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Higher dose of Novartis drug Exelon® Patch approved by FDA for patients with mild to moderate Alzheimer's disease

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- -- Approval based on efficacy and safety demonstrated in long-term study comparing 13.3 mg/24 h to 9.5 mg/24 h in declining mild to moderate Alzheimer's patients
- -- New higher dose of Exelon Patch offers another therapeutic option for appropriate patients and dosing flexibility for physicians
- -- Alzheimer's disease (AD) is the most common form of dementia in older adults with about 4 million Americans living with mild to moderate AD(1,2)

EAST HANOVER, N.J., Sept. 4, 2012 /PRNewswire/ -- The US Food and Drug Administration has approved a higher dose of Exelon® Patch (rivastigmine transdermal system) for the treatment of people with mild to moderate Alzheimer's disease. The new 13.3 mg/24 h dosage strength of Exelon Patch provides physicians with a new treatment option for patients who are experiencing a decline in overall function and cognition.

"Alzheimer's disease is marked by progressive symptomatic decline, resulting in an increasingly large physical and emotional challenge for the patient and caregiver," said Jeffrey Cummings, MD, Director of the Cleveland Clinic Lou Ruvo Center for Brain Health. "Having multiple options for the treatment of mild to moderate Alzheimer's disease will help physicians better care for patients with the hope of improving function and cognition."

Approval of Exelon Patch 13.3 mg/24 h was based on the 48-week double-blind phase of the OPTIMA study, a novel controlled trial in mild to moderate AD patients who met the pre-defined criteria for functional and cognitive decline on the 9.5mg/24 h dose. Patients treated with the 13.3 mg/24 h patch experienced statistically significant ($p<0.05$) improvement in their overall function compared to the 9.5 mg/24 h patch as measured by the instrumental activities of daily living scale (ADCS-IADL) at week 48 (a co-primary endpoint). Improvement in cognition (measured by ADAS-Cog) compared to the lower dose was nominally statistically significant at 24 weeks but not at 48 weeks (also a co-primary endpoint). This was one of the longest double-blind cholinesterase inhibitor trials to date.

During the 48-week dose-comparison phase of OPTIMA, no unexpected adverse events (AEs) leading to discontinuation were reported, and the safety profile of the higher dose was consistent with that of the currently approved doses of Exelon Patch. Overall, the percentage of patients with AEs leading to discontinuation was lower in the 13.3 mg/24 h group compared to the 9.5 mg/24 h group (9.6% vs. 12.7%, respectively).

"Family caregivers play a vital role in the Alzheimer's treatment journey by working closely with healthcare providers to choose the right treatment for their loved ones," said John Schall, Chief Executive Officer of the National Family Caregivers Association. "From the caregiver's standpoint, a patch can be visual evidence to help see if their loved one has actually received their medication, so to have an additional option is important."

Exelon Patch is the first transdermal (through the skin) therapy approved for the treatment of people with mild

to moderate Alzheimer's disease. It is also approved to treat people with mild to moderate Parkinson's disease dementia.

"Exelon Patch has been used to treat hundreds of thousands of patients over the years, so we are especially pleased that the higher dose is now available to help even more people," said Andre Wyss, President of Novartis Pharmaceuticals Corporation. "We believe in transdermal application and the efficacy of Exelon Patch, and we are committed to continuing our research in Alzheimer's disease."

Alzheimer's is a gradually progressing and fatal degeneration of the brain characterized by cognitive and memory determination, progressive impairment of activities of daily living, and behavioral disturbances.[3] It is the most common cause of dementia among people age 65 and older.[1] Approximately 70% of Alzheimer's disease patients receive care at home.[3]

INDICATIONS

EXELON® PATCH (rivastigmine transdermal system) 4.6 mg/24 hours, 9.5 mg/24 hours, and 13.3 mg/24 hours is indicated for the treatment of mild to moderate dementia of the Alzheimer's type and mild to moderate dementia associated with Parkinson's disease.

