



Therapeutic Class ReviewSM

Neurology – Rasagiline (Azilect[®])

February 2007

New Product for Review:

Dossier Provided by Manufacturer:

Dossier Evaluation: 2

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

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Prefer/Non-Formulary
<i>MAO B Inhibitors</i>	
selegiline (Eldepryl [®]) – generic	rasagiline (Azilect [®]) [Teva Neuroscience]
<i>Dopamine Agonists</i>	
pergolide (Permax [®]) – generic	
pramipexole (Mirapex [®]) [Boehringer-Ingelheim]	
ropinirole (Requip [®]) [GlaxoSmithKline]	
bromocriptine (Parlodel [®]) – generic	
<i>COMT Inhibitors</i>	
entacapone (Comtan [®]) [Novartis]	tolcapone (Tasmar [®]) [Valeant]

Executive Summary

- Rasagiline (Azilect) is an irreversible monoamine oxidase (MAO) inhibitor indicated for the treatment of idiopathic Parkinson’s disease (PD).
 - Rasagiline (Azilect) inhibits MAO type B (MAO-B), but adequate studies to establish whether it is selective for MAO-B in humans have not yet been conducted.
 - Rasagiline (Azilect) is indicated for the treatment of the signs and symptoms of idiopathic PD as initial monotherapy and as adjunct therapy to levodopa.

Evidence

- There is possibly useful evidence that rasagiline (Azilect) results in:
 - modest improvements in the symptoms of early PD.
 - improvements in the amount of daily “off” time experienced by PD patients treated with levodopa.

- a similar safety profile as entacapone (Comtan) in PD patients being treated with levodopa.
- There is no useful evidence that rasagiline (Azilect):
 - slows or otherwise affects the progression of PD.
 - is safer or better tolerated than selegiline.
- Considerations in Subpopulations:
 - **Pediatrics:** The safety and effectiveness of rasagiline (Azilect) in the pediatric population have not been studied.
 - **Geriatrics:** Approximately half of patients in the rasagiline (Azilect) clinical trials were 65 years and over. There were no significant differences in the safety profile of the geriatric and non-geriatric patients.
 - **Gender:** The pharmacokinetic profile of rasagiline (Azilect) is similar in men and women.
 - **Race, ethnicity:** No specific recommendations.

Conclusion

Rasagiline (Azilect) is non-preferred/non-formulary due to the lack of evidence of superior efficacy over available formulary/preferred options.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
MAO B Inhibitors					
selegiline (generic)	06/1989	- Parkinson's disease; Adjunct	5mg bid PO	\$19.20 (MAC)	- Alzheimer's disease – Dementia - Attention deficit hyperactivity disorder - Dementia - HIV infection - Depression - Narcolepsy - Parkinson's disease, initial treatment - Periodic limb movement disorder - Schizophrenia; Adjunct
rasagiline (Azilect)	05/2006	- Parkinson's disease - Parkinson's disease; Adjunct	1mg qd PO	\$255.75	- None noted
Dopamine Agonists					
pergolide (generic)	12/1988	- Parkinson's disease; Adjunct	1mg tid	\$268.20 (MAC)	- Acromegaly - Cocaine withdrawal - Depression - Gilles de la Tourette's syndrome - Hyperprolactinemia - Parkinson's disease - Restless legs syndrome - Supranuclear paralysis
pramipexole (Mirapex [®])	07/1997	- Parkinson's disease - Parkinson's disease; Adjunct - Restless legs syndrome	1mg tid	\$225.66	- Depression - Panic disorder - Schizophrenia
ropinirole (Requip [®])	09/1997	- Parkinson's disease - Parkinson's disease; Adjunct - Restless legs syndrome	2mg tid	\$189.90	- None noted
bromocriptine (generic)	06/1978	- Parkinson's disease - Parkinson's disease; Adjunct - Acromegaly - Hyperprolactinemia -Associated Dysfunctions	10 mg tid	\$619.20 (MAC)	- Numerous
COMT Inhibitors					
tolcapone (Tasmar [®])	01/1998	- Parkinson's disease; Adjunct	100mg tid	\$293.29	- Depression
entacapone (Comtan [®])	10/1999	- Parkinson's disease; Adjunct	200mg with each dose of levodopa (3 to 8 times daily)	\$227.70 - \$607.20	- Restless legs syndrome

^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 December 2006 for 1 month of therapy.

