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Governor

STATE OF NEVADA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
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MICHAEL J. WILLDEN
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NOTICE OF OPEN PUBLIC MEETING

The Division of Health Care Financing and Policy (DHCFP) Pharmacy and Therapeutics Committee conducted a public meeting on **March 27, 2014**, beginning at **1:00 p.m.** at the following location:

Palace Station Hotel and Casino
Salon A
2411 W. Sahara Ave
Las Vegas, NV 89102
702-367-2411

Committee Members Present:

Michael Hautekeet, RPh; Mark Decerbo, Pharm.D.; David Fluitt, RPh; Adam Zold, Pharm.D.; Evelyn Chu, Pharm.D.; Shamim Nagy, MD, Chairwoman, MD; Joseph Adashek, MD; Constance Kalinowski, MD

Committee Members Absent:

Weldon Havins, MD; Amir Qureshi, MD

Others Present:

DHCFP: Gabriel Lither, Deputy Attorney General; Coleen Lawrence, Chief Program Services; Mary Griffith, RN, Social Services Specialist

Catamaran: Carl Jeffery, PharmD; Kevin Whittington, RPh

HPES: Beth Slamowitz, Pharm.D.

Others: Evette Brooks, Actelion; Rupa Shah, Purdue; Patricia Moty, Supeanus; Phil Walsh, Sunovian; Ben Skoog, Biogen Idec; Camile Kerr, Allergan; Brooks Hubbard, BIPI; Bill O'Neill, BIPI; Brian Streng, GSK; Deron Grothe, Teva; Don Ceteuland, AZ; Tom O'Connor, Novartis; Marilyn Semenchun, Eisai; Carla McSpadden, Forest; Kara Sperandeo, Forest; Marcus Suon, Forest; Larry Curtis, Forest; Michael Sullivan, Biogen; Naresh Singh, MD; Sandy Sierawski, Pfizer; Sohyela Aziz Eisai; Anthony Duca, Eisai; Melissa Walsh, Novartis; Raphael Wilburn, AstraZeneca; Sital Patel, Student; Richard Tran, Student; Charissa

Anne, J&J; Lisa Wilson, J&J; Laura Litzenbuerger, Janssen; Peter Berggren, Janssen; Ekfran Arion, Merck; Cathy Gross, Vertex; Molly Meekin, Hyperion; Charlie Collins, Gilead; Betty Chan, Gilead; Jerry Cerae, UMC

I. CALL TO ORDER AND ROLL CALL

Meeting called to order at 1:02 PM by Chairwoman Nagy.

Roll call of Committee members:
Connie Kalinowski, MD
Adam Zold, Pharm.D.
Mark Decerbo, Pharm.D.
Joseph Adashek, MD
Shamim Nagy, MD, Chairwoman, MD
Mike Hautekeet, RPh
David Fluitt, RPh
Evelyn Chu, Pharm.D.

II. PUBLIC COMMENT

Shamin Nagy, MD, Chairwoman: No public comment.

III. Review and Approval of the September 26, 2013 Meeting Minutes

A motion was made and seconded to approve the minutes.

Shamin Nagy, MD, Chairwoman: All in favor?

Committee votes unaminous, Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

IV. STATUS UPDATE BY DHCFP

Shamin Nagy, MD, Chairwoman: Status update from DHCFP.

Shamim Nagy, MD, Chairwoman: Any public comment? No public comment, Coleen.

Coleen Lawrence: Good afternoon, for the record, my name is Coleen Lawrence, Chief of Program Services for Nevada Medicaid. The Ordering, Prescribing and Referring Physician initiative is still on track for implementation for pharmacies. Web announcements and other communications will be

forthcoming. The initiative is a mandate from the ACA. Nevada Medicaid will be phasing in the other providers for this requirement.

Nevada Medicaid did choose the 100% expansion for the newly eligibles, our childless adults. The benefit plan for the newly eligible is the same as what is offered to other Medicaid recipients. There is still a backlog of applications. These applicants will become retro-eligible.

We have another State Plan Amendment. A benzo and barb SPA was done last year because of the Part D coverage. Now another one is required, but no changes to coverage is coming.

ICD-10, Medicaid will be compliant in October 2014. All our ICD-9s are being converted to ICD-10s. Many of the pharmacy policies are based on coding for diagnosis. The public hearing for the policy changes will state that we are not changing policy. We are only updating the diagnosis codes. That will be scheduled for September. Watch the Public Hearing Page of our website.

The supplemental rebate state plan amendment. There is some confusion regarding our supplemental rebate agreement. The confusion is how to submit a State Plan Amendment. The rebate team has had some conversations, and I am working with CMS. We have been working with them for about 6 months. Our goal is July 1st. It is coming down to what technical information needs to be submitted.

With the ACA, we are doing a dispensing fee survey and ingredient cost review for our pharmacies. We have a survey out to all our pharmacies. That will be out for 6-8 weeks right now. Then we have to look at ingredient cost because of the change with FUL that has occurred at the Federal level. Pharmacy is very busy with Nevada Medicaid.

V. ESTABLISHED DRUG CLASSES

A. RESPIRATORY: Inhaled Anticholinergic Agents

Public Comment:

Bill O'Neil – representing Combivent, Respimat and Spiriva gave an overview of Combivent Inhaler information on dosing and delivery. Spiriva information was provided on clinical studies.

Dr. Naresh Singh – representing both Boehringer Ingelheim and Forrest, requested to continue to cover Spiriva but to add Tudorza. Because of dry mouth in some people with Spiriva and difficulty with packaging, he requested Tudorza be added as preferred.

Kara Sperandeo – representing Forest, requested Tudorza be preferred. She provided epidemiology data and clinical data.

Carl Jeffery, PharmD presented the following slides, and gave an overview of the agents and clinical information.

Indication	Single Entity Agents			Combination Products
	Aclidinium	Ipratropium	Tiotropium	Ipratropium and Albuterol
Long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema	✔			
Long-term, once-daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema			✔	
Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema		✔		
Reduce exacerbations in chronic obstructive pulmonary disease patients			✔	
Patients with chronic obstructive pulmonary disease on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator				✔ Combivent®, Combivent Respimat®
Treatment of bronchospasm associated with chronic obstructive pulmonary disease in patients requiring more than one bronchodilator				✔ DuoNeb®

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RESPIRATORY: Inhaled Anticholinergic Agents

- Class of bronchodilators primarily used in the management of COPD
- Work via the inhibition of acetylcholine at parasympathetic sites in bronchial smooth muscle resulting in bronchodilation
- Combivent MDI no longer available, switched to non-CFC Combivent Respimat

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Beier et al (abstract)[30] Aclidinium 400 µg BID vs tiotropium 18 µg QD vs placebo	AC, DB, MC, PC, RCT Patients with moderate-to-severe COPD	N=414 6 weeks	Primary: Mean change from baseline in FEV_1 $AUC_{0–24}$ at six weeks Secondary: Change from baseline in FEV_1 $AUC_{12–24}$, COPD symptom total score and, additional symptoms questionnaire and safety	Primary: Compared to placebo, there was a significant change from baseline in FEV_1 $AUC_{0–24}$ at six weeks with aclidinium (150 mL; *P*<0.0001) and tiotropium (140 mL; *P*<0.0001). Secondary: The change from baseline in FEV_1 $AUC_{12–24}$ at six weeks was significantly greater with aclidinium (160 mL; *P*<0.0001) and tiotropium (123 mL; *P*<0.0001) compared to placebo. Significant improvements in total symptom scores over six weeks were numerically greater with aclidinium (*P*<0.0001) than tiotropium (*P*<0.05) compared to placebo. Only aclidinium significantly reduced the severity of early-morning cough, wheeze, shortness of breath, and phlegm, and of nighttime symptoms compared to placebo (*P*<0.05). The incidence of adverse events was similar between treatments. Few anticholinergic adverse events (<1.5%) or serious events (<3%) occurred in any group.

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Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Van Noord et al[31] Tiotropium 18 µg QD vs ipratropium 40 µg QID	DB, DD, MC, PG Patients with stable COPD with mean age of 65 years and average FEV_1 41% of predicted values	N=288 15 weeks	Primary: Changes in FEV_1 and FVC Secondary: Daily records of PEF, use of albuterol	Primary: The FEV_1 response, at all time points on days eight, 50 and 92, was significantly greater following tiotropium compared to ipratropium (differences of 0.09, 0.11, and 0.08 L; *P*<0.05). The results for FVC closely reflect those obtained for FEV_1. Tiotropium performed consistently better than ipratropium. The differences in trough FEV_1 values were most pronounced (*P*<0.001), whereas differences in peak FEV_1 increase did not reach statistical significance (*P*>0.05). Secondary: The improvement in both morning and evening PEF was greater in the tiotropium group than in the ipratropium group. The difference in morning PEF between the groups was statistically significant up through week 10 (*P*<0.05). For evening PEF, the difference reached statistical significance during the first seven weeks of the treatment period (*P*<0.05). In both groups, there was a drop in the use of rescue albuterol, the reduction being greater in the tiotropium group than in the ipratropium group (*P*<0.05).

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Study and Drug Regimen	Study Design and Demographics	Sample Size Study Duration	End Points	Results
Niewoehner et al[33] Tiotropium 18 µg QD vs ipratropium and albuterol MDI QID (fixed-dose combination product) Concomitant medications allowed throughout the trial included ICSs, theophylline, and stable doses of prednisone (not to exceed 10 mg daily or its equivalent).	Pooled analysis of 2 RCTs Patients ≥40 years of age with COPD, current or former cigarette smoker with lifetime consumption of ≥10 pack-years, postbronchodilator FEV_1 ≤70% of predicted, pre bronchodilator FEV_1 ≤65% of predicted, and FEV1/FVC ≤70% who were receiving ipratropium and albuterol (18 to 103 µg) MDI for ≥1 month	N=676 12 weeks	Primary: Trough FEV_1, FEV_1 AUC_{0-6}, and FVC Secondary: PEF, albuterol rescue therapy, total albuterol use, and patient global evaluations	Primary: Mean change in trough FEV_1 was significantly larger in the tiotropium group compared to the ipratropium and albuterol group (difference, 86 mL; 95% CI, 49 to 133 mL; *P*<0.0001). Mean FEV_1 AUC_{0-6} in the tiotropium arm was statistically non-inferior to the ipratropium and albuterol arm (difference, 17 mL; 95% CI, -21 to 56 mL; *P*=0.0003), but not statistically superior (*P*=0.37). Mean peak FEV_1 responses were larger in the ipratropium/albuterol arm compared with the tiotropium arm, with differences ranging from 120 to 134 mL (*P*<0.001). Differences in FVC responses were similar to those observed with the FEV_1. Mean FVC trough for the tiotropium group was significantly larger on study days 42 and 84 (*P*<0.01) compared with the ipratropium and albuterol group, but the AUC_{0-6} was not (*P*>0.5). Secondary: Weekly mean morning PEF and FEV_1 were both significantly larger in the tiotropium arm compared with the ipratropium and albuterol arm for morning measurements (*P*<0.05), but not for evening measurements. No significant treatment-related differences were detected in albuterol rescue therapy, physician global evaluations, or patient reported shortness of breath. Total albuterol use was significantly lower in the tiotropium group compared to the ipratropium/albuterol group (5.3 vs 6.8 puffs per day based on weekly means; *P*<0.001). Mean patient global evaluations were statistically significantly better (*P*<0.05) for the tiotropium group on study day 42, but not on study day 84.

Study and Drug Regimen	Study Design and Demographics	Sample Size Study Duration	End Points	Results
Dorinsky et al[36] Albuterol 180 µg QID via MDI vs ipratropium 36 µg QID via MDI vs equivalent dose of ipratropium/albuterol via MDI	DB, MC, PG, RETRO, RCT Patients ≥40 years of age with COPD, >10 pack-year smoking history, regularly using at least two bronchodilators for symptom control during 3 months prior to the trials, FEV_1 ≤65% predicted, FEV_1/FVC ratio ≤70%	N=1,067 85 days	Primary: FEV_1 and FVC values before and after administration of the study medications (bronchodilator response defined as an increase in FEV_1 of 12 and 15% from baseline) Secondary: Not reported	Primary: The percentage of patients demonstrating a 15% increase in FEV_1 at 15 and 30 minutes after medication administration was significantly higher in the ipratropium/albuterol group compared to the individual treatment groups on all test days, and significantly higher than the individual treatment groups after 60 and 120 minutes on test day one and two (*P*<0.05). The overall decline in percentage of patients demonstrating a 15% increase in FEV_1 in all groups was small and ranged from two to eight percent (*P* value not reported). A significantly greater percentage of patients demonstrated a 12 or 15% increase in FEV_1 on three or more test days in the ipratropium/albuterol group compared to the individual treatment groups (*P*<0.05). Secondary: Not reported

Clinical Guideline	Recommendations
Global Initiative for Chronic Obstructive Lung Disease: **Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2013)**[1]	<u>Treatment</u> • Patients should be instructed to avoid the exacerbating exposure. This includes assisting the patient in smoking cessation attempts and counseling the patient on how to avoid pollutant exposures. • The management of COPD should be individualized to address symptoms and improve the patient's quality of life. • None of the medications for COPD have been shown to modify long-term decline in lung function. **<u>Treatment should be focused on reducing symptoms and complications.</u>** • Administer bronchodilator medications on an as needed or regular basis to prevent or reduce symptoms and exacerbations. • Principle bronchodilators include β_2-agonists, anticholinergics and theophylline used as monotherapy or in combination. • **<u>The use of long-acting bronchodilators is more effective and convenient than short-acting bronchodilators</u>**. • For single-dose, as needed use, there is no advantage in using levalbuterol over conventional nebulized bronchodilators. • Inhaled corticosteroids (ICSs) should be used in patients with an FEV_1 <60% of the predicted value. • Chronic treatment with systemic corticosteroids should be avoided due to an unfavorable risk-benefit ratio. • COPD patients should receive an annual influenza vaccine. • The pneumococcal polysaccharide vaccine is recommended for COPD patients ≥65 years old or for patients <65 years old with an FEV_1 <40% of the predicted value. • Exercise training programs should be implemented for all COPD patients. • Long-term administration of oxygen (>15 hours/day) increases survival in patients with chronic respiratory failure. <u>Management of exacerbations</u> • The most common causes of an exacerbation are bronchial tree infections and air pollution. • **<u>Inhaled β_2-agonists, with or without anticholinergics, and systemic corticosteroids are effective treatments for exacerbations of COPD.</u>** • Patients experiencing COPD exacerbations with clinical signs of airway infection may benefit from antibiotic treatment.

