Request for permission for pharmaceutical industry oral testimony at Idaho Medicaid's P&T Committee meeting on 11-18-2016.

Submission # 4

This request has not been approved for oral testimony (10/28/16).

Gennrich, Jane

From: Eide, Tamara J.
Sent: Wednesday, October 26, 2016 10:23 AM
To: Gennrich, Jane
Subject: FW: Upcoming Idaho P&T Meeting- Anticonvulsants
Attachments: Fycompa-perampanel-USPI-rev-April 2016.pdf; Idaho P&T Committee GrantWF Eisai FYCOMPA OS.pdf

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From: Wilmon_Grant@eisai.com [mailto:Wilmon_Grant@eisai.com]
Sent: Tuesday, October 25, 2016 4:36 PM
To: Eide, Tamara J.
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Subject: Upcoming Idaho P&T Meeting- Anticonvulsants

Dr Eide,
Thank you so much for the information you sent me regarding Idaho Medicaid and FYCOMPA. It was very helpful in guiding the preparation of this testimony. Please find attached my submission for testimony to be presented at the Idaho P&T meeting on November 18, 2016. This submission focuses on the recent FDA approval for FYCOMPA oral suspension. Included also is the most recent FYCOMPA package insert for your convenience. Provided the committee approves the attached information, verbal testimony at the meeting will be given by myself. Please do not hesitate to reach out with any questions.
Kind Regards,
Wilmon

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human health care

10/25/16

Idaho Medicaid Pharmacy & Therapeutics Committee
Attn: Tami Eide, PharmD
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RE: Idaho Medicaid Pharmacy and Therapeutics Committee

Dr. Eide,
My name is Wilmon Grant MCR, Ph.D. and I am a Senior Medical Science Liaison with Eisai Inc. U.S. Medical and Scientific Affairs. Thank you for the opportunity for Eisai Inc. to present on FYCOMPA (perampanel) for the management of epilepsy. I am providing written testimony to be considered for presentation by myself to the Idaho P&T Committee membership during the Public Testimony Meeting on November 18, 2016.

FYCOMPA (perampanel) is a first in class AMPA receptor antagonist approved by the FDA in the management of epilepsy. Fycompa was approved in October 2012 as adjunctive therapy for the treatment of Partial-onset (focal) seizures (POS) with or without secondary generalization in patients with epilepsy age 12 and older. In June 2015 the FDA approved Fycompa as add on therapy for the treatment of Primary Generalized Tonic-Clonic (PGTC) seizures in patients with epilepsy age 12 and older. Testimony that will be presented on Nov. 18th will refer to the April 2016 FDA approval of a new formulation: oral suspension Fycompa[1].

Approval for oral suspension was granted for adjunctive therapy for treatment of POS or PGTC seizures in patients with epilepsy ≥ 12 years of age based on a bioequivalence study conducted in 100 healthy male and female volunteers[2]. The study compared the rate and extent of adsorption of a single 12mg dose of perampanel oral suspension compared with a single dose of perampanel 12 mg tablet in the fed and fasted state. The results of this study demonstrated that FYCOMPA oral suspension has comparable bioavailability to FYCOMPA tablets under steady state, and both formulations may be used interchangeably. FYCOMPA is orally administered once daily as a single dose and is available in multiple tablet strengths and an oral suspension (Tablets: 2,4,6,8,10, & 12mg, Oral Suspension: 0.5mg/ml)[1].

I hope the information enclosed proves to be of help and interest. Please do not hesitate to contact me at 210-948-8965 or wilmon_grant@eisai.com should you require anything further.

Kind Regards,
Wilmon Grant

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To the Idaho Medicaid Pharmacy and Therapeutics Committee:
FYCOMPA is a first in class AMPA receptor antagonist approved by the FDA in the management of epilepsy.

First approved in October 2012 by the FDA as add on therapy for the treatment of Partial-onset (focal) seizures (POS) with or without secondary generalization in patients with epilepsy age 12 and older

In June 2015 the FDA approved Fycompa as add on therapy for the treatment of Primary Generalized Tonic-Clonic (PGTC) seizures in patients with epilepsy age 12 and older

In May 2016 the FDA granted approval of new formulation: oral suspension[1,2]

Basis for approval of FYCOMPA oral suspension:
Study 048: This was an open label, 2 arm, single dose randomized crossover study with 100 healthy males or females, ages 18 to 55 years with BMI of 18 to 32 kg/m^2 (50 each arm). Arm 1 evaluated the oral suspension and tablet forms of perampanel in fasted subjects. Fed subjects were evaluated in Arm 2. In both arms, subjects would be randomized to either receive a 12 mg perampanel tablet or 12 mg in the oral suspension formulation. Subjects were to return on day 43 for dosing of the other formulation (6 week washout). There were no significant demographic differences between the fasted (Treatment Arm 1) and fed (Treatment Arm 2) groups.

Subjects were randomized to 1 of 4 treatment allocations (AB, BA, CD, or DC), as defined below:

- Fasted (Arm 1):
  - Treatment A: Single oral dose of a 12-mg perampanel tablet
  - Treatment B: Single 12 mg dose of perampanel oral suspension.