IMPORTANT SAFETY INFORMATION

EXELON PATCH is contraindicated in patients with known hypersensitivity to rivastigmine, other carbamate derivatives, or other components of the formulation. Isolated cases of generalized skin reactions have been described in post-marketing experience.

Medication errors with EXELON PATCH have resulted in serious adverse events; some cases have required hospitalization, and rarely, led to death. The majority of medication errors have involved not removing the old patch when putting on a new one and the use of multiple patches at one time. Only one EXELON PATCH should be worn at a time.

EXELON PATCH can cause gastrointestinal adverse reactions, including significant nausea, vomiting, diarrhea, anorexia/decreased appetite, and weight loss. Dehydration may result from prolonged vomiting or diarrhea and can be associated with serious outcomes. The incidence and severity of these reactions are dose-related. For this reason, initiate treatment with EXELON PATCH at a dose of 4.6 mg/24 hours and titrate to a dose of 9.5 mg/24 hours and then to a dose of 13.3 mg/24 hours, if appropriate. If treatment is interrupted for more than three days because of intolerance, reinitiate EXELON PATCH with the 4.6 mg/24 hours dose to reduce the possibility of severe vomiting and its potentially serious sequelae.

In a 24-week clinical trial, the most commonly observed adverse events with EXELON PATCH occurring at a frequency of at least 5% and greater than placebo with administration of 9.5 mg/24 hours were nausea, vomiting, and diarrhea (7%, 6%, 6% for EXELON PATCH 9.5 mg/24 hours versus 5%, 3%, 3% for placebo, respectively).

Of the commonly reported adverse reactions (>/=3% in any treatment group) in a 48-week clinical trial, the most frequent events in the EXELON PATCH 13.3 mg/24 hours group were nausea, vomiting, fall, weight decreased, application site erythema, decreased appetite, diarrhea, and urinary tract infection. The percentage of these patients with these events was higher in the EXELON PATCH 13.3 mg/24 hours group than in the EXELON PATCH 9.5mg/24 hours group.

Weight should be monitored during therapy with EXELON PATCH. In a 24-week clinical trial, weight loss (>/=7% of baseline) with EXELON PATCH 9.5 mg/24 hours was 8% vs 6% for placebo; anorexia was 3% vs

2% for placebo. Weight loss (>/=7% of baseline) was 26% in women and 18% in men receiving doses >9 mg/day of EXELON capsules in clinical trials. Patients with body weight below 50 kg (110 lbs) may experience more adverse events and may be more likely to discontinue EXELON due to adverse events. In a 48-week clinical trial, weight loss equal to or greater than 7% of their baseline weight was 18.6% of those treated with EXELON PATCH 13.3 mg/24 hours and 15.2% of those treated with EXELON PATCH 9.5 mg/24 hours.

Like other cholinomimetics, rivastigmine may exacerbate or induce extrapyramidal symptoms. Parkinsonian symptoms, particularly tremor, have worsened in Parkinson's disease dementia patients treated with EXELON (rivastigmine tartrate) capsules.

In view of its pharmacodynamic effects, rivastigmine should not be given concomitantly with other cholinomimetic drugs and might interfere with the activity of anticholinergic medications.

Due to increased cholinergic activity, cholinesterase inhibitors may be expected to increase gastric acid secretion and/or have vagotonic effects on heart rate. As with other cholinomimetics, caution is recommended in patients with sick sinus syndrome, conduction defects, gastroduodenal ulcerative conditions (including those predisposed by concomitant medications), gastrointestinal bleeding, asthma or chronic obstructive pulmonary disease, urinary obstruction, seizures, or undergoing anesthesia. Patients' ability to drive should be routinely evaluated.

Please see Exelon Patch Full Prescribing Information, and Exelon Patch Patient Product Information

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Novartis is proud to offer Patient Assistance Now, an easy-to-use, comprehensive resource that allows you to access programs that may help you pay for your Novartis medicines.

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Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2011, the Group achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 126,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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