RESPIRATORY: Inhaled Anticholinergic Agents

- Conclusions:
  - Tiotropium is the only agent within the class that is FDA-approved for reducing exacerbations associated with COPD
  - Both aclidinium and tiotropium have a significantly longer duration of action compared to ipratropium and as a result are approved for twice- and once-daily dosing, respectively
  - All of the antimuscarinic agents have been shown to improve lung function and exercise tolerance in patients with COPD; however, comparative trials have noted improved outcomes with tiotropium over ipratropium
  - Meta-analyses have demonstrated significant clinical advantages when tiotropium is used in combination with a bronchodilator from a different pharmacologic class
  - Ipratropium, while effective, does not appear to offer any significant advantages in comparison to other short-acting bronchodilators

RESPIRATORY: Inhaled Anticholinergic Agents

- Conclusions cont.:
  - According to the Global Initiative for Chronic Obstructive Lung Disease guidelines, inhaled bronchodilators are preferred for the management of COPD.[1] Principle bronchodilators include β_2-agonists, anticholinergics and theophylline used as monotherapy or in combination

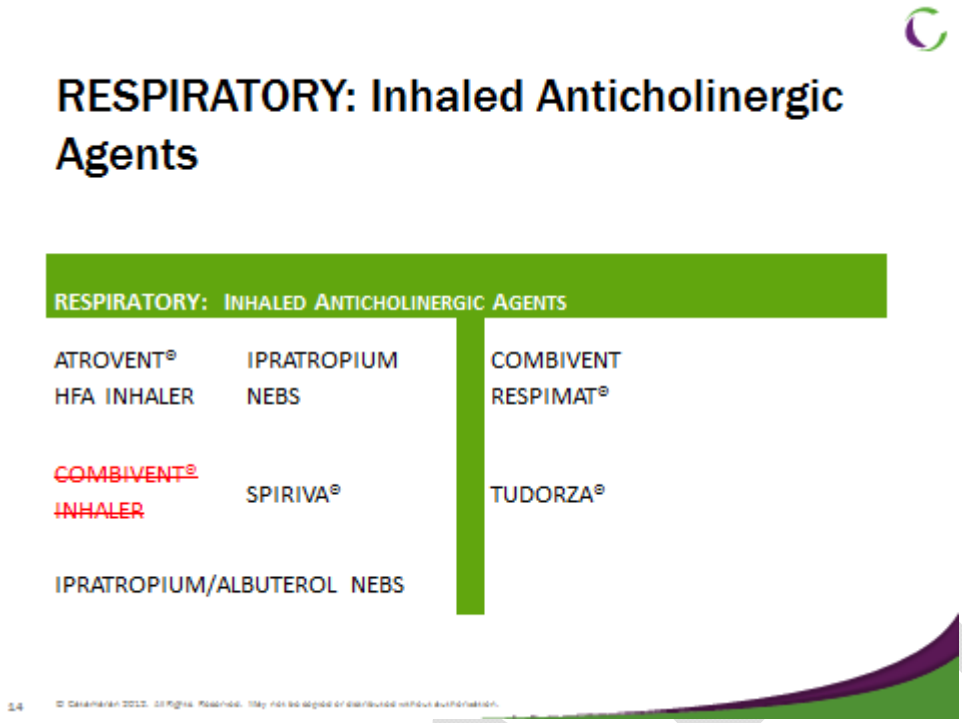
RESPIRATORY: Inhaled Anticholinergic Agents

- Products are Clinically and Therapeutically Equivalent
  - ATROVENT® HFA INHALER
  - IPRATROPIUM NEBS
  - COMBIVENT RESPIMAT®
  - SPIRIVA®
  - TUDORZA®
  - IPRATROPIUM/ALBUTEROL NEBS

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD – Presented the following slide to the Committee.



Carl Jeffery, PharmD recommended to remove Combivent Inhaler from the preferred side since it is no longer available and to keep the remaining products the same.

A motion was made and seconded that the Committee accept Catamaran's recommendation.

Shamim Nagy, MD, Chairwoman: All in favor?

Kalinowski: Aye.
Zold: Aye.
Decerbo: Nay.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion carries.

C. RESPIRATORY: Inhaled Corticosteroid/Beta-Adrenergic Combinations

Shamim Nagy, MD, Chairwoman: Any public comment?

Brian Streng – representing Glaxo Smith Kline,Breo Ellipta and Advair Diskus. He presented information on Breo Ellipta and requested Breo Ellipta be added as preferred.

Carl Jeffery, PharmD presented the following slides representing drug information to the Committee.

RESPIRATORY: Inhaled Corticosteroid/Beta-Adrenergic Combinations

- New Drug – Breo Ellipta (fluticasone furoate/vilanterol)

Generic Name	Treatment of Asthma in Adults and Children ≥4 Years of Age	Treatment of Asthma in Adults and Children ≥12 Years of Age	Maintenance Treatment of Airflow Obstruction in Patients with Chronic Obstructive Pulmonary Disease*
Budesonide/formoterol		✔	✔ †
Fluticasone propionate/ salmeterol	✔ (Advair Diskus®)	✔ (Advair HFA®)	✔ ‡ (Advair Diskus®)
Fluticasone furoate/vilanterol			✔
Mometasone/formoterol		✔	

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Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Martinez et al.[89] Fluticasone furoate/vilanterol 100/25 µg QD fluticasone furoate/vilanterol 200/25 µg QD fluticasone furoate 200 µg QD fluticasone furoate 100 µg QD vilanterol 25 µg QD placebo Albuterol was allowed for use as symptom relief, as was ipratropium bromide provided the dose was a stable dosing regimen from the screening visit onward.	DB, MC, PC, PG, RCT Patients aged ≥40 years of age with stable, moderate to severe COPD, a smoking history of ≥10 pack-years, a post-bronchodilator FEV_1/FVC ratio of ≤0.70, a post-bronchodilator FEV_1 ≤70% predicted and a score of ≥2 on the mMRC Dyspnea Scale	N=1,224 24 weeks	Primary: Zero to four hour weighted mean postdose-FEV_1 and trough-FEV_1 Secondary: CRQ-SAS, peak FEV_1, time to ≥100 mL improvement from baseline in FEV_1 on day one, time to ≥12% improvement in FEV_1 over the first four hours post-dose on day one, use of rescue medications, nighttime awakenings and safety parameters	Primary: The 100/25 µg and 200/25 µg combination regimens were associated with improvement in weighted mean postdose-FEV_1 compared to placebo (214 mL; 95% CI, 161 mL to 266 mL for the 100 µg dose comparison; and 209 mL; 95% CI, 157 mL to 261 mL for the 200 µg dose comparison, respectively) and fluticasone furoate monotherapy (168 mL; 95% CI, 116 mL to 220 mL for the 100 µg dose comparison; 168 mL; 95% CI, 117mL to 219 mL for the 200 µg dose comparison, respectively). In addition, the combination regimens were associated with an increase in trough FEV_1 compared to placebo (144 mL; 95% CI, 91 mL to 197 mL for the 100 µg dose comparison; and 131 mL; 95% CI, 80 mL to 183 mL for the 200 µg dose comparison, respectively). However, there was no significant difference between the combination regimen and vilanterol alone (45 mL; 95% CI, -8 mL to 97 mL for the 100 µg dose comparison; and 32 mL; 95% CI, -6 mL to 102 mL for the 200 µg dose comparison, respectively)

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Martinez et al.[89] Fluticasone furoate/vilanterol 100/25 µg QD fluticasone furoate/vilanterol 200/25 µg QD fluticasone furoate 200 µg QD fluticasone furoate 100 µg QD vilanterol 25 µg QD placebo Albuterol was allowed for use as symptom relief, as was ipratropium bromide provided the dose was a stable dosing regimen from the screening visit onward.	DB, MC, PC, PG, RCT Patients aged ≥40 years of age with stable, moderate to severe COPD, a smoking history of ≥10 pack-years, a post-bronchodilator FEV_1/FVC ratio of ≤0.70, a post-bronchodilator FEV_1 ≤70% predicted and a score of ≥2 on the mMRC Dyspnea Scale	N=1,224 24 weeks	Primary: Zero to four hour weighted mean postdose-FEV_1 and trough-FEV_1 Secondary: CRQ-SAS, peak FEV_1, time to ≥100 mL improvement from baseline in FEV_1 on day one, time to ≥12% improvement in FEV_1 over the first four hours post-dose on day one, use of rescue medications, nighttime awakenings and safety parameters	Secondary: From day one of the study postdose-FEV_1 and trough-FEV_1 were greater with fluticasone furoate/vilanterol and vilanterol compared with fluticasone furoate and placebo. Both parameters increased rapidly from day 1 to day 14 and were generally maintained thereafter. Over six months, scores on the dyspnea domain of the CRQ-SAS declined relative to placebo with both strengths of fluticasone furoate, but improved with both strengths of fluticasone furoate/vilanterol and with vilanterol alone. In the fluticasone furoate 100 µg and 200 µg arms adjusted mean peak FEV_1 was 24 mL (95% CI, -6 to 55) and 7 mL (95% CI, -23, to 37) respectively, greater than placebo while for vilanterol the adjusted mean increase from placebo was 147 mL (95% CI, 117 to 177). The equivalent values for fluticasone furoate/vilanterol 100/25 µg and 200/25 µg were 152 mL (95% CI, 122 to 182) and 141 ml (95% CI, 111 to 171), respectively. Other efficacy comparisons generally favored the use of fluticasone furoate/vilanterol compared to placebo. No increase was seen in on-treatment adverse events or serious adverse events, with active therapy vs. placebo. Exacerbations were infrequent but occurred more often in the placebo arm (21 events) than in any active treatment arm and more frequently in the vilanterol arm (18 events) than in the fluticasone furoate-containing arms (14 events).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Kerwin et al.[90] Fluticasone furoate/vilanterol 50/25 µg QD vs fluticasone furoate vilanterol 100/25 µg QD vs fluticasone furoate 200 µg QD vs vilanterol 25 µg QD vs placebo Albuterol was allowed for use as symptom relief, as was ipratropium bromide provided the dose was a stable dosing regimen from the screening visit onward.	DB, MC, PC, PG, RCT Patients aged ≥40 years of age with stable, moderate to severe COPD, a smoking history of ≥10 pack-years, a post-bronchodilator FEV_1/FVC ratio of ≤0.70, a post-bronchodilator FEV1 ≤70% predicted and a score of ≥2 on the mMRC Dyspnea Scale	N=1,030 24 weeks	Primary: Zero to four hour weighted mean postdose-FEV_1 and trough-FEV_1 Secondary: CRQ-SAS, peak FEV_1, time to ≥100 ml improvement from baseline in FEV_1 on day one, time to ≥12% improvement in FEV1 over the first four hours post-dose on day one, use of rescue medications, nighttime awakenings and safety parameters	Primary: The 100/25 µg combination regimen was associated with improvement in weighted mean postdose-FEV_1 compared to placebo (173 mL; 95% CI, 123 mL to 224 mL) and fluticasone furoate monotherapy (120 mL; 95% CI, 70 mL to 170 mL).). In addition, the combination regimen was associated with an increase in trough FEV_1 compared to placebo (115 mL; 95% CI, 60 mL to 169 mL). However, there was no significant difference between the combination regimen and vilanterol alone (48 mL; 95% CI, -6 mL to 102 mL). Similar results were observed with the 50 µg/25 µg compared to placebo. Secondary: For FEV_1 at other time points over 24 weeks, both strengths of fluticasone furoate/vilanterol showed rapid and sustained improvements over placebo, and were greater than the vilanterol monotherapy arm at all time points from day 14. Similarly, both combination strengths and vilanterol showed rapid and sustained effects on trough FEV_1 compared with placebo, and both combination strengths provided greater lung function effects than vilanterol at days 7, 28, 56, 84, 140 and 168, but only the 50 µg/25 µg strength provided greater lung function effects at day 2, day 112 and day 169, and only the 100 µg/25 µg strength provided greater lung function effects at day 14. Both fluticasone furoate/vilanterol arms showed greater improvements compared with placebo in diary card symptoms, rescue use or rescue-free 24-h periods, nighttime awakenings and morning peak flow. The incidence of on-treatment adverse events was higher with active therapy compared to placebo, but the reports of serious adverse events were similar across arms. Reported adverse events included nasopharyngitis, local steroidal effects (candidiasis, oropharyngeal pain) and upper respiratory tract infection.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Agusti et al[8] Fluticasone propionate/ salmeterol 500/50 µg BID vs fluticasone furoate/ vilanterol 100/25 µg QD	DB, DD, MC, PG, RCT Patients aged ≥40 years of age with a smoking history of ≥10 pack-years, a post-bronchodilator FEV_1/FVC ratio of ≤0.70, a post-bronchodilator FEV_1 ≤70% predicted and at least one moderate COPD exacerbation within the last 2 years.	N=528 12 weeks	Primary: 24-hour effect on lung function after 12 weeks assessed by change from baseline in weighted mean FEV_1 Secondary: Time to 100 mL increase from baseline from zero to four hours on day one, change from baseline in trough FEV_1 on day 85 and change in health status	Primary: On day 84, there was no significant difference in improvement from baseline between the fluticasone propionate/salmeterol (108±221 mL) and fluticasone furoate/vilanterol (130±222 mL) groups (P=0.282). Secondary: Because statistical significance was not achieved for the primary endpoint, statistical significance in the secondary endpoints could not be inferred. The mean change from baseline in trough FEV_1 on day 85 was 88 mL in the fluticasone propionate/salmeterol group compared to 111 mL in the fluticasone furoate/vilanterol (mean treatment different, 23 mL; 95% CI, -21 to 66). The median time to reach an increase of ≥100 mL in FEV_1 was 28 minutes in the fluticasone propionate/salmeterol group compared to 16 minutes in the fluticasone furoate/vilanterol. There was no significant difference in the proportion of rescue free 24-hour periods between the groups. The rate of adverse events was similar between the groups.

