

Alabama Medicaid DUR Board Meeting Minutes

April 23, 2014

Members Present: Paula Thompson, Kelli Littlejohn, Bernie Olin, Denyse Thornley-Brown, Frank Pettyjohn, , Dan McConaghy, Jimmy Jackson, Rhonda Harden, Richard Glaze, Robert Moon

Also Present: Tiffany Minnifield, Heather Vega, Lori Thomas, Clemice Hurst, Brooke Devore, Erin Grant, Kayla Brackett

Present via Conference Call: Kristian Testerman

Members Absent: Donald Marks, Jared Johnson

Call to Order: The DUR meeting was called to order by P. Thompson at approximately 1:10p.m.

Review and Adoption of Minutes: The minutes of the January 22, 2014 meeting were presented and reviewed. D. Thornley-Brown made a motion to approve the minutes as amended and F. Pettyjohn seconded the motion. The motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of November 2013. She reported 7,813 total requests. She then reported 17,567 electronic requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for November 2013, L. Thomas reported that approximately 76% of all manual PAs and overrides were responded to in less than two hours, about 93% in less than four hours and 99% in less than eight hours. For the month of December 2013, L. Thomas reported 7,646 manual PA requests and 16,725 electronic PA requests. She reported that approximately 82% of PAs were responded to in less than two hours, 96-97% in less than four hours and 99% in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary. She reported 4,248,160 total prescriptions, 224,134 average recipients per month using pharmacy benefits and an average paid per prescription of \$66.89 for the months of July 2013 through December 2013.

Cost Management Analysis: L. Thomas reported an average cost per claim of \$71.27 for December 2013. L. Thomas reminded the Board members that the Maintenance Supply was phased in on October 1st. L. Thomas reported that an average cost per claim for a maintenance supply prescription was \$39.00. L. Thomas also reminded the Board members that Synagis season began October 1st. From the 4th Quarter 2013 Drug Analysis, L. Thomas reported 80.2% generic utilization, 11.2% brand single-source, 5% brand multi-source (those requests which required a DAW override) and 3.6% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 10/01/2013 – 12/31/2013, L. Thomas reported the top five drugs: hydrocodone-acetaminophen, amoxicillin, ProAir[®] HFA, montelukast sodium, and azithromycin. She then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 10/01/2013 – 12/31/2013: Abilify[®], Synagis[®], Vyvanse[®], Focalin XR[®], and Invega[®] Sustenna[®]. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L. Thomas reported the top five classes: Antipsychotic Agents, Corticosteroids (Respiratory Tract), Amphetamines, Miscellaneous Anticonvulsants, and Hemostatics.

UPDATES

Hydrocodone Utilization: L. Thomas briefly reminded the Board members that in 2012 the Board voted to review hydrocodone utilization data and in early 2013 a special letter was hand-delivered to the top 100 prescribers of hydrocodone. L. Thomas reviewed the number of hydrocodone claims from the past three years. L. Thomas presented a chart comparing the top 100 prescribers of hydrocodone in 2012 and 2013. This chart will be revisited at the next meeting due to changes and updates from the Board. A sample letter will be presented to the Board members during the July meeting. This letter will be hand-delivered to the top 100 prescribers of hydrocodone. The letter will inform each physician of their ranking based on the number of hydrocodone prescriptions written.

RDUR Intervention Report: L. Thomas informed the Board members that HID and Alabama Medicaid entered into a new contract which began November 1st. With this new contract, HID will review 2000 profiles per quarter. L. Thomas informed Board members that HID also began Lock-In services for Alabama Medicaid on November 1st. L. Thomas explained that Lock-In criterion is similar to RDUR criterion and that HID will target 200 recipients per month which hit against the Lock-In criteria. L. Thomas presented the RDUR Activity Report for November 2013. She reported 676 profiles reviewed and 504 letters sent with 57 responses received as of the date of the report. She reported 37 of 53 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters were the use of benzodiazepines in patients with a history of drug abuse. L. Thomas then presented the RDUR Activity Report for December 2013. She reported 722 profiles reviewed and 508 letters sent with 89 responses received as of the date of the report. She reported 35 of 66 physicians indicated that they found the RDUR letters “useful” or “extremely useful”.

