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Clinical pharmacokinetics and pharmacodynamics demonstrate once-weekly CorplexTM donepezil transdermal system as a therapeutic alternative to daily oral Aricept

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Aricept® (donepezil hydrochloride) is the most commonly used therapy worldwide in the treatment of Alzheimer's disease as a daily tablet. Patient adherence to therapy is poor due to the required daily administration, and gastro-intestinal (GI) adverse effects that may be associated with the oral route of administration. The once-weekly delivery with the donepezil transdermal system (TDS) using the CorplexTM technology platform is expected to improve adherence by providing a convenient once-weekly patch, and potentially improve the GI tolerability profile by bypassing the GI tract. A phase 1, multiple-dose, randomized crossover study in healthy subjects was conducted, with the primary objective of comparing the steady-state pharmacokinetics (PK) and pharmacodynamics (PD) of CorplexTM Donepezil TDS, targeted to deliver 10 mg/day of donepezil, and the oral Aricept® 10 mg after several weeks of treatment. The secondary objectives were assessment of safety and tolerability (including skin tolerability). Based on the results of our earlier single-dose phase 1 PK study, we projected that at steady state, the maximum plasma concentration and the area under the curve of plasma concentration of donepezil with the CorplexTM Donepezil TDS would be similar to the same measurements of oral Aricept®. The steady state PKPD data from the current clinical study is consistent with our projections, and demonstrated bioequivalence between once-weekly CorplexTM Donepezil TDS and oral Aricept®. Sustained and controlled delivery of donepezil was observed in the plasma concentrations of all subjects treated with once-weekly CorplexTM Donepezil for four consecutive weeks. Subjects treated with once-weekly CorplexTM Donepezil, experienced acceptable skin tolerability and no systemic adverse events unique to transdermal delivery. The gastrointestinal tolerability was much improved with CorplexTM Donepezil TDS to oral Aricept®. The PKPD results from this phase 1 multiple dose study support the feasibility of a convenient, safe and effective once-weekly dosing regimen as compared to daily oral administration. A registration pivotal pharmacokinetic is underway to demonstrate bioequivalence between the once-weekly CorplexTM Donepezil TDS and oral Aricept® at steady-state. Bioequivalence studies are designed to assess the biological equivalence of pharmaceutical products based on their PK profiles. They are relatively short in duration of treatment, and provide a development path that is substantially less costly and more streamlined compared to standard clinical development programs.

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