RESPIRATORY: Inhaled Corticosteroid/Beta-Adrenergic Combinations

- Conclusion:
  - Head-to-head trials comparing budesonide/formoterol and fluticasone propionate/salmeterol failed to demonstrate that one product is consistently "superior" over the other
  - A single prospective head-to-head trial comparing mometasone/formoterol (Dulera®) to fluticasone propionate/salmeterol demonstrated non inferiority in regard to forced expiratory volume in 1 second (FEV_1) area under the curve from 0 to 12 hours, in addition to a significantly faster onset of action and increase in FEV_1
  - While one study comparing fluticasone propionate/salmeterol and fluticasone furoate/vilanterol did not demonstrate significant differences in improvement of 0 to 24 hour FEV_1

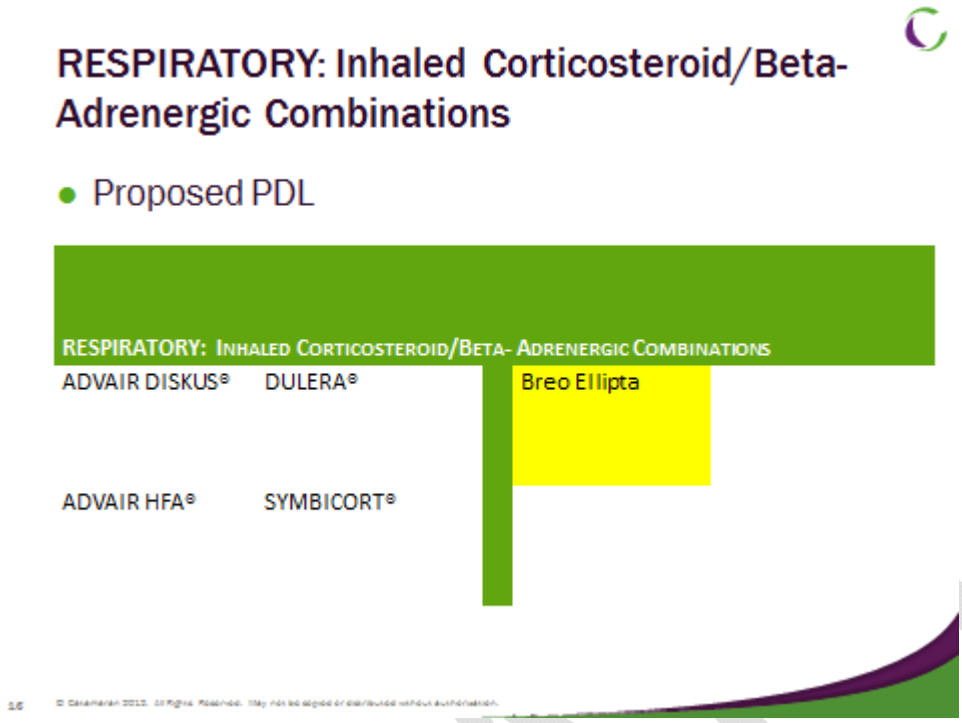
RESPIRATORY: Inhaled Corticosteroid/Beta-Adrenergic Combinations

- Therapeutic and Clinical Equivalence
  - ADVAIR DISKUS®
  - DULERA®
  - Breo Ellipta
  - ADVAIR HFA®
  - SYMBICORT®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide to the Committee:



He recommended Breo Ellipta remain as non-preferred, and no changes with the other preferred listed medications.

Dr. Adashek makes a motion to move Breo Ellipta to preferred.
The motion was not seconded.

Another motion was made and seconded to accept Catamaran's recommendation as presented, keeping Breo Ellipta as non-preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Nay.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion carries.

A. RESPIRATORY: Long Acting Beta-Adrenergic Agents

Public Comment: None

Carl Jeffery, PharmD presented slides representing an overview of products, clinical information and clinical studies.

RESPIRATORY: Long Acting Beta-Adrenergic Agents

- New Agents –
  - Brovana ® (Arfomoterol) – solution for nebulizer
  - Arcapta Neohaler® (Indacaterol)

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Arformoterol (Brovana®)	Long-term, twice daily, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema	Solution for nebulization: 15 µg (2 mL)	-
Formoterol (Foradil®, Perforomist®)	Treatment of asthma and prevention of bronchospasm as concomitant therapy with a long-term asthma control medication in patients with reversible obstructive airways disease, including patients with nocturnal symptoms (dry powder inhaler only), long-term, twice daily, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema, prevention of exercise-induced bronchospasm (dry powder inhaler only)	Capsule for inhalation: 12 µg Solution for nebulization: 20 µg/2 mL	-
Indacaterol (Arcapta Neohaler®)	The long term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema	Capsule for inhalation: 75 µg	-
Salmeterol (Serevent Diskus®)	Treatment of asthma and prevention of bronchospasm as concomitant therapy with a long-term asthma control medication in patients with reversible obstructive airways disease, including patients with nocturnal symptoms, long-term, twice daily, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema, prevention of exercise-induced bronchospasm	Dry powder inhaler: 50 µg (28 or 60 inhalations)	-

Kornmann et al[75] INLIGHT-2 Indacaterol 150 µg QD vs salmeterol 50 µg BID vs placebo Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening. Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed.	AC, DB, DD, MC, PC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=1,002 26 weeks	Primary: Trough FEV_1 at 12 weeks compared to placebo Secondary: Trough FEV_1 at 12 weeks compared to salmeterol, FEV_1 at day two and weeks 12 and 26, health status, diary assessments, dyspnea and safety	Primary: Trough FEV_1 at 12 weeks was significantly higher with indacaterol compared to placebo (*P*<0.001). Secondary: Trough FEV_1 at 12 weeks was significantly higher with indacaterol compared to salmeterol (treatment difference, 60 mL; *P*<0.001). Similar results were observed at 26 weeks (treatment difference, 70 mL; *P*<0.001). Indacaterol maintained a clinically significant increase in FEV_1 over placebo during the course of the trial, with an increase from 130 mL at day two to 170 mL at week 12 and 180 mL at week 26 (*P*<0.001 for all). The difference between salmeterol and placebo was smaller and did not increase with length of treatment (120, 110 and 110 mL at day two, week 12 and week 26, respectively; *P*<0.001 for all). Indacaterol was "superior" at weeks 12 and 26 compared to salmeterol (*P*<0.001 for both). Both indacaterol (treatment difference, -3.6, -4.1, -6.3 and -5.0 at weeks four, eight, 12 and 26; *P*<0.001 for all) and salmeterol (-2.5, -3.6, -4.2 and -4.1; *P*<0.01 for all) significantly improved SGRQ total scores compared to placebo, with the differences between indacaterol and salmeterol significantly favoring indacaterol at 12 weeks (*P*<0.05). The odds of indacaterol achieving a clinically important improvement from baseline in SGRQ total scores (at least four units) was significantly greater compared to salmeterol by 12 weeks (OR, 1.59; 95% CI, 1.12 to 2.25; *P*<0.01). (Cont.)

Kornmann et al[75] INLIGHT-2 Indacaterol 150 µg QD vs salmeterol 50 µg BID vs placebo Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening. Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed.	AC, DB, DD, MC, PC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=1,002 26 weeks	Primary: Trough FEV_1 at 12 weeks compared to placebo Secondary: Trough FEV_1 at 12 weeks compared to salmeterol, FEV_1 at day two and weeks 12 and 26, health status, diary assessments, dyspnea and safety	Secondary (cont): The mean percentage days of poor COPD control over 26 weeks was 34.10% with both indacaterol and salmeterol compared to 38.10% with placebo (*P*=0.058 and *P*=0.057). Compared to patients receiving salmeterol, patients receiving indacaterol used less salbutamol, had higher morning PEF measurements and had more days when they were able to perform usual activities. Adjusted mean total TDI scores at weeks four, eight, 12 and 26 were significantly higher with salmeterol (*P*<0.05) and indacaterol (*P*<0.001) compared to placebo. The mean differences compared to placebo were numerically larger with indacaterol than with salmeterol, with significance achieved at weeks four (0.95 vs 0.55; *P*<0.05) and 12 (1.45 vs 0.90; *P*<0.05). Patients receiving indacaterol were more likely to achieve a clinically important improvement from baseline in TDI total scores at all time points compared to patients receiving placebo (*P*<0.001 for all). The odds of this occurring with salmeterol compared to placebo only reached significance at weeks 12 and 26 (*P*≤0.001). The most commonly reported adverse events were COPD worsening, nasopharyngitis, upper and lower respiratory tract infections and back pain. The proportions of patients experiencing serious adverse events were similar among the treatments (8.8, 5.7 and 7.8%).

Dahl et al[76] INVOLVE Indacaterol 300 µg QD vs indacaterol 600 µg QD vs formoterol 12 µg BID vs placebo Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed. Other bronchodilators or ICSs were not allowed unless to treat a COPD exacerbation.	DB, DD, PC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=129 1 year	Primary: Trough FEV_1 at 12 weeks Secondary: Days of poor COPD control, SGRQ score, time to first exacerbation, spirometry, TDI score, exacerbation rates, BODE index, safety	Primary: Trough FEV_1 at week 12 with both indacaterol doses was significantly higher compared to placebo (treatment difference, 170 mL; *P*<0.001) and formoterol (treatment difference, 100 mL; *P*<0.001). Over the remainder of the trial, improvements with indacaterol compared to placebo were maintained at a similar level, while the difference between formoterol and placebo diminished. Secondary: Both doses of indacaterol were significantly "superior" to placebo in decreasing the number of days of poor COPD control (treatment difference, -4.7; 95% CI, -8.4 to -1.0; *P*<0.05 and -8.3; 95% CI, -12.0 to -4.6; *P*<0.001). Formoterol was also significantly "superior" to placebo (-4.8; 95% CI, -8.5 to -1.1; *P*<0.05). Both doses of indacaterol were significantly "superior" to placebo in improving SGRQ scores at weeks 12 (treatment difference, -3.8; 95% CI, -5.6 to -2.1 and -4.1; 95% CI, -5.9 to -2.3; *P*<0.001 for both) and 52 (-4.7; 95% CI, -6.7 to -2.7 and -4.6; 95% CI, -6.6 to -2.6; *P*<0.001 for both). Formoterol was also significantly "superior" to placebo (-3.2; 95% CI, -5.0 to -1.5 and -4.0; 95% CI, -6.0 to -2.0; *P*<0.001 for both). There were too few events to calculate COPD exacerbation free time; however, both doses of indacaterol were significantly "superior" to placebo in improving the time to first COPD exacerbation (HR, 0.77; 95% CI, 0.606 to 0.975 and HR, 0.69; 95% CI, 0.538 to 0.882; *P*<0.05 for both). Formoterol was also significantly "superior" to placebo (HR, 0.77; 95% CI, 0.605 to 0.981; *P*<0.05).

Dahl et al[76] INVOLVE Indacaterol 300 µg QD vs indacaterol 600 µg QD vs formoterol 12 µg BID vs placebo Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed. Other bronchodilators or ICSs were not allowed unless to treat a COPD exacerbation.	DB, DD, PC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=129 1 year	Primary: Trough FEV_1 at 12 weeks Secondary: Days of poor COPD control, SGRQ score, time to first exacerbation, spirometry, TDI score, exacerbation rates, BODE index, safety	(CONT) Both doses of indacaterol were significantly "superior" to placebo in improving change from baseline in morning and evening PEF (treatment difference, 28.3; 95% CI, 22.8 to 33.8; and 31.1; 95% CI, 25.6 to 36.7; *P*<0.001 for both [morning PEF], and 24.6; 95% CI, 19.2 to 30.1; and 28.3; 95% CI, 22.8 to 33.8; *P*<0.001 for both [evening PEF]). Formoterol achieved similar results (*P*<0.001 for both), and both doses of indacaterol were significantly "superior" to formoterol (*P*<0.001 for all comparisons). Both doses of indacaterol were significantly "superior" to placebo in improving TDI scores at week 12 (treatment difference, 1.17; 95% CI, 0.76 to 1.58 and 1.13; 95% CI, 0.71 to 1.54; *P*<0.001 for both) and week 52 (1.00; 95% CI, 0.53 to 1.47 and 0.98; 95% CI, 0.51 to 1.46; *P*<0.001 for both). Formoterol was also significantly "superior" to placebo (0.72; 95% CI, 0.300 to 1.013; *P*<0.001 and 0.71; 95% CI, 0.24 to 1.19; *P*<0.01). After 12 weeks, both doses of indacaterol were significantly "superior" to formoterol (*P*<0.05 for both doses). Exacerbations occurred at a rate of 0.60 (rate ratio, 0.82; 95% CI, 0.63 to 1.06; *P* value not significant vs placebo), 0.57 (0.74; 95% CI, 0.56 to 0.97; *P*<0.05 vs placebo) 0.56 (0.75; 95% CI, 0.58 to 0.99; *P*<0.05 vs placebo) and 0.74 per year with indacaterol 300 µg, 600 µg, formoterol and placebo. Both doses of indacaterol were significantly "superior" to placebo (least-squares mean, 2.67 and 2.90) in improving the BODE index at week 12 (treatment difference, -0.40; 95% CI, -0.56 to -0.25; *P*<0.001 and -0.24; 95% CI, -0.40 to -0.08; *P*<0.01) and week 52 (-0.55; 95% CI, -0.73 to 0.37 and -0.49; 95% CI, -0.68 to -0.31; *P*<0.001 for both). Formoterol was also significantly "superior" to placebo (-0.28; 95% CI, -0.43 to -0.12 and -0.53; 95% CI, -0.72 to -0.35; *P*<0.001 for both).

Dahl et al[76] INVOLVE Indacaterol 300 µg QD vs indacaterol 600 µg QD vs formoterol 12 µg BID vs placebo Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed. Other bronchodilators or ICSs were not allowed unless to treat a COPD exacerbation.	DB, DD, PC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=129 1 year	Primary: Trough FEV_1 at 12 weeks Secondary: Days of poor COPD control, SGRQ score, time to first exacerbation, spirometry, TDI score, exacerbation rates, BODE index, safety	(CONT) COPD worsening and nasopharyngitis were the only adverse events reported by >10% of patients with any treatment. Eight patients died during the trial and four died during follow up (two due to cardiac arrest [indacaterol 300 µg and placebo], one due to multiorgan failure [formoterol], one due to respiratory failure [formoterol] and four due to sudden death [one, formoterol; three, placebo]). Tremor was reported in 0.2, 1.9, 1.2 and 0.5% of patients, while tachycardia was reported in 0.9, 0.7, 0.5 and 1.2% of patients. Cough observed within five minutes of drug administration was observed in 19.1, 0.8 and 1.8% of patients receiving indacaterol, formoterol and placebo. (*P* values not reported).