Proposed Criteria: L. Thomas presented the proposed set of 36 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 36 criteria, results from the criteria vote returned 35 approved and 1 approved as amended (#15).

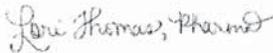
Medicaid Update: T. Minnifield began the Medicaid Update by reminding the Board members that all Medicaid information discussed is available online, as well as any new Medicaid ALERTs.

P & T Committee Update: C. Hurst began the P&T Update by informing the Board that the last meeting was scheduled for February 12, 2014, but was cancelled due to lack of a quorum. The next P&T meeting is scheduled for May 14, 2014 at 9am and will cover the Skin and Mucous Membrane Agents, Alzheimer’s Agents, Antidepressants, Cerebral Stimulants Used for ADHD, Wakefulness Promoting Agents, Genitourinary Smooth Muscle Relaxants, and Anxiolytics, Sedatives, and Hypnotics. C. Hurst also discussed the April 2014 PDL changes, which included name brand TOBI inhalation solution becoming the preferred agent with no PA required.

New Business: T. Minnifield notified the Board that the next DUR meeting will be held on July 23, 2014. P. Thompson made a motion to adjourn the meeting. The motion was seconded by D. Thornley-Brown. A voice vote to adjourn was unanimous. The meeting was adjourned at 1:55p.m.

Next Meeting Date: The next DUR Board meeting will be held on July 23, 2014.

Respectfully submitted,



Lori Thomas, PharmD

3. Levomilnacipran / Moderate Renal Impairment ___√___

Alert Message: Fetzima (levomilnacipran) is predominately excreted by the kidney so for patients with moderate renal impairment (CrCl 30-59 mL/min), the maintenance dose of levomilnacipran should not exceed 80 mg once daily. For patients with severe renal impairment (CrCl 15-29 mL/min), the maintenance dose should not exceed 40 mg once daily. No dosage adjustment is recommended in mild renal impairment. Levomilnacipran is not recommended for patients with ESRD.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C (Include)

Levomilnacipran

CKD Stage 3

Max Dose: 80mg/day

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

4. Levomilnacipran / Severe Renal Impairment & ESRD ___√___

Alert Message: Fetzima (levomilnacipran) is predominately excreted by the kidney so for patients with severe renal impairment (CrCl 15-29 mL/min), the maintenance dose should not exceed 40 mg once daily. Levomilnacipran is not recommended for patients with ESRD. For patients with moderate renal impairment (CrCl 30-59 mL/min), the maintenance dose of levomilnacipran should not exceed 80 mg once daily. No dosage adjustment is recommended in mild renal impairment.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C (Include)

Levomilnacipran

CKD Stage 4

CKD Stage 5

ESRD

Max Dose: 40 mg/day

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

5. Levomilnacipran / Non-adherence ___√___

Alert Message: Based on the refill history, your patient may be under-utilizing Fetzima (levomilnacipran). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence

Drugs/Diseases

Util A

Util B

Util C

Levomilnacipran

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Keene MS. Confusion and Complaints: The True Cost of Noncompliance in Antidepressant Therapy. Medscape Psychiatry & Mental Health. 2005;10(2). Available at: <http://www.medscape.com/viewarticle/518273>

9. Levomilnacipran / Serotonergic Agents

_____✓_____

Alert Message: Caution should be exercised when Fetzima (levomilnacipran) is administered with other serotonergic drugs due to the risk of serotonin syndrome. Levomilnacipran is a serotonin and norepinephrine reuptake inhibitor and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin. If concurrent use is clinically warranted, monitor closely for signs and symptoms of serotonin syndrome.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Levomilnacipran	SSRIs	Nefazodone	Buspirone
	SNRIs	Mirtazapine	Tramadol
	TCAs	Trazodone	Fentanyl
	Triptans	Lithium	Cyclobenzaprine
	Ergot Alkaloids	Meperidine	Rasagiline

