Drug Information

The following information is obtained from various newswires, published medical journal articles, and medical conference presentations.

Drug Name: Axona (caprylidene)

Company: Accera
Approval Status: Approved March 2009
Treatment Area: Alzherimer's disease

General Information

Axona is a medical food that is metabolized into ketone bodies, which the brain can use for energy even when its ability to process glucose is impaired. Brain-imaging scans of older adults and those with Alzheimer's disease reveal a dramatically decreased uptake of glucose, the brain's preferred source of energy. Axona is being developed to replace these depleted glucose levels to treat age-associated memory impairment (AAMI) and Alzheimer's disease.

Axona is specifically indicated for the clinical dietary management of the metabolic processes associated with mild to moderate Alzheimer's disease.

Axona is supplied as a powder for oral formulation. Axona should be administered once daily at breakfast. The recommended dosage is 40 grams (one packet of Axona powder, containing 20 grams MCTs) per day. The contents of each packet of Axona should be added to 4 to 8 ounces (118 to 236 milliliters) of water, as preferred, shaken until fully blended, and consumed immediately.

Clinical Results

FDA Approval

The FDA approval of Axona was based on the following studies:

Single-Administration Clinical Study in Patients With AD or MCI
This randomized, placebo-controlled, crossover-design study enrolled 20 subjects between the ages of 55-85 years old and diagnosed with probable AD or mild cognitive impairment (MCI). It was designed to measure the therapeutic effects of a single administration (40-80 grams) of medium-chain triglycerides (MCTs) on memory. Subjects were allowed to continue on stable concomitant AD treatments. A single 40-gram administration of MCTs led to elevated BHB serum levels (to approximately 0.5 mM at 90 minutes following administration) that were positively correlated with improvement in paragraph recall (a measure of cognition) ($P = 0.02$). APOE4(-) patients showed greater improvement compared to APOE4(+) patients in the AD Assessment Scale—Cognitive subscale (ADAS-Cog, which measures memory and other aspects of cognitive performance) ($P = 0.039$).

Clinical Study in Patients With Probable Mild to Moderate AD
This double blind, randomized, placebo-controlled, 90-day study enrolled 152 subjects with mild to moderate AD in the US. At day 45, ADASCog scores stabilized in the Axona group, whereas a decline in cognition was observed in the placebo group. The point difference in ADAS-Cog change from baseline scores at day 45 between groups was 1.91 ($P = 0.024$). This point difference in ADAS-Cog change from baseline scores at day 90 between groups was 1.54 ($P = 0.0767$). Final ADAS-Cog evaluations were performed following a 2-week washout period (day 104): the Axona group maintained a slight improvement from baseline, whereas the placebo group still demonstrated a decline, although the difference between groups was no longer statistically significant ($P = 0.405$). The ADAS-Cog change from baseline score was also analyzed in subgroups of patients based on APOE4 genotype. The APOE4(-) patients receiving Axona showed improved cognitive function when compared with APOE4(-) patients receiving placebo. The point difference in change from baseline ADAS-Cog scores for APOE4(-) Axona and placebo patients at day 45 was 4.77 ($P < 0.0005$), and was 3.36 at day 90 ($P = 0.015$; see Figure 2). In APOE4(+) patients, the mean change in ADAS-Cog total scores for the 2 groups was essentially identical at all time points, with more patients showing decline rather than improvement at day 45 and day 90.

Bridging Study in Healthy Elderly Volunteers
This open-label, randomized bridging study enrolled 66 healthy elderly subjects and was designed to establish the tolerability, safety, and pharmacokinetic (PK) profile of 3 different formulations of Axona administered for 14 days either with a 7-day titration (7 days at 10 grams MCTs followed by 7 days at 20 grams MCTs) or without titration (14 days at 20 grams MCTs). The original formulation of Axona used in the AD controlled clinical trial required reconstitution with a meal replacement drink, (i.e Ensure), in order to enhance product tolerability. The two new

formulations tested each contained an identical amount of MCTs as the original formulation, but different amounts of proteins and carbohydrates, and allowed for reconstitution in 6-8 ounces of water. The highest mean BHB levels (Cmax) and area-under-the-curve (AUC) values were observed in the cohort of subjects receiving the high-protein formulation at the 20-gram MCT level. This cohort of subjects receiving the high-protein formulation at the 20-gram MCT level also experienced the latest onset of most GI AEs.

Side Effects

Adverse events associated with the use of Axona may include, but are not limited to, the following:

- Diarrhea
- Flatulence
- Dyspepsia
- Dizziness
- Headache

Mechanism of Action

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Literature References

Henderson ST, Vogel JL, Barr LJ, Garvin F, Jones JJ, Costantini LC Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. *Nutrition & Metabolism* 2009 Aug 10;6:31

Costantini LC, Barr LJ, Vogel JL, Henderson ST Hypometabolism as a therapeutic target in Alzheimer's disease. *BMC Neuroscience* 2008 Dec 3;9 Suppl 2:S16

Additional Information

For additional information regarding Axona or Alzheimer's disease, please visit the Axona web page.