Korn et al[77] INSIST Indacaterol 150 µg QD vs salmeterol 50 µg BID Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening. Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed.	DB, DD, MC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥10 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=1,123 12 weeks	Primary: Change in FEV_1 AUC from five minutes post dose to 11 hours and 45 minutes postdose at 12 weeks Secondary: Trough FEV_1, FEV_1 AUC five minutes to four hours, five minutes to eight hours and eight to 11 hours at 12 weeks, FVC at 12 weeks; dyspnea; safety	Primary: FEV_1 AUC measurements at 12 weeks were significantly higher with indacaterol compared to salmeterol, with an adjusted mean difference of 57 mL (95% CI, 35 to 79; *P*<0.001). The mean (percent) changes from baseline for indacaterol and salmeterol were 0.19 (16.6%) and 0.13 L (11.4%), respectively. Secondary: Trough FEV_1 significantly favored indacaterol compared to salmeterol after 12 weeks, (adjusted mean difference, 60 mL; 95% CI, 37 to 83; *P*<0.001). Indacaterol maintained significance over salmeterol at all visits (*P*<0.001), except on day two (*P* value not significant). Results for other FEV_1 AUC measurements after 12 weeks all significantly favored indacaterol over salmeterol (*P*<0.001 for all). The adjusted mean differences were 0.06 (95% CI, 0.03 to 0.08), 0.05 (95% CI, 0.03 to 0.08) and 0.07 L (95% CI, 0.04 to 0.09). FEV_1 at week 12 with indacaterol was significantly higher compared to salmeterol at all time points (*P*<0.001 for all). At 12 weeks, FVC with indacaterol was significantly higher compared to salmeterol at all time points (*P* values not reported). With regards to dyspnea, TDI total scores with indacaterol were significantly "superior" compared to salmeterol after 12 weeks (adjusted mean difference, 0.63; 95% CI, 0.30 to 0.97; *P*<0.001). There was also a significantly greater proportion of patients receiving indacaterol that achieved a clinically important improvement from baseline (at least one point) in TDI total score (69.4 vs 62.7%; OR, 1.41; 95% CI, 1.07 to 1.85; *P*<0.05).

Korn et al[77] INSIST Indacaterol 150 µg QD vs salmeterol 50 µg BID Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening. Patients previously on LABA/ICS combination products were switched to ICS monotherapy at an equivalent dose. Salbutamol was provided for use as needed.	DB, DD, MC, PG, RCT Patients ≥40 years of age with moderate to severe COPD, smoking history ≥10 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=1,123 12 weeks	Primary: Change in FEV_1 AUC from five minutes post dose to 11 hours and 45 minutes postdose at 12 weeks Secondary: Trough FEV_1, FEV_1 AUC five minutes to four hours, five minutes to eight hours and eight to 11 hours at 12 weeks, FVC at 12 weeks; dyspnea; safety	(CONT) Over the 12 weeks, the use of rescue salbutamol was significantly lower with indacaterol (mean difference, -0.18 puffs/day; 95% CI, -0.36 to 0.00; *P*<0.05) and patients had a greater proportion of days with no rescue medication use (mean difference, 4.4 days; 95% CI, 0.6 to 8.2; *P*<0.05). Overall incidences of adverse events were similar between the two treatments; at least one adverse event was reported by 33.8 and 33.5% of patients receiving indacaterol and salmeterol. The most frequently reported adverse events were COPD worsening (4.5 vs 5.7%) and headache (3.6 vs 3.6%). Overall, 3.6 and 2.8% of patients experienced a serious adverse event, with cardiac disorders being the most frequently reported (1.1 vs 0.4%; *P* values not reported).

Magnussen et al[78] INPUT Indacaterol 300 µg QD in the AM indacaterol 300 µg QD in the PM salmeterol 50 µg BID placebo Patients were randomly assigned to one of 12 treatment sequences, each comprising 3 DB, 14 day treatment periods, with each treatment period separated by a 14 day washout period. In each treatment sequence, patients received 3 of the 4 treatments listed above. Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening.	DB, DD, PC, RCT, XO Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=96 12 weeks	Primary: Trough FEV_1 at 14 days Secondary: FEV_1 at individual time points on day one of each treatment period, trough FVC at 14 days, patient-reported symptom assessment and safety	Primary: Trough FEV_1 was significantly higher with indacaterol PM (treatment difference, 200 mL; *P*<0.001) and indacaterol AM (200 mL; *P*<0.001) compared to placebo. The difference between indacaterol PM and AM (10 mL) was not significant (*P* value not reported). Trough FEV_1 was significantly higher with indacaterol PM compared to the evening dose of salmeterol (*P*<0.001). No significant difference between indacaterol AM and the morning dose of salmeterol was observed (*P* value not significant). Secondary: For individual time point FEV_1 values on day one, all active treatments produced significantly higher measurements compared to placebo at all time points. At five minutes, the differences between indacaterol AM and indacaterol PM compared to placebo were 150 and 140 mL (*P*<0.001 for both). The FEV_1 with both indacaterol AM and indacaterol PM was numerically higher compared to salmeterol at all time points. Significance was observed between indacaterol AM and salmeterol at all time points until the second salmeterol dose was administered (*P* values not reported). Similar results were observed for trough FVC.

Magnussen et al[78] INPUT Indacaterol 300 µg QD in the AM indacaterol 300 µg QD in the PM salmeterol 50 µg BID placebo Patients were randomly assigned to one of 12 treatment sequences, each comprising 3 DB, 14 day treatment periods, with each treatment period separated by a 14 day washout period. In each treatment sequence, patients received 3 of the 4 treatments listed above. Permitted concomitant medications included ICS, if the dose and regimen were stable for 1 month prior to screening.	DB, DD, PC, RCT, XO Patients ≥40 years of age with moderate to severe COPD, smoking history ≥20 pack years, post-bronchodilator FEV_1 <80 and ≥30% predicted and FEV_1/FVC <70%	N=96 12 weeks	Primary: Trough FEV_1 at 14 days Secondary: FEV_1 at individual time points on day one of each treatment period, trough FVC at 14 days, patient-reported symptom assessment and safety	(CONT) Over 14 days of treatment, both indacaterol AM and indacaterol PM significantly improved the proportion of nights with no awakenings (*P*<0.001 and *P*<0.01), days with no daytime symptoms (*P*<0.05 for both) and days able to perform usual activities (*P*<0.05 for both) compared to placebo. Improvements in all of these analyses were consistently in favor of indacaterol over salmeterol, with the difference reaching significance for indacaterol PM analysis of proportion of nights with no awakenings (*P*<0.05). No differences were observed between the two indacaterol regimens. The overall incidence of adverse events was comparable between treatments (25.0, 23.1, 19.1 and 20.6%), with most being of mild to moderate severity. Cough was the most frequently reported suspected drug-related adverse event with indacaterol (5.9 and 7.7% compared to 1.5 and 0.0% with salmeterol and placebo). Serious adverse events were reported in two patients receiving indacaterol; neither was suspected to be drug-related.

RESPIRATORY: Long Acting Beta-Adrenergic Agents

- Conclusion
  - Salmeterol and formoterol have been found to improve FEV_1 in patients with mild to moderate asthma who require persistent use of SABAs
  - Overall, data from published clinical trials demonstrate that treatment with indacaterol consistently results in significantly higher mean trough FEV_1 after 12 weeks of treatment compared to placebo, formoterol, salmeterol and tiotropium. Patients treated with indacaterol also achieved significant improvements in COPD symptoms, as well as health-related quality of life compared to those treated with placebo
  - In general, treatment with indacaterol is favored over other long acting bronchodilators for these outcomes, but significant “superiority” is not consistently achieved

RESPIRATORY: Long Acting Beta-Adrenergic Agents

- Clinical and Therapeutic Equivalence
  - FORADIL®
  - SEREVENT DISKUS®
  - Arcapta Neohaler®
  - Brovana ®

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A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD, presented the following slide:

RESPIRATORY: Long Acting Beta-Adrenergic Agents

RESPIRATORY: Long Acting Beta Adrenergics		
FORADIL®	SEREVENT DISKUS®	Brovana ®
Arcapta Neohaler®		

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Carl Jeffery, PharmD recommended that Arcapta Neohaler be considered preferred and Brovana be considered non-preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, that Arcapta Neohaler be preferred and Brovana be nonpreferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion carries.

ANALGESICS: Long Acting Narcotics

Public Comment:

Rupa Shah -- representing Purdue, presented clinical information on Butrans and OxyContin. He requested both Butrans and OxyContin be made preferred.

Carl Jeffery, PharmD – gave a brief explanation that this class is being reviewed for housekeeping. The following slides were presented.

ANALGESICS: Long Acting Narcotics

- Evaluation of Fentanyl Patches
- Generic fentanyl patches AB rated to Brand Duragesic® Patches.

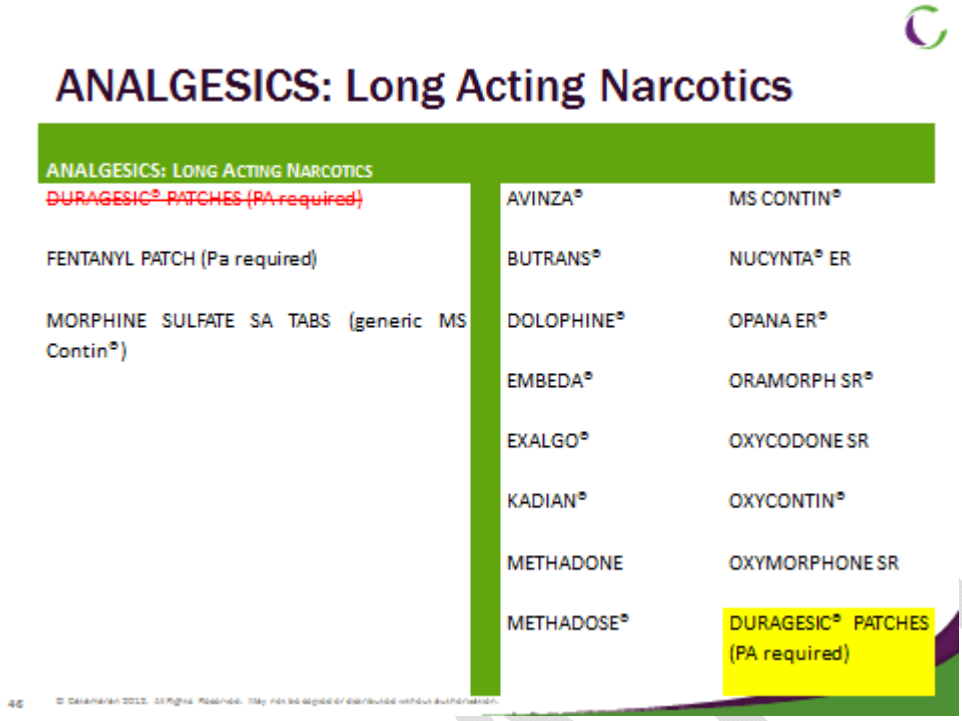
ANALGESICS: Long Acting Narcotics

- Clinical and Therapeutic Equivalence
  - DURAGESIC® PATCHES (PA required)
  - AVINZA®
  - MS CONTIN®
  - FENTANYL PATCH (Pa required)
  - BUTRANS®
  - NUCYNTA® ER
  - MORPHINE SULFATE SA TABS (generic MS Contin®)
  - DOLOPHINE®
  - OPANA ER®
  - EMBEDA®
  - ORAMORPH SR®
  - EXALGO®
  - OXYCODONE SR
  - KADIAN®
  - OXYCONTIN®
  - METHADONE
  - OXYMORPHONE SR
  - METHADOSE®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide:



He recommended the Brand Duragesic be made non-preferred and no other changes for the remaining list.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make Brand Duragesic non-preferred with no other changes.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion carries.

DIABETIC AGENTS: Incretin Mimetics

Public Comment

Raphael Wilburn – representing Astra-Zeneca for Byetta and Bydureon. He gave an overview of products, clinical information, dosing, and treatment guidelines.

Shamim Nagy, MD, Chairwoman, MD, Chair: Dr. Jeffery.

Carl Jeffery, PharmD presented the following slides, clinical information, accepted guidelines, and product differences.