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

10. Levomilnacipran / Drugs Affecting Coagulation

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Alert Message: Concurrent use of Fetzima (levomilnacipran) and medications that enhance bleeding potential (e.g., anticoagulants, thrombolytics and NSAIDs) may increase the risk of a bleeding complication. Levomilnacipran, which inhibits serotonin reuptake, may cause impaired platelet aggregation due to platelet serotonin depletion.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Levomilnacipran	NSAIDs	Dipyridamole	Dabigatran
	Aspirin	Cilostazol	Dalteparin
	Warfarin	Clopidogrel	Anagrelide
	Apixaban	Prasugrel	Enoxaparin
	Fondaparinux	Ticagrelor	
	Rivaroxaban	Ticlopidine	

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Bismuth-Evenzal Y, Gonopolsky Y, Gurwitz D, et al. Decreased Serotonin Content and Reduced Agonist-induced Aggregation in Platelets of Patients Chronically Medicated with SSRI Drugs. J Affect Disord. 2012 Jan;136(1-2):99-103.

11. Levomilnacipran / Hypertension, Cardiovascular Disorders

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Alert Message: Caution should be exercised in treating patients with pre-existing hypertension, cardiovascular, or cerebrovascular conditions that might be compromised by increases in blood pressure and/or heart rate as Fetzima (levomilnacipran) has been shown to increase both. For patients who experience a sustained increase in heart rate and/or blood pressure while receiving levomilnacipran, discontinuation or other medical intervention should be considered.

Conflict Code: MC – Drug (Actual) Diseased Precaution/Warning
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Levomilnacipran	Hypertension	Ischemic Heart Disease	
	Stroke	Heart Failure	
	Conduction Disorders	Cerebral Ischemia	
	Dysrhythmias	Myocardial Infarction	

References:

Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

12. Posaconazole / CYP3A4 Substrates that Prolong QT Interval ✓ _____

Alert Message: Noxafil (posaconazole) is contraindicated with CYP3A4 substrates that prolong the QT interval. Posaconazole is a strong CYP3A4 inhibitor and concurrent use with a CYP3A4 substrate may result in increased substrate plasma concentrations, leading to QTc prolongation and torsades de pointes. In addition, posaconazole has been associated with prolongation of the QT interval.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Posaconazole	Trazodone	Sunitinib	Erythromycin	Solifenacin
	Vardenafil	Dasatinib	Clarithromycin	Vemurafenib
	Pimozide	Lapatinib	Telithromycin	Mifepristone
	Venlafaxine	Nilotinib	Haloperidol	
	Disopyramide	Indacaterol	Chloroquine	
	Amiodarone	Rilpivirine	Mefloquine	
	Telithromycin	Clozapine	Iloperidone	
	Alfuzosin	Quetiapine	Ondansetron	
	Crizotinib	Dofetilide	Propafenone	
	Ziprasidone	Methadone	Quinine	
	Asenapine	Citalopram	Ranolazine	
	Dronedarone	Ranolazine	Saquinavir	

References:

Noxafil Prescribing Information, Nov. 2013, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2013 Elsevier/Gold Standard.

Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

13. Posaconazole / Sirolimus ✓ _____

Alert Message: The concurrent use of Noxafil (posaconazole) is contraindicated with Rapamune (sirolimus) due to risk of sirolimus toxicity. Co-administration of these agents has been shown to increase sirolimus blood concentrations by approximately 9-fold. Posaconazole is a strong inhibitor of sirolimus CYP3A4-mediated metabolism and both drugs are substrates for P-gp efflux protein.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Posaconazole Sirolimus

References:

Noxafil Prescribing Information, Nov. 2013, Merck Sharp & Dohme corp.

Clinical Pharmacology, 2013 Elsevier/Gold Standard.

14. Posaconazole / Cyclosporine & Tacrolimus ✓ _____

Alert Message: Caution should be exercised when co-administering Noxafil (posaconazole) with a calcineurin-inhibitor (cyclosporine and tacrolimus). Concurrent use of posaconazole with these agents has been shown to increase the whole blood trough concentrations of the calcineurin-inhibitor. Frequent monitoring of cyclosporine or tacrolimus whole blood concentrations should be performed during and at discontinuation of posaconazole treatment and the calcineurin-inhibitor dose adjusted accordingly.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Posaconazole Cyclosporine
 Tacrolimus

References:

Noxafil Prescribing Information, Nov. 2013, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2013 Elsevier/Gold Standard.