- Co-administered with a high fat meal (Arm 2)
  - Treatment C: Single oral dose of a 12-mg perampanel tablet.
  - Treatment D: Single 12 mg dose of perampanel oral suspension.

The **treatment** phase consisted of 2 identical study periods. The only difference between periods was the treatment administered (either single 12 mg tablet or single 12 mg dose of oral suspension).

- Fasted Treatment: Subjects fasted overnight (10 hours), and then were given a single 12 mg dose of perampanel with 240 mL of water. No food was allowed for at least 4 hours after dosing.
- Fed Treatment: Subjects fasted overnight (≥ 10 hours) then consumed a high fat (~50% of caloric content) and high calorie (800-1000 calories) meal 30 minutes before dosing. The meal was to be eaten within 30 minutes. No food was allowed for 4 hours after dosing.

Pharmacokinetic results demonstrated that mean apparent $T^{1/2}$ was 122 hours for the tablet in the fasted group and 134 hours for the suspension in fasted subjects. The mean plasma concentration-time profiles for single dose administrations of perampanel 12 mg tablet and 12 mg oral suspension were very similar after long-term testing and when truncated to 12 hours.

- Bioequivalence criteria were met for all primary endpoints ($AUC_{(0-t)}$, $AUC_{(0-inf)}$, and C_{max} under fasted conditions.
- Bioequivalence criteria for primary endpoints were also met in the fed state.

Safety Summary:

The safety data of 116 subjects exposed to perampanel oral suspension in two bioequivalence trials were evaluated by the FDA. The clinical safety tests conducted in the trial were appropriate and capable of identifying major safety signals. Study 048 (as previously described), and Study 028; a randomized, open-label, 2-period, 2-sequence crossover study that compared the relative bioavailability of a single dose of perampanel 4 mg oral suspension to a single dose of perampanel 4 mg tablet (reference formulation) in 16 healthy subjects.

- Safety findings are consistent with data previously reported for partial-onset seizures and primary generalized tonic-clonic seizures[3-7]. No new safety signals were identified in either Study 048 or Study 028.
- The most common adverse reactions observed with FYCOMPA include dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, headache, vomiting, contusion, abdominal pain, and anxiety.

FYCOMPA has a boxed warning:

- To alert prescribers and patients about the risk of serious and life-threatening neuropsychiatric events, including: irritability, aggression, anger, hostility, and homicidal ideation and threats.
- Patients should be monitored for these reactions as well as for changes in mood, behavior, or personality that are not typical for the patient, particularly during the titration period and at higher doses.
- FYCOMPA should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening[1].

Dosing and administration of FYCOMPA is simple:

A favorable kinetic profile allows it to be dosed as a single tablet once-daily at bedtime

- POS: the recommended maintenance dose range is 4 – 12 mg daily.
- PGTC: the recommended maintenance dose is 8 mg daily[1].

Historically FYCOMPA is:

- approved in >45 countries,
- doses received in over 75,000 patients worldwide
- more than 1,600 patients have received FYCOMPA in epilepsy clinical trials
- available worldwide since 2012

In summary, FYCOMPA is:

- The first AMPA receptor antagonist with FDA-approval for management of Epilepsy
- FYCOMPA is orally administered once daily as a single dose (tablet or oral suspension)
- Available in multiple tablet strengths and an oral suspension
- Tablets: 2,4,6,8,10, & 12mg
- Suspension: 0.5mg/ml

With FDA approved indications for focal and primary generalized epilepsy Fycompa is considered a broad spectrum anti-seizure medication. Eisai recommends FYCOMPA be available in the Idaho Medicaid Program with access consistent to its label for the management of focal and generalized epilepsy.

References:

1. Food and Drug Administration. Fycompa prescribing information. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208277s000lbl.pdf. Accessed Oct. 25, 2016.
2. Food and Drug Administration. Available at: http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM503585.pdf. Accessed Oct. 25, 2016.
3. French JA, Krauss GL, Biton V et al. Adjunctive perampanel for refractory partial-onset seizures: randomized phase III study 304. Neurology. 2012 Aug 7;79(6):589-96.
4. French JA, Krauss GL, Steinhoff BJ et al. Evaluation of adjunctive perampanel in patients with refractory partial-onset seizures: results of randomized global phase III study 305. Epilepsia. 2013 Jan;54(1):117-25.
5. Krauss GL, Serratosa JM, Villanueva V et al. Randomized phase III study 306: adjunctive perampanel for refractory partial-onset seizures. Neurology. 2012 May 1;78(18):1408-15.
6. Krauss GL, Perucca E, Ben-Menachem E et al. Long-term safety of perampanel and seizure outcomes in refractory partial-onset seizures and secondarily generalized seizures: results from phase III extension study 307. Epilepsia. 2014 Jul;55(7):1058-68.
7. French JA, Krauss GL, Wechsler RT et al. Perampanel for tonic-clonic seizures in idiopathic generalized epilepsy. Neurology 2015; 85:1-8.