DIABETIC AGENTS: Incretin Mimetics

Generic Name	Adjunct to Diet and Exercise to Improve Glycemic Control in Adults with Type 2 Diabetes Mellitus
Exenatide	✔
Liraglutide	✔

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
Exenatide	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus: Extended-release injection: initial, 2 mg SC once weekly Injection: initial, 5 µg SC BID; maintenance, 10 µg SC BID after one month of therapy	Safety and efficacy in children have not been established.	Extended-release injection (Bydureon®): 2 mg/vial* Injection (Byetta®): 250 µg/mL†
Liraglutide	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus: Injection: initial, 0.6 mg SC QD for one week; maintenance, 1.2 to 1.8 mg SC QD	Safety and efficacy in children have not been established.	Injection: 6 mg/mL‡

DIABETIC AGENTS: Incretin Mimetics

Meta-analyses and Cochrane Reviews evaluating incretin-based therapies (dipeptidyl peptidase-4 inhibitors and incretin mimetics) have been conducted and demonstrate similar decreases in HbA_{1c} and significant decreases in body weight compared to other antidiabetic agents

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Anti-hyperglycemia Therapy in Type 2 Diabetes: General Recommendations

Initial Drug Monotherapy	**Metformin**				
Efficacy (↓HbA_{1c})	High				
Hypoglycemia	Low risk				
Weight	Neutral/loss				
Side Effects	Gastrointestinal/lactic acidosis				
If needed to reach individualized HbA_{1c} target after approximately three months, proceed to two drug combination therapy (order not meant to denote any specific preference)					
Two Drug Combin-ations	Metformin + sulfonylurea	Metformin + thia-zolidinedione (TZD)	Metformin + DPP-4 inhibitor	Metformin + GLP-1 receptor agonist	Metformin + insulin (usually basal)
Efficacy (↓HbA_{1c})	High	High	Inter-mediate	High	Highest
Hypoglycemia	Moderate risk	Low risk	Low risk	Low risk	High risk
Weight	Gain	Gain	Neutral	Loss	Gain
Major Side Effects	Hypo-glycemia	Oedema, heart failure, bone fracture	Rare	Gastro-intestinal	Hypo-glycemia
If needed to reach individualized HbA_{1c} target after approximately three months, proceed to three drug combination therapy (order not meant to denote any specific preference)					
Three Drug Combin-ations	Metformin + sulfonylurea +	Metformin + TZD +	Metformin + DPP-4 inhibitor +	Metformin + GLP-1 receptor agonist +	Metformin + insulin therapy +
	TZD, DDP-4 inhibitor, GLP-1 receptor agonist, or insulin	Sulfonylurea, or DPP-4 inhibitor, GLP-1 receptor agonist, or insulin	Sulfonyl-urea, TZD, or insulin	Sulfonyl-urea, TZD, or insulin	TZD, DPP-4 inhibitor, or GLP-1 receptor agonist
If combination therapy that includes basal insulin has failed to achieve HbA_{1c} target after three to six months, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents					
More Complex Insulin Strategies	Insulin (multiple daily doses)				

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DIABETIC AGENTS: Incretin Mimetics

- Clinical and Therapeutic Equivalence
  - BYETTA®
  - VICTOZA®
  - BYDUREON®

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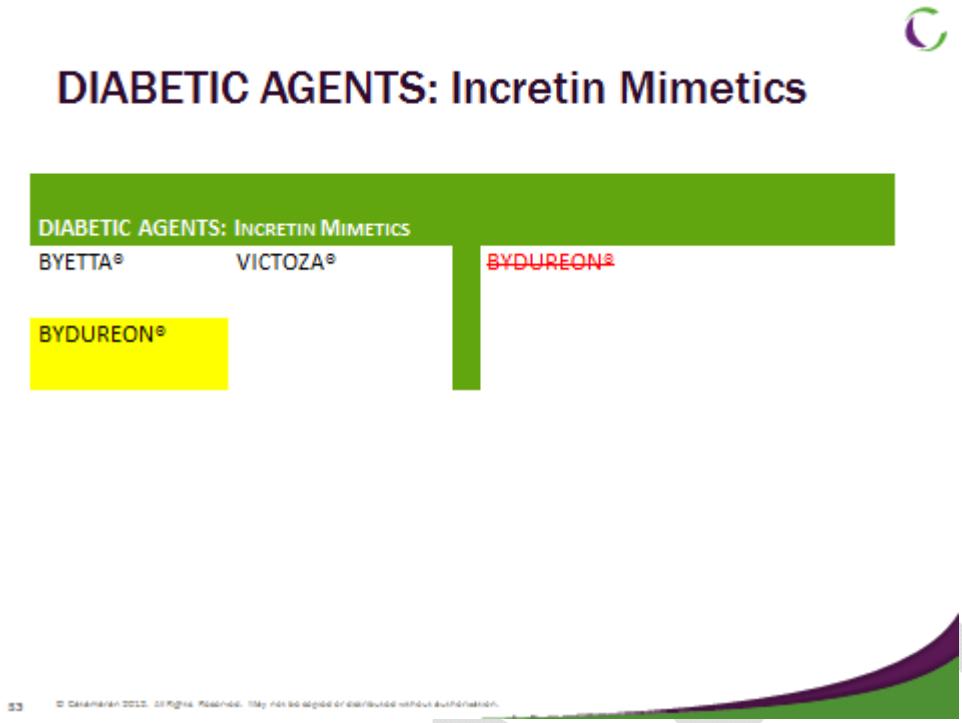
A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide:



Dr. Jeffery made the recommendation that Bydureon move to preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make Bydureon preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Nay.
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

CENTRAL NERVOUS SYSTEM: Oral Anticonvulsants, Misc.

Public Comment

Marilyn Semenchun – representing Eisai for Fycompa. She provided clinical information, study information and dosing information.

Shamim Nagy, MD, Chairwoman, MD, Chair; Dr. Jeffery.

Carl Jeffery, PharmD presented information on the new product in the class, Fycompa. The following slides were presented.

CENTRAL NERVOUS SYSTEM: Oral Anticonvulsants, Misc.

- **Perampanel (Fycompa®)**
  - Labeled Indication: Adjunctive therapy in the treatment of partial-onset seizures (with or without generalized seizures)
  - Study 304 – reduction in seizure frequency to placebo, however no significant difference for patients achieving a seizure reduction of > 50% from baseline compared to placebo.
  - Study 305 – Similar to 304, but achieved the > 50% reduction.
  - Study 306 – Similar to 304 and 305, but a greater proportion of patients achieved a reduction in seizure frequency.

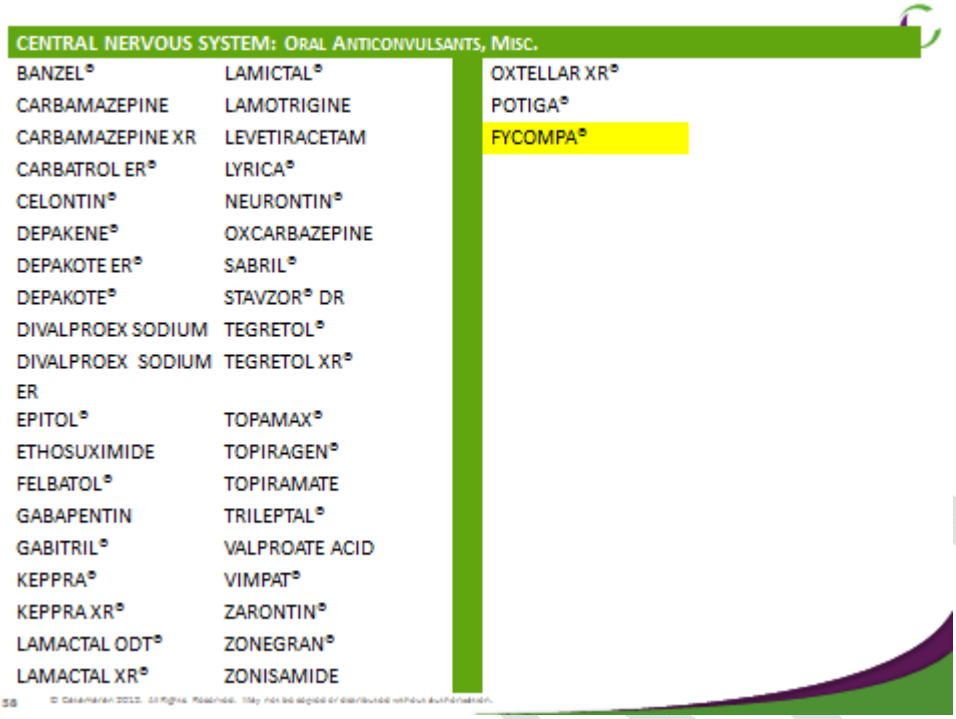
Clinical and Therapeutic Equivalence

- BANZEL®
- LAMICTAL®
- CARBAMAZEPINE
- LAMOTRIGINE
- CARBAMAZEPINE XR
- LEVETIRACETAM
- CARBATROL ER®
- LYRICA®
- CELONTIN®
- NEURONTIN®
- DEPAKENE®
- OXCARBAZEPINE
- DEPAKOTE ER®
- SABRIL®
- DEPAKOTE®
- STAVZOR® DR
- DIVALPROEX SODIUM
- TEGRETOL®
- DIVALPROEX SODIUM ER
- TEGRETOL XR®
- EPITOL®
- TOPAMAX®
- ETHOSUXIMIDE
- TOPIRAGEN®
- FELBATOL®
- TOPIRAMATE
- GABAPENTIN
- TRILEPTAL®
- GABITRIL®
- VALPROATE ACID
- KEPPRA®
- VIMPAT®
- KEPPRA XR®
- ZARONTIN®
- LAMACTAL ODT®
- ZONEGRAN®
- LAMACTAL XR®
- ZONISAMIDE
- OXTELLAR XR®
- POTIGA®
- FYCOMPA®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide:



CENTRAL NERVOUS SYSTEM: ORAL ANTICONVULSANTS, MISC.

BANZEL®	LAMICTAL®	OXTELLAR XR®
CARBAMAZEPINE	LAMOTRIGINE	POTIGA®
CARBAMAZEPINE XR	LEVETIRACETAM	FYCOMPA®
CARBATROL ER®	LYRICA®	
CELONTIN®	NEURONTIN®	
DEPAKENE®	OXCARBAZEPINE	
DEPAKOTE ER®	SABRIL®	
DEPAKOTE®	STAVZOR® DR	
DIVALPROEX SODIUM	TEGRETOL®	
DIVALPROEX SODIUM ER	TEGRETOL XR®	
EPITOL®	TOPAMAX®	
ETHOSUXIMIDE	TOPIRAGEN®	
FELBATOL®	TOPIRAMATE	
GABAPENTIN	TRILEPTAL®	
GABITRIL®	VALPROATE ACID	
KEPPRA®	VIMPAT®	
KEPPRA XR®	ZARONTIN®	
LAMACTAL ODT®	ZONEGRAN®	
LAMACTAL XR®	ZONISAMIDE	

Carl Jeffery, PharmD made the recommendation that Fycompa should remain non-preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, to keep Fycompa non-preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

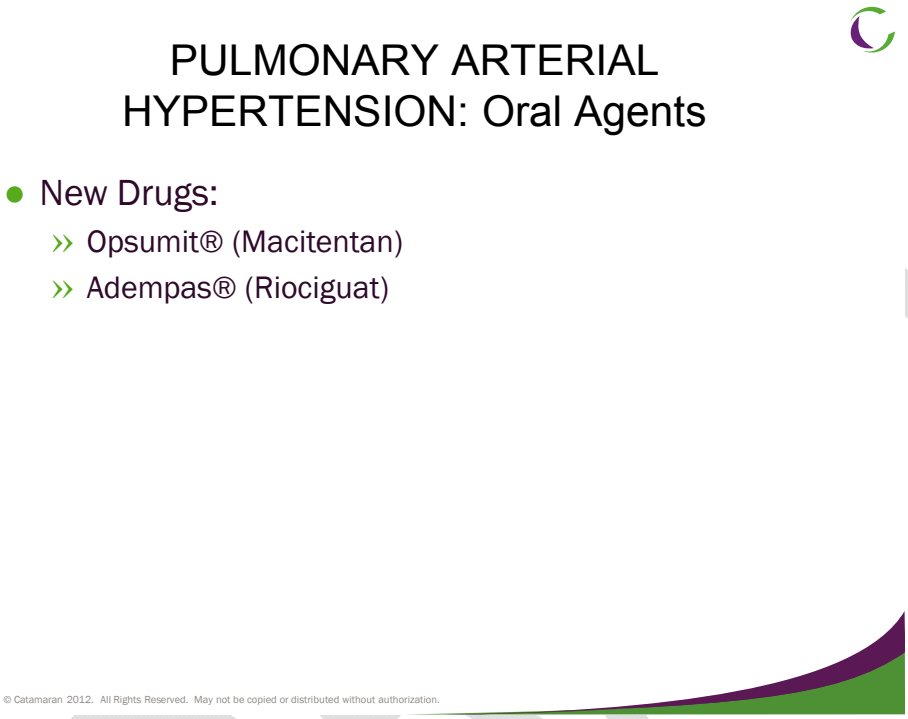
PULMONARY ARTERIAL HYPERTENSION: Oral Agents

Public Comment

Greg Morrill – representing Bayer for Adempas. He provided clinical information and requested Adempas be made preferred.

Evette Brooks – representing Actelion for Opsumit. She provided clinical information and requested Opsumit be made preferred.

Carl Jeffery, PharmD presented the following slides, clinical information, dosage forms, and product comparisons.



Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Ambrisentan (Letairis®)	Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening*	Tablet: 5 mg 10 mg	-
Bosentan (Tracleer®)	Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening†	Tablet: 62.5 mg 125 mg	-
Macitentan (Opsumit®)	Treatment of PAH (WHO Group I) to delay disease progression‖#	Tablet: 10 mg	-
Riociguat (Adempas®)	Treatment of PAH (WHO Group I) to improve exercise ability, improve WHO functional class and delay clinical worsening and treatment of persistent/recurrent CTEPH after surgical treatment or inoperable CTEPH to improve exercise capacity‖	Tablet: 0.5 mg 1 mg 1.5 mg 2 mg 2.5 mg	-
Sildenafil (Revatio®)	Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening§‖	Tablet: 20 mg Vial for injection: 0.8 mg/mL	✔
Tadalafil (Adcirca®)	Treatment of PAH (WHO Group I) to improve exercise ability¶	Tablet: 20 mg	-

PULMONARY ARTERIAL HYPERTENSION: Oral Agents

Class	Generic (Trade) Name	Dosage Form
Prostanoids	Iloprost (Ventavis®) Treprostinil (Tyvaso®)	Inhalation, Others available as IV or SQ
Endothelin Receptor Antagonists (ERAs)	Ambrisentan (Letaris®) Bosentan (Tracleer®) Macitentan (Opsumit®)	Oral only
Phosphodiesterase (PDE)-5 Inhibitors	Sildenafil (Revatio®) Tadalafil (Adcirca®)	Oral and IV forms available
Soluble Guanylate Cyclase Stimulators	Riociguat (Adempas®)	Oral only

PULMONARY ARTERIAL HYPERTENSION: Oral Agents

- Clinical trials have demonstrated the safety and efficacy of the PAH agents, however, there are no head-to-head trials comparing the agents within classes or between classes
- The national and European consensus guidelines recommend oral therapy with either a PDE-5 inhibitor or an ERA as first-line agents in patients considered lower risk
- Higher risk and patients with poor prognosis indexes, parenteral therapy with prostanoids should be considered first-line.
- Guidelines have not been updated since the introduction of soluble guanylate cyclase stimulators

Generic (Trade Name)	Test	Results
Ambrisentan (Letairis®)	6MWD	25, 28, 37M (2.5, 5, 10mg dose)
Bosentan (Tracleer®)	6MWD	11.2M increase vs 7.9M decrease for placebo, not statistically significant. But significant delay in clinical worsening
Iloprost (Ventavis®)	6MWD	16.7% achieved 10% improvement, improvement by at least one NYHA class vs. 4.9% in placebo
Macitentan (Opsumit®)	6MWD	Placebo-corrected average increases of 16.8 and 22.0 m vs. decrease of 9.4 m in the placebo group
Riociguat (Adempas®)	6MWD	Increase of 39 m vs. 6 m in the placebo group
Sildenafil (Revatio®)	6MWD	46% increased from baseline, 18% decreased, 19% died and 17% discontinued treatment or were lost to follow-up
Tadalafil (Adcirca®)	6MWD	Treatment with tadalafil significantly improved exercise capacity, as measured by the 6MWD and reduced clinical worsening compared to placebo
Treprostinil (Tyvaso®)	6MWD	There was a significant increase in the 6MWD in the treprostinil group compared to placebo

PULMONARY ARTERIAL HYPERTENSION: Oral Agents

- Clinical and Therapeutic Equivalence
  - ADCIRCA®
  - ADEMPAS®
  - LETAIRIS®
  - TRACLEER®
  - OPSUMIT®
  - SILDENAFIL
  - REVATIO®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide to the Committee:

PULMONARY ARTERIAL HYPERTENSION: Oral Agents

PULMONARY ARTERIAL HYPERTENSION: ORAL AGENTS		
ADCIRCA®	~~REVATIO®~~	Adempas®
LETAIRIS®	TRACLEER®	Opsumit®
Sildenafil		REVATIO®

He made the recommendation to make generic sildenafil preferred, and Adempas, Opsumit and brand Revatio as non-preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make generic sildenafil preferred and Adempas, Opsumit and brand Revatio to be non-preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

PULMONARY ARTERIAL HYPERTENSION: Inhaled Agents

Evette Brooks – representing of Actelion for Ventavis, offers to answer any questions the Committee may have.