15. Non First-line Antihypertensives / Hypertension / JNC 8 4 Classes _____ ✓ _____

Alert Message: The JNC 8 recommends the use of either a CCB, ACEI, ARB or thiazide-type diuretic as initial therapy to control hypertension in non black adult patients 18 years of age and older, if no contraindication or compelling indication exists. Recommended initial therapy in black patients is a thiazide-type diuretic or CCB, alone or in combination. If goal blood pressure is not achieved with an initial drug refer to the JNC 8 for recommended strategies for adding antihypertensive agents.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A

Other Antihypertensives:
Alpha/Beta-Adrenergic Blockers
Antiadrenergics-Centrally Acting
Antiadrenergics-Peripherally Acting
Selective Aldosterone Receptor Antagonist
Beta-Blockers

Util B

Hypertension

Util C (Negating)

Chronic Kidney Disease
ACE Inhibitors
ARBs
CCBs
Thiazide-type Diuretics

Age Range: 18 – 999 yoa

References:

James PA, Oparil S, Carter BL, et al. 2014 Evidence-based Guideline for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eight Joint National Committee (JNC 8). JAMA 2014; DOI:10.1001/jama.2013.284427. Available at: <http://jama.jamanetwork.com/journal.aspx>.

16. Vortioxetine / Overutilization / Negating CYP Inducers & Inhibitors _____ ✓ _____

Alert Message: The manufacturer’s maximum recommended daily dose of Brintellix (vortioxetine) is 20 mg in extensive CYP2D6 metabolizers. The efficacy and safety of doses above 20 mg/day have not been evaluated in controlled clinical trials. The vortioxetine dose should not exceed 10mg/day in CYP2D6 poor metabolizers.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A

Vortioxetine

Util B

Util C (Negating)

Bupropion	Rifampin	Phenytoin	Carbamazepine
Fluoxetine	Rifabutin	Phenobarbital	Quinidine
Paroxetine	Rifapentine	Primidone	

Max Dose: 20mg/day

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

17. Vortioxetine 15 & 20 mg / Strong CYP2D6 Inhibitors _____ ✓ _____

Alert Message: The manufacturer recommends that the daily dose of Brintellix (vortioxetine) be reduced by half when patients are receiving a strong CYP2D6 inhibitor (i.e., bupropion, fluoxetine, paroxetine and quinidine) concomitantly. The dose should be increased to the original level when the CYP2D6 inhibitor is discontinued.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A

Vortioxetine 15mg
Vortioxetine 20mg

Util B

Bupropion
Fluoxetine
Paroxetine
Quinidine

Util C

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

18. Vortioxetine / Strong CYP Inducers

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Alert Message: The concurrent use of Brintellix (vortioxetine) with a strong CYP inducer (e.g., rifampin, carbamazepine, and phenytoin) for greater than 14 days may necessitate an increase in the vortioxetine dose but the dose should not exceed three times the original dose. Vortioxetine is extensively metabolized via multiple cytochrome isozymes (e.g., CYP2D6, CYP3A4/5, CYP2C9 and CYP2C8) and use with CYP inducers may result in decreased vortioxetine plasma concentrations.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>			<u>Util C</u>
Vortioxetine	Carbamazepine Phenytoin	Rifapentine Phenobarbital	Rifampin Rifabutin	Primidone

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
FDA Drug Development and Approval Process (Drugs): Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Available at:
<http://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/druginteractionslabeling/ucm093664.htm>

19. Vortioxetine / Non-adherence

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Alert Message: Based on the refill history, your patient may be underutilizing Brintellix (vortioxetine). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vortioxetine		

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Keene MS. Confusion and Complaints: The True Cost of Noncompliance in Antidepressant Therapy. Medscape Psychiatry & Mental Health. 2005;10(2). Available at: <http://www.medscape.com/viewarticle/518273>

20. Vortioxetine /Pediatric Use (Black Box)

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Alert Message: The safety and effectiveness of Brintellix (vortioxetine) in the pediatric population has not been established.

