

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

Submission # 3

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

Gennrich, Jane

From: Eide, Tamara J.
Sent: Wednesday, October 26, 2016 10:22 AM
To: Gennrich, Jane
Subject: FW: Abilify Maintena and Rexulti Medicaid Testimony
Attachments: Abilify Maintena & Rexulti Idaho Medicaid Cover Letter & Testimony for Samantha Sweeney_October 2016.pdf; Abilify Maintena PI- Aug 2016.pdf; Rexulti PI- Sept 2016.pdf

Tami Eide, Pharm.D., BCPS

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208-364-1829
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From: Amy Moy [mailto:otsuka_amoy@irmsonline.net] **On Behalf Of** Otsuka-ProfessionalServices@otsuka-us.com
Sent: Wednesday, October 26, 2016 9:38 AM
To: Eide, Tamara J.
Cc: samantha.min@otsuka-us.com
Subject: Abilify Maintena and Rexulti Medicaid Testimony

Dear Dr. Tami Eide:

Thank you for your inquiry regarding Abilify Maintena® (aripiprazole) extended-release suspension, for intramuscular use and Rexulti® (brexpiprazole) for oral use.

Please find attached, the information you have requested:

- Abilify Maintena & Rexulti Idaho Medicaid Cover Letter & Testimony for Samantha Sweeney_October 2016
- Abilify Maintena PI- Aug 2016
- Rexulti PI- Sept 2016

Depending on the nature of your inquiry, some of the information contained in this response may be outside the approved prescribing information for Abilify Maintena and/or Rexulti. This response is not intended to offer recommendations for administering Abilify Maintena and/or Rexulti in a manner inconsistent

with its approved labeling.

I trust this information is helpful. Please consult the enclosed package inserts for complete prescribing information. If you have further questions or require additional information, please feel free to contact your Managed Market Liaison, Dr. Samantha Sweeney at samantha.min@otsuka-us.com.

Thank you for your interest in Abilify Maintena and Rexulti.

Yours truly,

Medical Information

Otsuka Pharmaceutical Development & Commercialization, Inc.

Samantha Sweeney, PharmD, MBA
Otsuka Pharmaceutical Development & Commercialization, Inc.

October 21, 2016

Idaho Medicaid
Pharmacy & Therapeutics Committee
Attention: Tami Eide, Pharm.D.

Dear Dr. Eide:

On behalf of Otsuka Pharmaceutical Development & Commercialization, Inc., I would like to submit the following new data for ABILIFY MAINTENA[®] (aripiprazole) and REXULTI[®] (brexpiprazole) for consideration for the Pharmacy & Therapeutics Committee meeting on November 18, 2016.

As noted in the enclosed proposed testimony:

- The post-hoc analysis from the first head-to-head study with ABILIFY MAINTENA versus paliperidone palmitate long-acting injectable (PLAI) showed statistically significant improvement for ABILIFY MAINTENA in the Readiness for Work Questionnaire (WoRQ) at 28 weeks (page 1, paragraph 9, line 47). The study also showed that the odds of being rated as ready for work at Week 28 were significantly better with ABILIFY MAINTENA vs PLAI treatment in patients 18-35 years (page 1, paragraph 9, line 51).
- The prescribing information for REXULTI was recently updated with the 52-week, randomized, double-blind, placebo-controlled maintenance study evaluating the efficacy and safety of REXULTI in adult patients with schizophrenia. It demonstrated significantly delayed time to exacerbation of psychotic symptoms/impending relapse for REXULTI compared to placebo (page 2, paragraph 13, line 69).
- A cost-effectiveness model that evaluated incremental cost per schizophrenia hospitalization averted showed REXULTI was a dominant strategy compared with lurasidone. Additionally, REXULTI treatment resulted in fewer relapses and hospitalizations, lower total cost of treatment, and higher quality of life compared to lurasidone (page 2, paragraph 14, line 82).

Thank you kindly for your consideration.

Sincerely,
Samantha Sweeney
West Managed Market Liaison

1 **ABILIFY MAINTENA[®] (aripiprazole) and REXULTI[®] (brexpiprazole) New Data Testimony – Idaho**
2 **Medicaid**

3
4 My name is Samantha Sweeney, and I am a Managed Market Liaison with Otsuka Pharmaceutical
5 Development & Commercialization, Inc. Thank you for this opportunity to provide new information on ABILIFY
6 MAINTENA and REXULTI to Idaho Medicaid. I will first highlight the new clinical points for ABILIFY MAINTENA
7 and then will transition the update to REXULTI.

8
9 **ABILIFY MAINTENA**

10 **INDICATIONS AND USAGE¹**

11 ABILIFY MAINTENA for extended-release injectable suspension is an atypical antipsychotic indicated for the
12 treatment of schizophrenia. ABILIFY MAINTENA is for deep intramuscular (IM) deltoid or gluteal injection to be
13 administered by a healthcare professional (HCP) only.