Carl Jeffery, PharmD presented slides, clinical information and product comparisons.

PULMONARY ARTERIAL HYPERTENSION: Inhaled Agents

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Iloprost (Ventavis®)	Treatment of PAH (WHO Group I) to improve a composite endpoint consisting of exercise tolerance symptoms (NYHA class) and lack of deterioration‡	Ampule for inhalation: 10 µg/mL 20 µg/mL	-
Treprostinil (Tyvaso®)	Treatment of PAH (WHO Group I) to improve exercise ability	Ampule for inhalation: 0.6 mg/mL	-

Class	Generic (Trade) Name	Dosage Form
Prostanoids	Iloprost (Ventavis®) Treprostinil (Tyvaso®)	Inhalation, Others available as IV or SQ
Endothelin Receptor Antagonists (ERAs)	Ambrisentan (Letaris®) Bosentan (Tracleer®) Macitentan (Opsumit®)	Oral only
Phosphodiesterase (PDE)-5 Inhibitors	Sildenafil (Revatio®) Tadalafil (Adcirca®)	Oral and IV forms available
Soluble Guanylate Cyclase Stimulators	Riociguat (Adempas®)	Oral only

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Generic (Trade Name)	Test	Results
Ambrisentan (Letairis®)	6MWD	25, 28, 37M (2.5, 5, 10mg dose)
Bosentan (Tracleer®)	6MWD	11.2M increase vs 7.9M decrease for placebo, not statistically significant. But significant delay in clinical worsening
Iloprost (Ventavis®)	6MWD	16.7% achieved 10% improvement, improvement by at least one NYHA class vs. 4.9% in placebo
Macitentan (Opsumit®)	6MWD	Placebo-corrected average increases of 16.8 and 22.0 m vs. decrease of 9.4 m in the placebo group
Riociguat (Adempas®)	6MWD	Increase of 39 m vs. 6 m in the placebo group
Sildenafil (Revatio®)	6MWD	46% increased from baseline, 18% decreased, 19% died and 17% discontinued treatment or were lost to follow-up
Tadalafil (Adcirca®)	6MWD	Treatment with tadalafil significantly improved exercise capacity, as measured by the 6MWD and reduced clinical worsening compared to placebo
Treprostinil (Tyvaso®)	6MWD	There was a significant increase in the 6MWD in the treprostinil group compared to placebo

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PULMONARY ARTERIAL HYPERTENSION: Inhaled Agents

- Clinical and Therapeutic Equivalence
  - VENTAVIS®
  - TYVASO®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following slide to the Committee:

PULMONARY ARTERIAL HYPERTENSION: Inhaled Agents

PULMONARY ARTERIAL HYPERTENSION AGENTS: INHALED AGENTS
VENTAVIS®
TYVASO®

Carl Jeffery, PharmD recommended adding Tyvaso as preferred, and keeping Ventavis as preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make Tyvaso preferred and keep Ventavis as preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

OPHTHALMIC GLAUCOMA AGENTS

Shamim Nagy, MD, Chairwoman, MD, Chair: Public Comment? None. Dr. Jeffery.

Carl Jeffery, PharmD presented slides and clinical information for the new product, Simbrinza.

OPHTHALMIC GLAUCOMA AGENTS

Generic Name (Trade name)	Medication Class	Generic Availability
Brimonidine/timolol maleate (Combigan®*)	Ophthalmic glaucoma combinations	✔
Brinzolamide/brimonidine (Simbrinza®)	Ophthalmic glaucoma combinations	-
Dorzolamide/timolol maleate (Cosopt®)	Ophthalmic glaucoma combinations	✔
Dorzolamide/timolol maleate (Cosopt PF®*)	Ophthalmic glaucoma combinations	✔

OPHTHALMIC GLAUCOMA AGENTS

- Two studies compared the efficacy of ophthalmic brinzolamide/brimonidine in a fixed-dose combination to the efficacy of ophthalmic brinzolamide or ophthalmic brimonidine as monotherapy. Both studies demonstrated that treatment with ophthalmic brinzolamide/brimonidine as a fixed-dose combination resulted in a significantly greater reduction in IOP compared to monotherapy with either agent ($P<0.005$ for both studies).

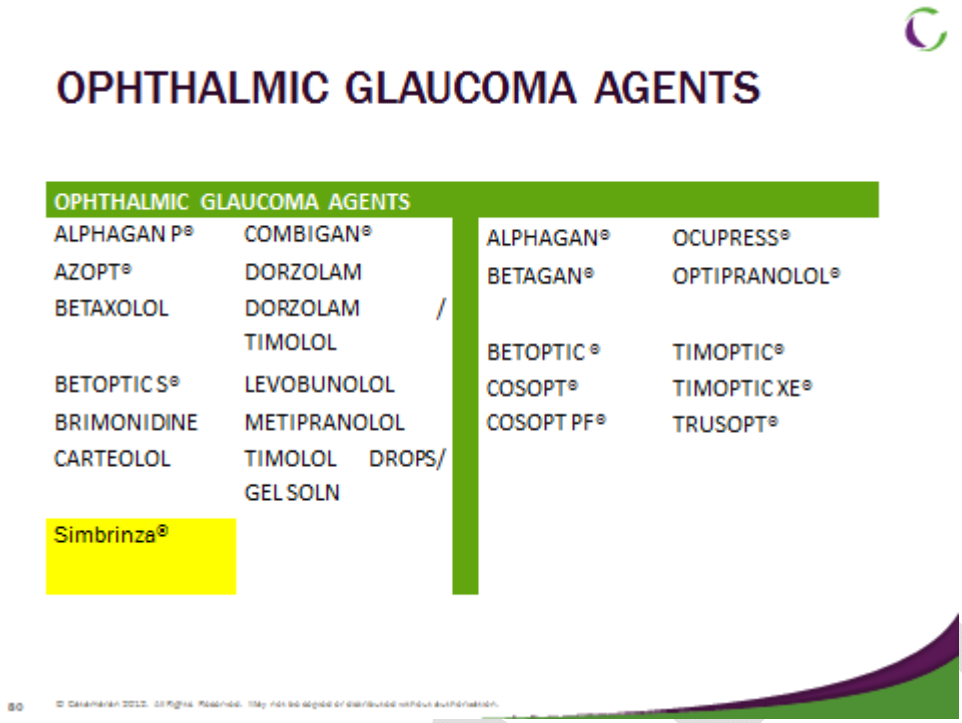
Clinical and Therapeutic Equivalence

- ALPHAGAN P®
- COMBIGAN®
- AZOPT®
- DORZOLAM
- BETAXOLOL
- DORZOLAM / TIMOLOL
- BETOPTIC S®
- LEVOBUNOLOL
- BRIMONIDINE
- METIPRANOLOL
- CARTEOLOL
- TIMOLOL DROPS/ GEL SOLN
- SIMBRINZA®
- ALPHAGAN®
- OCUPRESS®
- BETAGAN®
- OPTIPRANOLO®
- BETOPTIC ®
- TIMOPTIC®
- COSOPT®
- TIMOPTIC XE®
- COSOPT PF®
- TRUSOPT®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following:



Carl Jeffery, PharmD made the recommendation to make Simbrinza preferred.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make Simbrinza preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

ANAPHYLAXIS: Self-Injectable Epinephrine

Shamim Nagy, MD, Chairwoman, MD, Chair: Public Comment? None. Dr. Jeffery.

Carl Jeffery, PharmD presented slides, a brief overview of the class and explained the new generic epinephrine now available.

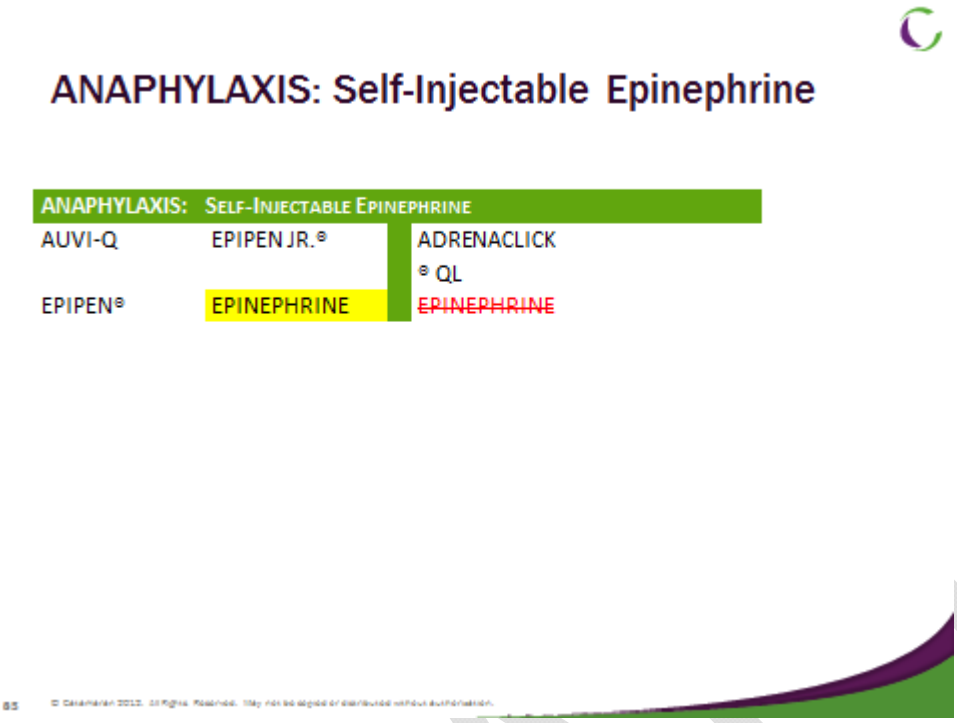
Generic Name	Usual Dose	Availability
Epinephrine	Emergency treatment of severe allergic reactions (Type 1) including anaphylaxis to stinging insects (e.g., order Hymenoptera, which include bees, wasps, hornets, yellow jackets and fire ants), biting insects (e.g., triatoma, mosquitoes), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as anaphylaxis to unknown substances (idiopathic anaphylaxis) or exercise-induced anaphylaxis: Injection: 0.15 (15 to 30 kg) or 0.3 mg (≥30 kg) Vial for injection:* <30 kg: 0.01 mg/kg, up to a maximum of 0.3 mg, repeated every 5 to 10 minutes as necessary; ≥30 kg: 0.3 to 0.5 mg repeated every 5 to 10 minutes as necessary	Injection: 0.15 mg/0.15 mL (Adrenaclick®†, Auvi-Q®†, epinephrine†) 0.15 mg/0.3 mL (EpiPen Jr®†) 0.3 mg/0.3 mL (Adrenaclick®†, Auvi-Q®†, epinephrine†, EpiPen®†) Vial for injection: 1 mg/1mL (Adrenalin®*)

- Clinical and Therapeutic Equivalence
  - AUVI-Q
  - EPIPEN JR.®
  - ADRENACLICK® QL
  - EPIPEN®
  - EPINEPHRINE

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following:



He made the recommendation that generic epinephrine injector be added as preferred, with no other changes.

A motion was made and seconded to accept Catamaran's recommendation as presented, to make generic epinephrine injector preferred with no other changes.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

ANTIDEPRESSANTS: Other

Representative of Lundbeck for Brintellix provided clinical information and requested Brintellix be made preferred.

Carla McSpadden – speaking on behalf of Forest for Fetzima, provided clinical information and requested Fetzima be made preferred.

Carl Jeffery, PharmD presented slides, and clinical information for two new products, Fetzima and Brintellix.

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Nefazodone*	Depression	Tablet: 50 mg 100 mg 150 mg 200 mg 250 mg	✔
Trazodone* (Oleptro®)	Major depressive disorder	Tablet (extended release): 150 mg 300 mg Tablet (immediate release): 50 mg 100 mg 150 mg 300 mg	✔
Vilazodone (Viibryd®)	Major depressive disorder	Tablet: 10 mg 20 mg 40 mg	-
Vortioxetine (Brintellix®)	Major depressive disorder	Tablet: 5 mg 10 mg 15 mg 20 mg	-

Vortioxetine (Brintellix®)

- Inhibits reuptake of serotonin (5-HT); also has agonist activity at the 5-HT_{1A} receptor and antagonist activity at the 5-HT_3 receptor
- Vortioxetine has been shown to be more effective than placebo in clinical trials, with effects seen as early as one week.[10-13] Vortioxetine has been compared to placebo and although studies have shown a significant improvement vs placebo these results were not consistent across trials and outcomes.
- **Substrate** of CYP2A6 (minor), CYP2B6 (minor), CYP2C19 (minor), CYP2C8 (minor), CYP2C9 (minor), CYP2D6 (major), CYP3A4 (major)

Heisenberg N, et. al.[14] (2012) Vortioxetine 1 mg once daily or vortioxetine 5 mg once daily or vortioxetine 10 mg once daily vs placebo once daily	DB, MC, PC, PG, RCT Patients 18 to 75 years of age, had a current MDE per DSM-IV-TR criteria, ambulatory and a baseline MADRS total score ≥26	N=556 (N=505 completed study) 8 weeks	Primary: Change from baseline in HAMD-24 after eight weeks of treatment Secondary: Decrease from baseline on SDS, CGI-I score and decrease from baseline on MADRS	Primary: At eight weeks, all treatment groups had a significantly greater decrease from baseline in HAMD-24 compared to placebo. Vortioxetine 1 mg had a decrease from baseline on the HAMD-24 of -14.82 (*P*<0.001). Vortioxetine 5 mg had a decrease from baseline of -15.42 (*P*<0.001), and vortioxetine 10 mg had a decrease from baseline on the HAMD-24 of -16.23 (*P*<0.001). Secondary: None of the vortioxetine treatment groups had statistically significant decrease from baseline on the SDS as compared to placebo for (*P* values not reported). Vortioxetine 1, 5 and 10 mg all met the secondary endpoint of CGI-I compared to placebo; 2.37, 2.37 and 2.29 respectively (*P*<0.001 for all comparators). Vortioxetine 1, 5, and 10 mg all met statistical significance for the endpoint of decrease from baseline on the MADRS total score; -14.89, -15.09 and -15.65, respectively (*P*<0.001 for all).