^c As listed in © 1974 - 2005 Thomson MICROMEDEX database or as referenced.

References

1. Klasco RK (Ed): DRUGDEX[®] System (electronic version). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at: <http://www.thomsonhc.com> (cited: 6/22/2006).
2. Azilect[®] [package insert]. Kansas City, MO: Teva Neuroscience, Inc.; May 2006
3. Parkinson Study Group. A controlled trial of rasagiline in early Parkinson disease: the TEMPO Study. *Arch Neurol*. 2002 Dec;59(12):1937-43.
4. Parkinson Study Group. A controlled, randomized, delayed-start study of rasagiline in early Parkinson disease. *Arch Neurol*. 2004 Apr;61(4):561-6.
5. Stern MB, Marek KL, Friedman J, Hauser RA, LeWitt PA, Tarsy D, et. al. Double-blind, randomized, controlled trial of rasagiline as monotherapy in early Parkinson's disease patients. *Mov Disord*. 2004 Aug;19(8):916-23.
6. Rascol O, Brooks DJ, Melamed E, Oertel W, Poewe W, Stocchi F, et. al; LARGO study group. Rasagiline as an adjunct to levodopa in patients with Parkinson's disease and motor fluctuations (LARGO, Lasting effect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial. *Lancet*. 2005 Mar 12-18;365(9463):947-54.
7. Parkinson Study Group. A randomized placebo-controlled trial of rasagiline in levodopa-treated patients with Parkinson disease and motor fluctuations: the PRESTO study. *Arch Neurol*. 2005 Feb;62(2):241-8.
8. Rabey JM, Sagi I, Huberman M, Melamed E, Korczyn A, Giladi N, et. al.; Rasagiline Study Group. Rasagiline mesylate, a new MAO-B inhibitor for the treatment of Parkinson's disease: a double-blind study as adjunctive therapy to levodopa. *Clin Neuropharmacol*. 2000 Nov-Dec;23(6):324-30.
9. Pharmacy Budget Model for Treatment of Parkinson's Disease. Product Dossier: Azilect[®] (rasagiline), Teva Neuroscience, Inc; Kansas City, MO. Data reviewed November 30, 2006.
10. Macleod AD, Counsell CE, Ives N, Stowe R. Monoamine oxidase B inhibitors for early Parkinson's disease. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004898. DOI: 10.1002/14651858.CD004898.pub2.
11. Clarke C, Moore AP. Parkinson's disease. *Clin Evid*. 2005 Jun;(13):1658-77.
12. Suchowersky O, Gronseth G, Perlmutter J, Reich S, Zesiewicz T, Weiner WJ, Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: neuroprotective strategies and alternative therapies for Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2006 Apr 11;66(7):976-82.
13. Pahwa R, Factor SA, Lyons KE, Ondo WG, Gronseth G, Bronte-Stewart H, Hallett M, Miyasaki J, Stevens J, Weiner WJ, Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2006 Apr 11;66(7):983-95
14. Drug Facts and Comparisons. Drug Facts and Comparisons 4.0 [online]. 2006. Available from Wolters Kluwer Health, Inc. Accessed November 29, 2006.
15. Eldepryl[®] [package insert]. Tampa, FL: Somerset Pharmaceuticals, Inc.; July 1998. Available at http://www.somersetpharm.com/products/product_labeling.html. Accessed December 1, 2006.
16. Siderowf A, McDermott M, Kieburtz K, Blindauer K, Plumb S, Shoulson I; Parkinson Study Group. Test-retest reliability of the unified Parkinson's disease rating scale in patients with early Parkinson's disease: results from a multicenter clinical trial. *Mov Disord*. 2002 Jul;17(4):758-63.
17. Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The Unified Parkinson's Disease Rating Scale (UPDRS): status and recommendations. *Mov Disord*. 2003 Jul;18(7):738-50.
18. Product Dossier: Azilect[®] (rasagiline), Teva Neuroscience, Inc; Kansas City, MO. Data reviewed November 30, 2006.