotics for the management of patients with schizophrenia.
- Considerations in Subpopulations:
 - **Pediatrics** - The safety and effectiveness of paliperidone (Invega) in pediatric patients has not been established.
 - **Geriatrics**: No overall differences in safety or effectiveness were observed between subjects 65 years and over and younger subjects. Dosage must be adjusted for decreased renal function.
 - **Gender**: No dosage adjustment is necessary based on gender.
 - **Race, ethnicity**: No dosage adjustment is necessary based on race or ethnicity.

Conclusion

Paliperidone (Invega) is non-preferred/non-formulary because:

- It has unproven advantages compared to current formulary alternatives; and
- There is a lack of long-term safety data with this product.

Products^[1-3]

| Drug Products | FDA approval ^a | Patent Expiration(s) ^d | FDA approved indications | Usual Dose/Route | Cost ^b | Potential Off-label Uses ^c |
|--------------------------------|---------------------------|-----------------------------------|--|--------------------|-------------------|---|
| clozapine (Clozaril®, generic) | 09/1989 | N/A | - Tx resistant schizophrenia - Suicidal behavior, recurrent | 400 mg daily PO | \$166.50 (MAC) | - Aggressive behavior - Bipolar disorder - Borderline personality disorder - Dementia - Excessive thirst - HIV psychosis disorder - Involuntary movement disorder - Parkinson's disease – psychotic disorder - Schizoaffective disorder, Refractory |

Products (Continued)^[1-3]

| Drug Products | FDA approval^a | Patent Expiration(s)^d | FDA approved indications | Usual Dose/Route | Cost^b | Potential Off-label Uses^c |
|--|---------------------------------|---|---|---|-------------------------|--|
| risperidone (Risperdal [®]) | 12/1993 | 12/2007 | - Schizophrenia - Bi-polar mania - Irritability in autism | 4 - 8 mg daily PO 25 mg/q 2wk IM | \$350 - \$700 | - Behavioral syndrome – Dementia - Behavioral syndrome - Mental retardation - Bipolar disorder - Borderline personality disorder - Cocaine dependence - Cognitive function finding - Delusional disorder - Dementia - Psychotic disorder - Depression, Refractory - Drug-induced psychosis - Levodopa adverse reaction - Gilles de la Tourette's syndrome - Huntington's disease - Obsessive-compulsive disorder, Refractory - Organic psychotic condition - Parkinson's disease - Psychotic disorder - Pervasive developmental disorder - Posttraumatic stress disorder - Schizotypal personality disorder - Stuttering - Trichotillomania |
| olanzapine (Zyprexa [®]) | 09/1996 | 04/2011 | - Schizophrenia - Bi-polar mania | 5 mg – 20 mg daily PO 2.5-10 mg IM | \$256 - \$771 | - Cannabis induced psychotic disorder - Alzheimer's disease - Psychotic disorder - Anorexia nervosa - Anxiety – Dementia - Borderline personality disorder - Cancer – Nausea - Cocaine dependence - Delirium - Depressed bipolar I disorder - Drug-induced psychosis - Methamphetamine adverse reaction - Essential tremor - Gilles de la Tourette's syndrome - Headache - Huntington's disease - Neuroleptic adverse reaction – Tremor - Obsessive-compulsive disorder, Refractory - Parkinson's disease - Psychotic disorder - Pervasive developmental disorder - Posttraumatic stress disorder - Repetitive self-excoriation - Schizophrenic prodrome |
| olanzapine (Zyprexa [®]) - continued | | | | | | - Senile dementia of the Lewy body type - Severe major depression with psychotic features - Trichotillomania |

Products (Continued)^[1-3]

| Drug Products | FDA approval ^a | Patent Expiration(s) ^d | FDA approved indications | Usual Dose/Route | Cost ^b | Potential Off-label Uses ^c |
|--------------------------------------|---------------------------|-----------------------------------|--------------------------------------|---|--------------------|---|
| quetiapine (Seroquel [®]) | 09/1997 | 09/2011 | - Schizophrenia - Bi-polar mania | 400 mg – 800 mg daily PO | \$338 - \$676 | - Bipolar disorder - Delirium - Diffuse Lewy body disease - Psychotic disorder - Gilles de la Tourette's syndrome - Obsessive-compulsive disorder - Parkinson's disease - Psychotic disorder - Tardive dyskinesia |
| ziprasidone (Geodon [®]) | 02/2001 | 03/2012 | - Schizophrenia - Bi-polar mania | 20 mg – 80 mg BID PO 10-20 mg/day IM | \$345 - \$391 | - Major depressive disorder, Treatment-resistant; Adjunct - Schizoaffective disorder |
| aripiprazole (Abilify [®]) | 11/2002 | 10/2014 | - Schizophrenia - Bi-polar mania | 10 mg – 30 mg daily PO | \$395 - \$579 | - Asperger's disorder |
| paliperidone (Invega [™]) | 12/2006 | 10/2009 | - Schizophrenia | 3 mg to 12 mg daily PO | \$366 - \$732 | - None identified |
| For Comparison | | | | | | |
| haloperidol (Haldol, generic) | 04/1967 | N/A | - Schizophrenia | 0.5 mg to 10 mg BID to TID | \$4 to \$95 (MAC) | - Numerous |
| perphenazine (Trilafon, generic) | 02/1957 | N/A | - Schizophrenia - Nausea/vomiting | 4 mg to 16 mg TID | \$37 to \$92 (MAC) | - Numerous |

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of January 2007 for 1 month of therapy.

^c As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

^d Based on patents listed in Orange Book as of January 2007

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