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Baldwin et al.[15] (2012) Vortioxetine 2.5 mg once daily or vortioxetine 5 mg once daily or vortioxetine 10 mg once daily	OL Patients with MDD	N=535 52 weeks	Primary: Safety and tolerability, MADRS Secondary: Not reported	Primary: Adverse events reported by >10% of patients were nausea, headache, and nasopharyngitis. Six patients had eight adverse events related to sexual dysfunction. There were no clinically significant safety findings with respect to mean changes of vital signs, weight, ECG parameters, or clinical laboratory values. Patients entered the extension study with a mean MADRS total score of 13.5+8.7. The mean MADRS total score decreased (improved) by approximately 8 points to 5.5+6.0 at week 52. By the end of the study, the proportion of responders had increased from 63 to 94%, as had the proportion in remission (MADRS <10), increasing from 42 to 83%. Patients in remission (n=226) at the start of this study had a relapse rate (MADRS >22) of 9.7%. Secondary: Not reported

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Jain et al.[16] (2013) Vortioxetine 5 mg once daily vs placebo once daily	DB, PC Patients 18 to 75 years of age with MDD and a baseline MADRS total score >30	N=600 8 weeks	Primary: Change from baseline in HAMD-24 total score at week six compared to placebo Secondary: Response and remission rates, CGI-I, HAMA, MADRS-S total score, adverse events	Primary: There were no significant differences in efficacy measures between subjects in the 5 mg vortioxetine and placebo groups at week six. Secondary: HAMD-24 total score in subjects with baseline HAMA >19 in the 5 mg vortioxetine group was improved at weeks three to six compared to the placebo group (P<0.05). The most common adverse events for the vortioxetine and placebo groups were nausea (19.1 and 9.4%), headache (17.1 and 15.1%) and diarrhea (11.4 and 7.0%), respectively.

Katona C, et. al.[17] (2012) Vortioxetine 5 mg once daily or duloxetine 60 mg once daily vs placebo once daily	AC, DB, MC, PC, PG, RCT Patients ≥65 years of age, with a primary diagnosis of MDD per DSM-IV-TR criteria and a MADRS score ≥26	N=453 (N=392 completed the study) 8 weeks	Primary: Change from baseline in HAMD-24 total score at weeks one, two, four, six, and eight. Secondary: Change in baseline from CGI-I, MADRS total score, HAMA and CGI-S at week eight. Cognitive changes from baseline assessed via the RAVLT and DSST at week eight	Primary: The vortioxetine treatment group did not meet the primary endpoint until week six of the study, and it was not reported when the duloxetine treatment group began to separate from placebo for the primary endpoint. The vortioxetine treatment group began to separate on the HAMD-24 scale from placebo at week six (P=0.024). At week eight, vortioxetine 5 mg had a mean change from baseline in HAMD-24 score of -13.7 (P<0.01), and duloxetine 60 mg had a mean change from baseline on the HAMD-24 of -15.8 (P<0.0001). Secondary: Vortioxetine 5 mg and duloxetine 60 mg both met all secondary endpoints at week eight. A change in CGI-I of -0.56 (P<0.001) was reported for the vortioxetine group, along with a decrease in MADRS total change of -4.29 (P<0.001), a decrease in HAMA scores of -2.35 (P<0.01) and a decrease of CGI-S of -0.60 (P<0.001). Duloxetine showed similar results for these secondary endpoints with a P<0.001 for all of these measures. The cognitive measures also showed positive results for both treatment groups. Vortioxetine 5 mg showed a difference from placebo on the DSST change of 2.79 (P>0.05), and vortioxetine showed a difference from placebo in RAVLT for acquisition change of 1.14 (P<0.05) and delayed recall change of 0.47 (P<0.05). The duloxetine group did not show statistical significance for DSST change with a value of 0.77 (no P value reported). The duloxetine group did show statistical significance on the RAVLT for acquisition of change of 1.41 (P<0.01) and delayed recall change of 0.64 (P<0.01)

Mahableshwarkar, et. al.[18] (2013) Vortioxetine 2.5 mg once daily or vortioxetine 5 mg once daily vs duloxetine 60 mg once daily vs placebo once daily	DB, PC Adult patients with MDD	N=611 8 weeks	Primary: Change from baseline in the HAM-D24 Secondary: Responder rate, CGI-I), and remission rate; adverse events, ASEX	Primary: Both doses of vortioxetine were associated with declines in HAM-D24 total scores compared to placebo but were not statistically significant. At eight weeks, changes from baseline were [mean]: -10.50 (0.76) placebo, -12.04 (0.74) 2.5 mg vortioxetine, and -11.08 (0.74) 5 mg vortioxetine. Secondary: CGI-I and remission rate were not significantly different from placebo. Duloxetine treatment was associated with declines in HAM-D24 total score [-13.47(0.75); *P*=0.005] as well as significant improvements in secondary outcome measures vs placebo (*P*<0.05). The most common adverse events for vortioxetine were nausea, dry mouth, and headache. Rates of sexual dysfunction (ASEX) were 51.0, 37.5, 46.9, and 33.3% in the vortioxetine 2.5 mg, vortioxetine 5 mg, duloxetine, and placebo groups, respectively.

Vortioxetine (Brintellix®)

- Vortioxetine is a novel antidepressant that could provide a therapeutic option for patients unable to tolerate or achieve therapeutic goals with more traditional antidepressants. The nature of the treatment of depression is very individualized, and vortioxetine could make a positive impact in the setting of major depressive disorder. Vortioxetine use is associated with a high incidence of nausea at therapeutic doses, and lack of an established position in consensus treatment guidelines

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Desvenlafaxine succinate (desvenlafaxine ER, Pristiq®, Khedezla®)	Treatment of major depressive disorder	Extended-release tablet:	-
Duloxetine (Cymbalta®)	Management of chronic musculoskeletal pain*; management of fibromyalgia; management of neuropathic pain associated with diabetic peripheral neuropathy; treatment of generalized anxiety disorder; treatment of major depressive disorder	Delayed-release capsule:	-
Levomilnacipran (Fetzima®)	Treatment of major depressive disorder	Extended-release capsules:	-
Venlafaxine (Effexor®, Effexor XR®, venlafaxine ER)	Treatment of generalized anxiety disorder (extended-release capsule); treatment of major depressive disorder (extended-release capsule, extended-release tablet, tablet); treatment of panic disorder, with or without agoraphobia (extended-release capsule); treatment of social anxiety disorder (extended-release capsule)	Extended-release capsule (Effexor XR®): Extended-release tablet: Tablet:	

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Levomilnacipran (Fetzima®)

- Levomilnacipran, is a potent inhibitor of norepinephrine and serotonin reuptake
- The statistical analyses for all of the endpoints were calculated and reported as the least squares mean difference from placebo, using the changes from baseline on all scales at week eight. Overall levomilnacipran showed significant reduction in Montgomery-Åsberg Depression Rating Scale scores compared to placebo
- **Substrate** of CYP2C19 (minor), CYP2C8 (minor), CYP2D6 (minor), CYP3A4 (major), P-glycoprotein;

Asnis GM et al.[37] (2013) Levomilnacipran 40 mg QD or levomilnacipran 80 mg QD or levomilnacipran 120 mg QD vs placebo	DB, MC, PC, RCT Patents 18 to 65 years of age, met the diagnostic criteria of MDD per the DSM-IV-TR, current ongoing depressive episode ≥8 weeks in duration, MADRS score ≥30 at baseline, MADRS-SR ≥26 at baseline	N=708 N=506 completed study 8 weeks	Primary: Mean reduction of MADRS score from baseline at week eight (reported as LSMD from placebo) Secondary: Mean reduction of SDS score from baseline at week eight, mean reduction on $HDRS_{17}$ from baseline at week eight, mean change from baseline of CGI-S total score at week eight and mean reduction from baseline of CGI-I total score at week eight (all reported as LSMD from placebo)	Primary: The LSMD from placebo of MADRS scores for levomilnacipran 40, 80 and 120 mg at week eight were -3.23; *P*=0.0186, -3.99; *P*=0.0038 and -4.86; *P*=0.0005, respectively. Secondary: The LSMD from placebo on the SDS total score for levomilnacipran 40, 80 and 120 mg was -1.4; *P*>0.05, -2.51; *P*<0.05, -2.57; *P*<0.05, respectively. The LSMD from placebo on the $HDRS_{17}$ for levomilnacipran 40, 80 and 120 mg was -1.2; *P*>0.05; -2.09; *P*<0.05 and -2.34; *P*<0.05, respectively. The LSMD from placebo on the CGI-S for levomilnacipran 40, 80 and 120 mg was -.04; *P*>0.05, -0.43; *P*<0.01 and -0.35; *P*<0.05, respectively. The LSMD from placebo on the CGI-I score for levomilnacipran 40, 80 and 120 mg was -0.1; *P*>0.05, -0.34; *P*<0.05 and -0.32; *P*<0.05, respectively.

Bakish D et al.[38] (2013) Levomilnacipran 40 mg QD or levomilnacipran 80 mg QD vs placebo	DB, MC, PC, RCT Patients 18 to 75 years of age, met diagnostic criteria per the DSM-IV-TR for recurrent MDD, current ongoing depressive episode 6 weeks to 12 months in duration, 5 or fewer major depressive episodes within the previous 5 years, MADRS score ≥26 at baseline, CGI-S score ≥4 at baseline	N=557 N=441 completed study 8 weeks	Primary: Mean reduction of MADRS score from baseline at week eight (reported as LSMD from placebo) Secondary: Mean reduction of SDS score from baseline at week eight, mean reduction on $HDRS_{17}$ from baseline at week eight and mean reduction from baseline of CGI-S total score at week eight (all reported as LSMD from placebo)	Primary: The LSMD from placebo week eight for levomilnacipran 40 and 80 mg was -3.3; *P*=0.003 and -3.1; *P*=0.004, respectively. Secondary: The LSMD from placebo at week eight for levomilnacipran 40 and 80 mg was -1.8; *P*=0.046 and - 2.7; *P*=0.003, respectively. The LSMD from placebo on $HDRS_{17}$ scores for levomilnacipran 40 and 80 mg were -2.2; *P*=0.007 and -1.6; *P*=0.043. The LSMD from placebo on CGI-S scores for levomilnacipran 40 and 80 mg was -0.3 for both arms with *P*=0.020 and *P*=0.015, respectively.

Sambunaris A et al.[39] (2013) Levomilnacipran 40 to 120 mg vs placebo	DB, FD, MC, PC, RCT Patients 18 to 80 years of age, met the diagnostic criteria for MDD per the DSM-IV-TR, ongoing major depressive episode of at least 4 weeks in duration, MADRS score ≥30 at baseline and MADRS-SR ≥26 at baseline	N=429 N=335 completed study 8 weeks	Primary: Mean reduction of MADRS score from baseline at week eight (reported as LSMD from placebo Secondary: Mean reduction of SDS score from baseline at week eight, mean reduction on $HDRS_{17}$ from baseline at week eight, mean change from baseline of CGI-I total score at week eight, mean reduction from baseline of CGI-S total score at week eight and mean change from baseline on MEI-SF total score at week eight (all reported as LSMD from placebo)	Primary: The LSMD from placebo on the MADRS score at week eight was -3.095; *P*=0.0051 for levomilnacipran 40 to 120 mg. Secondary: The LSMD from placebo on the SDS at week eight was -2.632; *P*=0.0010 for levomilnacipran 40 to 120 mg. The LSMD from placebo on the $HDRS_{17}$ score for levomilnacipran 40 to 120 mg was -2.146; *P*=0.0038. Levomilnacipran 40 to 120 mg did not show statistically significant results for the LSMD from placebo on the CGI-I total score at week eight (-0.207; *P*=0.0881). Levomilnacipran 40 to 120 mg showed a LSMD from placebo on the CGI-S at week eight of -0.352; *P*=0.0083. The LSMD from placebo on the MEI-SF for levomilnacipran 40 to 120 mg at week eight was 5.048; *P*=0.0382.

Montgomery et al.[40] (2013) Levomilnacipran 75 or 100 mg QD Levomilnacipran dose was increased to 100 mg/day over 12 days.	DB, FD, MC, PC, RCT Outpatients 18 to 70 years of age who met DSM-IV criteria for MDD (duration > 1 month) with a HDRS17 score > 22 and SDS score > 10	N=553 10 weeks	Primary: MADRS score change from baseline to week 10 Secondary: HDRS17, SDS, CGI-I, MADRS response (>50% decrease from baseline) and remission (score <10), safety	Primary: Levomilnacipran was significantly "superior" to placebo on MADRS total score change from baseline to week 10 (LSMD, -4.2; 95% CI, -5.7 to -2.6; *P*<.0001). Secondary: Statistical significance in favor of levomilnacipran was demonstrated on change from baseline to week 10 in HDRS17 total score (LSMD, -3.4; 95% CI, -4.7 to -2.2; *P*<0.0001) and SDS total score (LSMD, -3.4; 95% CI, -4.6 to -2.2; *P*<0.0001) and subscales. Significantly more levomilnacipran patients vs placebo patients achieved MADRS response (59.1 vs 42.2%; *P*<0.0001) and remission (46.4 vs 26.0%; *P*<0.0001). Levomilnacipran was generally safe and well tolerated; more levomilnacipran patients (9.4%) vs placebo patients (6.5%) discontinued due to adverse events, but more placebo patients vs levomilnacipran patients discontinued overall (24.9 vs 20.2%).