14
15 **MECHANISM OF ACTION¹**

16 The mechanism of action of aripiprazole in the treatment of schizophrenia is unknown. However, the efficacy of
17 aripiprazole may be mediated through a combination of partial agonist activity at D₂ and 5-HT_{1A} receptors and
18 antagonist activity at 5-HT_{2A} receptors.

19
20 ABILIFY MAINTENA is the first approved D₂ partial agonist in a once-monthly extended-release injectable
21 suspension.

22
23 **PHARMACOKINETICS^{1,2}**

24 ABILIFY MAINTENA is formulated to contain aripiprazole and no biotransformation is needed to derive the active
25 drug form. Based on unpublished pharmacokinetic modeling data of ABILIFY MAINTENA and oral aripiprazole
26 tablets, the estimated oral aripiprazole dose equivalence, calculated based on median area under the curve,² are
27 approximately 16mg for ABILIFY MAINTENA 300mg dose and 21mg for ABILIFY MAINTENA 400mg dose.

28
29 The T_{max} following administration of ABILIFY MAINTENA is 4 days for the deltoid muscle and 5 - 7 days for the
30 gluteal muscle. Additionally, Otsuka has a Starter Program that has been well established in numerous hospitals in
31 ID, which can help to provide timely treatment for your patients with schizophrenia.

32
33 **EFFICACY AND SAFETY^{1,3,4}**

34 The efficacy of ABILIFY MAINTENA for the treatment of schizophrenia was established in one short-term (12-
35 week) trial in acutely relapsed adults and one longer-term (52 week) maintenance trial in adults, details of which are
36 provided in the Full Prescribing Information (PI).

37
38 In addition to the aforementioned pivotal trials, ABILIFY MAINTENA was evaluated in the QUALIFY study, one of the
39 few randomized studies to directly compare two different atypical long-acting injectable antipsychotics (LAIs),
40 ABILIFY MAINTENA and paliperidone palmitate. This study was also the first to assess LAI treatment effectiveness
41 on a measure of health-related quality of life (QOL) as the primary outcome. Data demonstrating ABILIFY
42 MAINTENA's significant improvement on health-related QOL was previously presented to the ID P&T Committee. In
43 addition, superior improvements on the primary endpoint were accompanied after 28 weeks of treatment by
44 significantly lower risk for sexual dysfunction and also less prolactin elevation with ABILIFY MAINTENA versus
45 paliperidone palmitate.³

46
47 A post-hoc analysis of QUALIFY by Potkin et al⁴ investigated the effectiveness of ABILIFY MAINTENA 400 mg and
48 paliperidone palmitate on work readiness specifically in patients 18-35 years and >35 years. The Readiness for
49 Work Questionnaire (WoRQ) was included as an additional endpoint in the QUALIFY study and may reflect broader
50 functioning capacity in patients with schizophrenia. Significantly greater improvements in WoRQ total scores with
51 ABILIFY MAINTENA vs paliperidone palmitate were found in patients 18-35 years (P=0.0026). Also, the odds of
52 being rated as ready for work at Week 28 were significantly better with ABILIFY MAINTENA vs paliperidone palmitate
53 treatment in patients 18-35 years (P=0.003).

54
55 This concludes the update for ABILIFY MAINTENA and now, I will transition to REXULTI.

56
57 **REXULTI**

58 **INDICATIONS AND USAGE⁵**

59 REXULTI is an atypical antipsychotic indicated for use as an adjunctive therapy to antidepressants for the
60 treatment of major depressive disorder (MDD) and the treatment of schizophrenia.

61

62 **MECHANISM OF ACTION^{6,6,7}**

63 The mechanism of action of REXULTI in the treatment of MDD or schizophrenia is unknown. However, the efficacy of
64 REXULTI may be mediated through a combination of partial agonist activity at serotonin 5-HT1A and dopamine D2
65 receptors, and antagonist activity at serotonin 5-HT2A receptors. REXULTI is a distinct chemical entity that is not an
66 isomer or metabolite of any compound.⁶ In addition to the previously mentioned pharmacologic activities, REXULTI
67 exerts antagonistic activity at adrenergic alpha1B and alpha2C receptors.⁷

68
69 **52-WEEK MAINTENANCE STUDY⁸**

70 Fleischhacker et al conducted a 52-week, randomized, double-blind, placebo-controlled study to evaluate the efficacy
71 and safety of REXULTI as maintenance treatment in adults with schizophrenia (n=202 randomized). Patients with
72 acute exacerbation of schizophrenia were cross titrated from current antipsychotic treatment(s) to REXULTI over 1-4
73 weeks, prior to entering a 12-36 week single-blind stabilization phase on REXULTI 1-4 mg/day. Patients progressed
74 to the double-blind maintenance phase if they met a set of criteria for stability for 12 consecutive weeks. The study
75 showed a beneficial effect of REXULTI relative to placebo on the primary endpoint of time to exacerbation of
76 psychotic symptoms / impending relapse and significantly fewer patients relapsed in the REXULTI group compared
77 with placebo. During the stabilization phase, 8.8% of patients were withdrawn due to adverse events. During the
78 maintenance treatment phase, the withdrawal rates due to adverse events were 5.2% and 11.5% in the REXULTI and
79 placebo groups, respectively.

