DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF DIRECTOR

ACTION REFERRAL

TO	DATE
Bowling/FOIA	4-10-07

DIRECTOR'S USE ONLY	ACTION REQUESTED
1. LOG NUMBER 000635	[ ] Prepare reply for the Director's signature DATE DUE _____
2. DATE SIGNED BY DIRECTOR cc: Singleton, Stenoland Cleared 4/20/07, letter attached.	[ ] Prepare reply for appropriate signature DATE DUE _____ [X] FOIA DATE DUE 4-24-07 [ ] Necessary Action

APPROVALS (Only when prepared for director's signature)	APPROVE	* DISAPPROVE (Note reason for disapproval and return to preparer.)	COMMENT
1.			
2.			
3.			
4.			

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Log. Boulis
"FOIA"
cc: Singleton
Stensland

Bryan Kost
Department of Health and Human Services
1801 Main St.
Columbia, SC 29201

RE: Freedom of Information Act request

Dear Mr. Kost:

This is a request under the Freedom of Information Act.

I request that a copy of the following documents be provided to me: handouts submitted by pharmaceutical manufacturers for the public testimony portion of any Pharmacy & Therapeutics meetings held from January 1, 2006, to March 31, 2007. This material would include only handouts that were voluntarily submitted to the committee and not any information submitted as a result of an unsolicited request by the committee.

The requested materials may be sent to me at the following address:

Attn: Robert Dean
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Should you have any questions, I can be reached at 301-796-1200 ext 2215.

Sincerely,

Robert Dean, MBA
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

State of South Carolina
Department of Health and Human Services

Mark Sanford
Governor

Robert M. Kerr
Director

TO:

FROM:

SUBJECT: Cost of Processing FOIA Request #

The South Carolina Department of Health and Human Services has received and processed your FOIA request. The cost for processing this information is as follows:

Staff processing time at $10.00 per hour	_____ Hours	$_____
Pages copied at $.10 per page	_____ Pages	$_____
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Other costs associated with the FOIA request: _____		$_____
Total Amount Due SCDHHS:		$_____

Please remit the above amount to the following address:

Bureau of Fiscal Affairs
South Carolina Department of Health and Human Services
Post Office Box 8297
Columbia, South Carolina 29202-8297

Please contact _____ should you have any questions.

_____ _____

Signature Date:

Finance and Administration
P. O. Box 8206 Columbia South Carolina 29202-8206
(803) 898-2503 Fax (803) 255-8235

Log 000635
FOIA

State of South Carolina
Department of Health and Human Services

Mark Sanford
Governor

Robert M. Kerr
Director

April 20, 2007

Mr. Robert Dean
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing Advertising and Communication
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

Dear Mr. Dean:

Thank you for your letter requesting that I provide you with handouts submitted by pharmaceutical manufacturers for the public testimony portion of any of our Pharmacy & Therapeutics (P&T) meetings held from January 1, 2006 to March 31,2007. The South Carolina Medicaid P & T Committee met five times during that time period and at two of the meetings, handouts were distributed by certain pharmaceutical manufacturers. I have enclosed the agendas for all five meetings and a copy of the handouts from the two applicable P&T meetings.

I hope this information is of assistance. If I may be of any further assistance, please contact me.

Sincerely,

James M. Assey, R.Ph.
Division Director

JMA/r

Division of Pharmacy and DME Services
P. O. Box 8206 • Columbia, South Carolina 29202-8206
(803) 898-2876 • Fax (803) 255-8353

South Carolina Medicaid Pharmacy and Therapeutics Committee

Location: South Carolina Pharmacy Association (SCPhA) Office*
1350 Browning Road, Columbia, SC 29210

Wednesday, February 7, 2007, 4:00 P.M.

AGENDA

I. **Welcome**.....Dr. LaCroix, Chairperson

Freedom of Information Act/Americans With Disabilities Act Compliance Pledge – This body's official minutes will indicate that this meeting is in compliance with the Freedom of Information Act's mandate that the public be notified when the public's business is being done, and that furthermore, the public has been notified that this facility is accessible to individuals with disabilities, and special accommodations could have been provided if requested in advance.

II. **Approval of Minutes from the November 1, 2006 meeting**.....P&T Committee

III. **Public Comment**

a. Presenters must pre-register with DHHS no less than seven days in advance of the meeting. Testimony will be limited to three minutes and there will be only one speaker per pharmaceutical agent under consideration. P&T Committee members may use an additional two minutes to ask the speaker questions if warranted.

b. Criteria for Re-Reviews: Previously reviewed therapeutic classes from PDL phases subject to re-review may be opened for re-review if one or more of the following has occurred: a) a new drug in the therapeutic class, b) a new indication for an existing drug in the therapeutic class, c) a new study recognized and generally accepted by the medical community or three peer-reviewed studies for a drug in the therapeutic class.