Clinical and Therapeutic Equivalence

- BUPROPION
- MIRTAZAPINE
- BUPROPION SR
- MIRTAZAPINE RAPID TABS
- BUPROPION XL
- TRAZODONE
- CYMBALTA
- SAVELLA®
- PRISTIQ®
- Brintellix®
- Fetzima®
- Duloxetine

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A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following:

ANTIDEPRESSANTS: Other

ANTIDEPRESSANTS: OTHER		
BUPROPION	MIRTAZAPINE	~~SAVELLA®~~
BUPROPION SR	MIRTAZAPINE RAPID TABS	~~PRISTIQ®~~
BUPROPION XL	TRAZODONE	Brintellix®
CYMBALTA®(PA not required for ICD-9 code 729.1 or 250.6)		Fetzima®
SAVELLA®	PRISTIQ®	Duloxetine

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Carl Jeffery, PharmD made the recommendation to move Savella and Pristiq to preferred status and keep Brintellix, Fetzima and duloxetine as non-preferred.

The Committee discussed moving Viibryd that is listed in the "Antidepressant: SSRIs" to "Antidepressants: Other" since it is not truly an SSRI.

A motion was made and seconded to move Viibryd to "Antidepressants: Other" keeping it non-preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

The Committee discussed, with input from the audience, that Savella, while it has a similar mechanism of action of other antidepressants, is only indicated for Fibromyalgia. The Committee decided to address this at a future meeting.

A motion was made and seconded to accept Catamaran's recommendation to move Savella and Pristiq to preferred. Brintellix, Fetzima and duloxetine will be non-preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Protease Inhibitors

Public Comment

Laura Litzenberger – representing Janssen for Olysio. She presented an overview of new products, including dosing and effectiveness.

Carl Jeffery, PharmD presented slides, clinical information and accepted treatment guidelines.

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Boceprevir (Victrelis®)	Treatment of chronic hepatitis genotype 1 infection, in combination with peg interferon alfa and ribavirin, in adults with compensated liver disease, including cirrhosis, who are treatment-naïve or who have previously been treated with interferon based treatment, including prior null responders, partial responders and relapsers	Capsule: 200 mg	-
Simeprevir (Olysio®)	Treatment of chronic hepatitis genotype 1 infection, in combination with peg interferon alfa and ribavirin, in adults with compensated liver disease, including cirrhosis, who are treatment-naïve or who have previously been treated with interferon based treatment, including prior null responders, partial responders and relapsers	Capsule: 150 mg	-
Telaprevir (Incivek®)	Treatment of chronic hepatitis genotype 1 infection, in combination with peg interferon alfa and ribavirin, in adults with compensated liver disease, including cirrhosis, who are treatment naïve or who have previously been treated with interferon based treatment, including prior null responders, partial responders and relapsers	Tablet: 375 mg	-

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HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Protease Inhibitors

- Boceprevir is available as a 200 mg capsule and is dosed 800 mg three times daily.[1]
  - Boceprevir is initiated after a four week lead-in period of peg interferon alfa and ribavirin alone.[1]
- Telaprevir is available as a 375 mg tablet and is dosed 1,125 mg twice daily.[2]
  - Telaprevir is initiated with peg interferon alfa and ribavirin.[2]
- Simeprevir is available as a 150 mg capsule and is dosed 150 mg once daily.[3]
  - Simeprevir is initiated with peg interferon alfa and ribavirin.[3]

Genotype	Recommended	Alternative	NOT Recommended
1	IFN eligible: SOF + PEG/RBV x 12 weeks IFN ineligible IFN ineligible is defined as one or more of the below: • Intolerance to IFN • Autoimmune hepatitis and other autoimmune disorders • Hypersensitivity to PEG or any of its components • Decompensated hepatic disease • History of depression, or clinical features consistent with depression • A baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL • A history of preexisting cardiac disease: SOF + SMV ± RBV x 12 weeks	IFN eligible: SMV x 12 weeks + PEG/RBV x 24 weeks* IFN ineligible IFN ineligible is defined as one or more of the below: • Intolerance to IFN • Autoimmune hepatitis and other autoimmune disorders • Hypersensitivity to PEG or any of its components • Decompensated hepatic disease • History of depression, or clinical features consistent with depression • A baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL • A history of preexisting cardiac disease: SOF + RBV x 24 weeks	TVR + PEG/RBV x 24 or 48 weeks (RGT) BOC + PEG/RBV x 28 or 48 weeks (RGT) PEG/RBV x 48 weeks Monotherapy with PEG, RBV, or a DAA Do not treat decompensated cirrhosis with PEG or SMV

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Genotype	Recommended	Alternative	NOT Recommended
2	SOF + RBV x 12 weeks	None	PEG/RBV x 24 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR, BOC, or SMV
3	SOF + RBV x 24 weeks	SOF + PEG/RBV x 12 weeks	PEG/RBV x 24-48 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR, BOC, or SMV

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Genotype	Recommended	Alternative	NOT Recommended
4	IFN eligible: SOF + PEG/RBV x 12 weeks IFN ineligible IFN ineligible is defined as one or more of the below: • Intolerance to IFN • Autoimmune hepatitis and other autoimmune disorders • Hypersensitivity to PEG or any of its components • Decompensated hepatic disease • History of depression, or clinical features consistent with depression • A baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL • A history of preexisting cardiac disease: SOF + RBV x 24 weeks	SMV x 12 weeks + PEG/RBV x 24-48 weeks	PEG/RBV x 48 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR or BOC
5 or 6	SOF + PEG/RBV x 12 weeks	PEG/RBV x 48 weeks	Monotherapy with PEG, RBV, or a DAA Any regimen with TVR or BOC

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HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Protease Inhibitors

Drug	Study	SVR
Boceprevir	SPRINT-2 RESPOND-2 Flamm et al[20]	67-68% 59-66% 64%
Telaprevir	ADVANCE ILLUMINATE Kumada et al REALIZE Hayashi et al[19]	83-89% 88-92% 73% 83-88% 88%
Simeprevir	QUEST 1 & 2	80%

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Protease Inhibitors

- Clinical and Therapeutic Equivalence
  - INCIVEK®
  - VICTRELIS®
  - OLYSIO®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following:

Carl Jeffery, PharmD made the recommendation to make Olysio preferred with no other changes.

A motion was made and seconded to accept Catamaran's recommendation to make Olysio preferred with no other changes.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

NEW DRUG CLASSES

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Polymerase Inhibitors

Public Comment

Betty Chan with Dr. Kevin Prince – representing Gilead for Solvaldi, provided a brief introduction and offered availability for questions. Dr. Prince requested the Committee make Sovaldi preferred.

Carl Jeffery, PharmD presented slides, clinical information for Sovaldi and accepted treatment guidelines.

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Polymerase Inhibitors

Generic Name (Trade name)	Medication Class	Generic Availability
Sofosbuvir (Sovaldi®)	Hepatitis C virus NS5B polymerase inhibitor	-

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Polymerase Inhibitors

Indication	Sofosbuvir
Treatment of chronic HCV genotype 1 infection, including HCV/HIV-1 co-infection, in combination with peg interferon alfa and ribavirin; treatment in combination with ribavirin alone (without peg interferon alfa) can be considered for hepatitis C patients with genotype 1 infection who are ineligible to receive an interferon-based regimen	✔
Treatment of chronic HCV genotype 4 infection, including HCV/HIV-1 co-infection, in combination with peg interferon alfa and ribavirin	✔
Treatment of chronic HCV genotype 2 or 3 infection, including HCV/HIV-1 co-infection, in combination with ribavirin	✔
Prevention of post-transplant HCV reinfection in combination with ribavirin in patients with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation), including patients with HCV/HIV-1 co-infection	✔

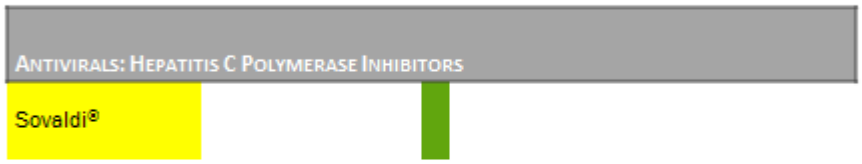
HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Polymerase Inhibitors

- NEUTRINO – GT 1, 4, 5 or 6
  - SVR of 90% compared to Boc/Tel of 60%
- FISSION – GT 2 or 3
  - SVR of 67% (lower in 3 vs. 2, 56 vs. 97%)
- POSITRON - GT 2 or 3
  - SVR of 78% (lower in 3 vs. 2, 61 vs 93%)
- FUSION – GT 2 or 3
  - SVR of 50% in 12-week group, 73% in 16-week

Carl Jeffery, PharmD: With only one agent in this class, a vote for clinical/therapeutic equivalency is not necessary.

Carl Jeffery, PharmD presented the following:

HEPATITIS C AGENTS: ANTIVIRALS: Hepatitis C Polymerase Inhibitors



Carl Jeffery, PharmD PharmD made the recommendation that Sovaldi be made preferred.

A motion was made and seconded to accept Catamaran's recommendation to make Solvaldi preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

MULTIPLE SCLEROSIS AGENTS: Oral Disease Modifying

Public Comment

Tom O'Connor – Representing Novartis for Gilenya, provided a brief overview of indications and clinical studies supporting use and treatment guidelines.

Michael Sullivan – representing Biogen for Tecfidera, offered to answer any questions about Tecfidera.

Carl Jeffery, PharmD presented slides, and gave a brief overview of the class. He explained this class is being reviewed so it can be broken out from the injectable agents.

MULTIPLE SCLEROSIS AGENTS: Oral Disease Modifying

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Dimethyl fumarate (Tecfidera®)	Relapsing-remitting multiple sclerosis*	Delayed-release capsule: 120 mg 240 mg	-
Fingolimod (Gilenya®)	Relapsing-remitting multiple sclerosis†	Capsule: 0.5 mg	-
Teriflunomide (Aubagio®)	Relapsing-remitting multiple sclerosis*	Tablet: 7 mg 14 mg	-

MULTIPLE SCLEROSIS AGENTS: Oral Disease Modifying

- Clinical and Therapeutic Equivalence
  - AUBAGIO®
  - GILENYA®
  - TECFIDERA®

A motion was made and seconded that these products are therapeutic equivalents.

The Committee voted unanimous: Aye.

Carl Jeffery, PharmD presented the following:

MULTIPLE SCLEROSIS AGENTS: Oral Disease Modifying

MULTIPLE SCLEROSIS AGENTS: DISEASE MODIFYING – ORAL AGENTS

Trial of only one agent is required before moving to a non-preferred agent

AUBAGIO®

GILENYA®

TECFIDERA®

~~AUBAGIO®~~

~~GILENYA®~~

He made the recommendation to add Aubagio and Gilenya as preferred and keeping Tecfidera as preferred.

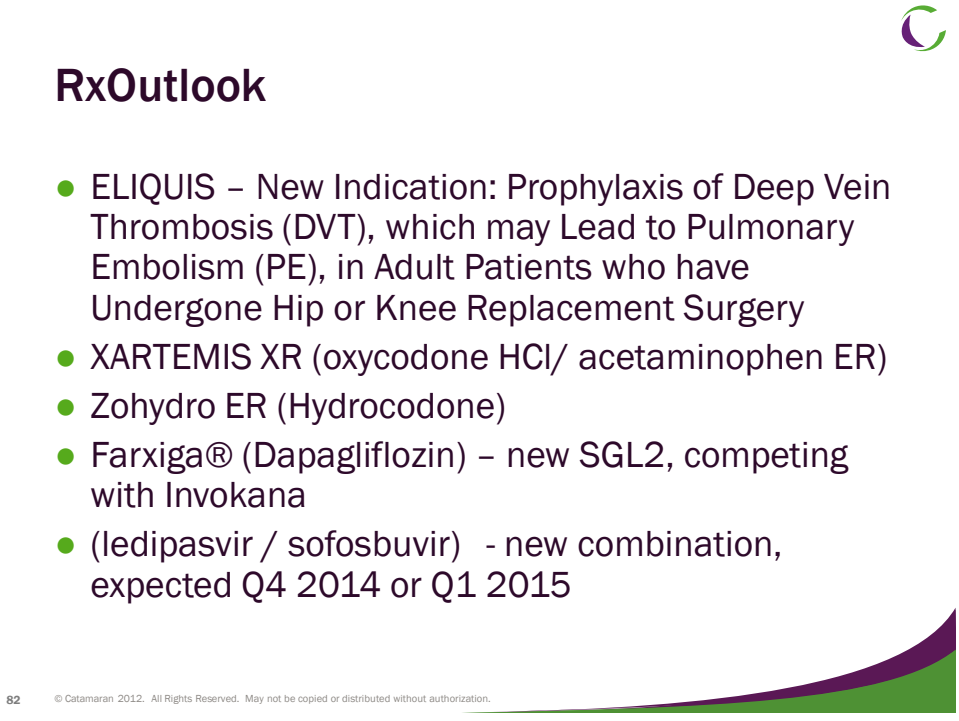
A motion was made and seconded to accept Catamaran's recommendation to make Aubagio and Gilenya preferred and keeping Tecfidera preferred.

Kalinowski: Aye.
Zold: Aye.
Decerbo: Aye.
Adashek: Aye.
Nagy: Aye.
Hautekeet: Aye.
Fluitt: Aye
Chu: Aye.

Shamim Nagy, MD, Chairwoman: Motion approved.

REPORT BY CATAMARAN ON NEW DRUGS TO MARKET, NEW GENERIC DRUGS TO MARKET, AND NEW LINE EXTENSIONS

Carl Jeffery, PharmD presented the following slide and gave a brief summary of products with new indications, new products coming out and expected generic product launches.



REVIEW OF NEXT MEETING LOCATION, DATE, AND TIME

The Committee agreed the next meeting will be June 26, 2014 at 1:00PM with a location to be determined.

PUBLIC COMMENT

None.

ADJOURNMENT

Chairperson Nagy adjourned the meeting at 3:04pm.