Conflict Code: TA – Therapeutic Appropriateness
Util A Util B Util C

Vortioxetine

Age Range: 0-18 yoa

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

21. Vortioxetine /MAOIs

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Alert Message: Brintellix (vortioxetine) is contraindicated for concurrent use in patients receiving MAOI therapy intended to treat psychiatric disorders due to risk of serotonin syndrome. Vortioxetine should not be used within 14 days of discontinuing treatment with an MAOI and treatment with an MAOI should not be initiated within 21 days of discontinuation of vortioxetine.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vortioxetine	Isocarboxazid Phenelzine Tranylcypromine Selegiline Transdermal	

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

22. Vortioxetine /Linezolid

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Alert Message: Brintellix (vortioxetine) is contraindicated for concurrent use with Zyvox (linezolid), a reversible, non-selective inhibitor of MAOI, due to risk of serotonin syndrome. There may be circumstances when it is necessary to initiate treatment with linezolid in a patient taking vortioxetine. If so, vortioxetine should be discontinued before initiating linezolid treatment.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vortioxetine	Linezolid	

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

23. Vortioxetine /Serotonergic Agents

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Alert Message: Caution should be exercised when Brintellix (vortioxetine) is administered with other serotonergic drugs. Vortioxetine is a serotonin modulator/stimulator and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin and increase the risk of serotonin syndrome (e.g., mental status changes, hypertension, vasoconstriction, and neuronal aberrations).

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vortioxetine	SSRIs SNRIs TCAs Tryptans Ergot Alkaloids Buspirone Tramadol	Nefazodone Mirtazapine Trazodone Lithium Meperidine Fentanyl

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

Criteria Recommendations

*Accepted Approved Rejected
As
Amended*

24. Vortioxetine /Drugs Affecting Coagulation

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Alert Message: Concurrent use of Brintellix (vortioxetine) and medications that enhance bleeding potential (e.g., anticoagulants, thrombolytics and NSAIDS) may increase the risk of a bleeding complication. Vortioxetine, which inhibits serotonin reuptake, may cause impaired platelet aggregation due to platelet serotonin depletion.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vortioxetine	NSAIDS Aspirin Warfarin Apixaban Fondaparinux Rivaroxaban Dabigatran Dalteparin	Dipyridamole Cilostazol Clopidogrel Prasugrel Ticagrelor Ticlopidine Anagrelide Enoxaparin

References:

Brintellix Prescribing Information, September 2013, Takeda Pharmaceuticals.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

25. Perampanel / Overuse

___✓___ ___ ___

Alert Message: The manufacturer's maximum recommended dose of Fycompa (perampanel) is 12 mg once daily at bedtime.

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Perampanel		Hepatic Impairment

Max Dose: 12mg/day

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

26. Perampanel / Overuse Hepatic Impairment

___✓___ ___ ___

Alert Message: The manufacturer's maximum recommended daily dose of Fycompa (perampanel) is 6 mg and 4 mg once daily at bedtime for patients with mild and moderate hepatic impairment, respectively. Perampanel use is not recommended in patients with severe hepatic impairment.

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Perampanel		Hepatic Impairment

Max Dose: 6mg/day

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

27. Perampanel / Renal Impairment & Hemodialysis

Alert Message: Fycompa (perampanel) use is not recommended in patients with severe renal impairment or on hemodialysis.

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Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel	CKD Stage 4 & 5 Hemodialysis	

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

28. Perampanel / Levonorgestrel Contraceptives

Alert Message: Use of Fycompa (perampanel) with oral or implant contraceptives containing levonorgestrel may render them less effective. Concurrent use of perampanel at a dose of 12mg/day reduced levonorgestrel exposure by approximately 40%. Additional non-hormonal forms of contraception are recommended.

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Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel	Levonorgestrel Contraceptives	

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

29. Perampanel / CYP3A4 Inducers Anticonvulsants

Alert Message: The concurrent use of Fycompa (perampanel) with an antiepileptic drug (AED) that induces CYP3A4-mediated metabolism can result in decreased plasma levels of perampanel and loss of therapeutic effect. The starting dose of perampanel should be increased in the presence of enzyme-inducing AEDs. When an enzyme-inducing AED is introduced or withdrawn, patients should be closely monitored and perampanel dose adjusted if needed.