80
81 **COST EFFECTIVENESS DATA⁹**

82 Aigbogun et al conducted a decision analytic model evaluating a hypothetical cohort initiating treatment with
83 REXULTI 1-4 mg or lurasidone 40-80 mg over a 1-year period. At 6 months, patients with schizophrenia remained
84 on initial treatment or discontinued due to relapse, adverse events, or for other reasons. Data were obtained from
85 comparable long-term maintenance/acute trials and product labeling. Placebo-adjusted relative risks were used to
86 estimate treatment efficacy. Costs included treatment and drug costs. Primary outcomes were incremental cost per
87 relapse and hospitalizations avoided with REXULTI. Results of the model indicated that the use of REXULTI was a
88 dominant strategy (e.g., less costly and more effective) compared to lurasidone for the treatment of adults with
89 schizophrenia. In addition, per patient, REXULTI treatment resulted in fewer relapses and hospitalizations, lower
90 total cost of treatment, and higher quality of life (as estimated by health state utilities), compared to lurasidone.
91 Sensitivity analyses suggested that discontinuation rates due to relapse for both treatments and the daily cost of
92 REXULTI were major drivers of the incremental cost-effectiveness ratios.

93
94 **SAFETY^{1,5}**

95 In fair balance, I call your attention to the **BOXED WARNINGS** for ABILIFY MAINTENA and REXULTI which include
96 increased mortality in elderly patients with dementia-related psychosis and for REXULTI only, suicidal thoughts and
97 behaviors in children, adolescents, and young adults. For the complete **BOXED WARNING** and additional
98 information, please refer to the Full Prescribing Information for ABILIFY MAINTENA and REXULTI.

99
100 **SUMMARY**

101 In closing, Otsuka Pharmaceutical Development & Commercialization, Inc., respectfully asks that ABILIFY
102 MAINTENA and REXULTI be included on the preferred drug list. Thank you.

103
104 **REFERENCES:**

- 105 1. ABILIFY MAINTENA® (ARIPIPRAZOLE) FULL PRESCRIBING INFORMATION.
- 106 2. DATA ON FILE. ABIMAI-007
- 107 3. Potkin SG, et al. Reduced Sexual Dysfunction With Aripiprazole Once-Monthly Versus Paliperidone Palmitate: Results From
108 Qualify, A Head-To-Head Study In Schizophrenia. [Poster] Presented At The American Society Of Clinical
109 Psychopharmacology Annual Meeting, May 30-June 3, 2016; Scottsdale, AZ
- 110 4. Potkin SG, et al. Effects Of Aripiprazole Once-Monthly And Paliperidone Palmitate On Work Readiness In Patients From The
111 Qualify Study Stratified By Age. [Poster] Presented At The American Society Of Clinical Psychopharmacology Annual Meeting,
112 May 30-June 3, 2016; Scottsdale, AZ.
- 113 5. Rexulti Prescribing Information, September 2016
- 114 6. Maeda K, et al. Brexpiprazole I: in vitro and in vivo characterization of a novel serotonin-dopamine activity modulator. *J*
115 *Pharmacol Exp Ther.* 2014;350(3):589-604.
- 116 7. Citrome L et al. Brexpiprazole for schizophrenia and as adjunct for major depressive disorder: a systemic review of the efficacy
117 and safety profile for this newly approved antipsychotic – what is the number needed to treat, number needed to harm and
118 likelihood to be helped or harmed? *Int J Clin Pract* doi: 10.1111/ijcp.12714.
- 119 8. Fleischhacker WW, Hobart M, Ouyang J. Efficacy and Safety of Brexpiprazole (OPC-34712) as Maintenance Treatment in
120 Adults with Schizophrenia: A Randomized, Double-blind, Placebo-controlled Study. *Int J Neuropsychopharm.* 2016 Aug 26.
121 [Epub ahead of print]
- 122 9. Aigbogun et al. Relapse prevention: a cost-effectiveness analysis of brexpiprazole treatment in adult patients with
123 schizophrenia in the United States. [Poster] Presented at: *28th Annual U.S. Psychiatric and Mental Health Congress.*
124 September 10-13, 2015.