____√____ _____ _____

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel	Carbamazepine Oxcarbazepine Phenytoin Phenobarbital Primidone	

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

30. Perampanel / Strong CYP3A4 Inducers (Non-AEDs) ✓ _____

Alert Message: The concurrent use of Fycompa (perampanel) with a strong CYP3A4 inducer (e.g., rifampin and nevirapine) should be avoided. Perampanel is a CYP3A4 substrate and concomitant use with a potent inducer may result in significantly decreased perampanel plasma levels and loss of therapeutic effect.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel	Rifampin Rifapentine Rifabutin Nevirapine	

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

31. Perampanel / CNS Depressants ✓ _____

Alert Message: The concurrent use of Fycompa (perampanel) and CNS depressants including alcohol may increase CNS depression. Patients should limit activity until they have experience with concomitant use of CNS depressants.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel	Antidepressants Antihistamines - Sedating Antipsychotics Barbiturates Benzodiazepines Muscle Relaxants Narcotics Hypnotics	

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

32. Perampanel / Therapeutic Appropriateness (0-11 yoa) ✓ _____

Alert Message: The safety and effectiveness of Fycompa (perampanel) in pediatric patients less than 12 years old have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Perampanel		

Age Range 0-11 yoa

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

33. Perampanel / Black Box Warning

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Alert Message: Serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, homicidal ideation and threats have been reported in patients taking Fycompa (perampanel). Perampanel dosage should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Perampanel

References:

Fycompa Prescribing Information, June 2013, Eisai.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

34. Perampanel / Non-adherence

___√___

Alert Message: Based on refill history, your patient may be under-utilizing Fycompa (perampanel). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence

Drugs/Diseases

Util A

Util B

Util C

Perampanel

References:

Fycompa Prescribing Information, June 2013, Eisai.
Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.
Faught ER, Weiner JR, Guerin A, et al. Impact of Nonadherence to Antiepileptic Drugs on Health Care Utilization and Costs: Findings from the RANSOM Study. Epilepsia 2009;50(3):501-509.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.

35. Canagliflozin / Nonadherence

___√___

Alert Message: Based on refill history, your patient may be under-utilizing Invokana (canagliflozin). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR - Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Canagliflozin

References:

Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.

36. Testosterone / History of Cardiovascular/Cerebrovascular Disease ✓

Alert Message: The FDA is evaluating the risk of stroke, heart attack and death in men taking FDA-approved testosterone products. Reassessment of this testosterone safety issue is based on the recent publication of two separate studies that suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy. Prescribers should consider whether the benefits of testosterone treatment is likely to exceed the potential risks of treatment.

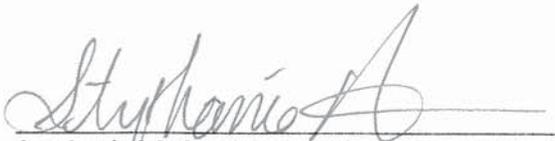
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Testosterone		Myocardial Infarction Stroke Angina Arrhythmia Heart Failure Hypertension Peripheral Vascular Disease Ischemic Heart Disease

Gender: Male

References:

FDA Drug Safety Communications; FDA Evaluating Risk of Stroke, Heart Attack and Death with FDA-approved Testosterone Products. [01-21-2014].
Vigen R, O'Donnell CI, Baron AE, et al. Association of Testosterone Therapy with Mortality, Myocardial Infarction and Stroke in Men with Low Testosterone Levels. JAMA 2013;310(17):1829-1836.
Finkle WD, Greenland S, Ridgeway GK, Adams JL, Frasco MA, et al. (2014) Increased Risk of Non-Fatal Myocardial Infarction Following Testosterone Therapy Prescription in Men. PLoS ONE 9(1): e85805.
doi:10.1371/journal.pone.0085805


Stephanie McGee Azar, Acting Commissioner

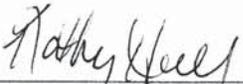
Approve () Deny

7-16-14
Date


Robert Moon, M.D., Deputy Commissioner
and Medical Director

Approve () Deny

7-16-14
Date


Kathy Hall, Deputy Commissioner

Approve () Deny

7/14/14
Date