IV. **Discussion and Selection from the Reviewed Drug Classes**.....P&T Committee
DHHS Staff
First Health Staff

- Electrolyte Depleters
- Hematopoietic Agents
- Immunomodulators
- Ophthalmic antihistamines
- Ophthalmic quinolones
- Otic quinolones
- Thiazolidinedione-sulfonylurea combinations

V. **Old Business**.....P&T Committee

VI. **New Business**

a. PDL Savings, S. C. Medicaid Pharmacy Expenditures/Demographics.....DHHS and First Health Staff

b. Next P&T Meeting (May 2, 2007)

VII. **Adjournment**

*** Directions to SCPhA Office**

Exit I-20 onto I-26 (toward Spartanburg). Stay in right lane. Exit at the first exit for St. Andrew's Road (Exit 106B). Once on the exit ramp (Exit 106B), veer to the right for Browning/Burning Tree Road. At the stop sign, turn right onto Browning/Burning Tree Road and remain on this road for about one mile. The SCPhA building is on the left just past the Center Point business area.

From I-26 (from Spartanburg). Exit at the St. Andrew's Road exit. At the end of the exit ramp, turn left onto St. Andrew's Road. Get into the right lane and turn right at the first stop light onto Browning/Burning Tree Rd. The SCPhA building is on the left just past the Center Point business area.

No Voluntarily Submitted Handouts at the February 7, 2007 Pharmacy and Therapeutics Committee Meeting.

South Carolina Medicaid Pharmacy and Therapeutics Committee

Location: South Carolina Pharmacy Association (SCPhA) Office*

1350 Browning Road, Columbia, SC 29210

Wednesday, November 1, 2006, 4:00 P.M.

AGENDA

I. **Welcome**.....Dr. LaCroix, Chairperson

Freedom of Information Act/Americans With Disabilities Act Compliance Pledge – This body's official minutes will indicate that this meeting is in compliance with the Freedom of Information Act's mandate that the public be notified when the public's business is being done, and that furthermore, the public has been notified that this facility is accessible to individuals with disabilities, and special accommodations could have been provided if requested in advance.

II. **Approval of Minutes from the August 2, 2006 meeting**.....P&T Committee

III. **Public Comment - Drug Classes for Review To Be Determined**

a. Presenters must pre-register with DHHS no less than seven days in advance of the meeting. Testimony will be limited to three minutes and there will be only one speaker per pharmaceutical agent under consideration. P&T Committee members may use an additional two minutes to ask the speaker questions if warranted.

b. Criteria for Re-Reviews: Previously reviewed therapeutic classes from PDL phases subject to re-review may be opened for re-review if one or more of the following has occurred: a) a new drug in the therapeutic class, b) a new indication for an existing drug in the therapeutic class, c) a new study recognized and generally accepted by the medical community or three peer-reviewed studies for a drug in the therapeutic class.

IV. **Drug Classes for P&T Committee Review**..... P&T Committee
Insulins — DHHS Staff
Hypoglycemics, Oral: Sulfonylureas-Second Generation — First Health Staff
Lipotropics: Fibric Acid Derivatives
Glaucoma Agents: Alpha-2 Adrenergic Agents
Gastrointestinals: Proton Pump Inhibitors

V. **Validation of Prior Selections from PDL Therapeutic Classes Not Subject to Review**.....P&T Committee

VI. **Old Business**.....P&T Committee
DHHS Staff

VII. **New Business**.....P&T Committee
DHHS Staff

a. Next P&T Meeting (February 1, 2007)

VIII. **Adjournment**

*** Directions to SCPhA Office**

Exit I-20 onto I-26 (toward Spartanburg). Stay in right lane. Exit at first St. Andrew's Rd. exit (Exit 106B). Once on off ramp, veer right for Browning/Burning Tree Rd. Turn right at stop sign onto Browning/Burning Tree Rd. and follow for about one mile. Building is on left just past Center Point business area.

From I-26 (from Spartanburg). Exit at St. Andrew's Road. Take a left off of ramp onto St. Andrew's Rd. Get into right lane and take a right at the first stop light onto Browning/Burning Tree Rd. The SCPhA building is on left just past Center Point business area.

NEXIUM® (esomeprazole magnesium) Delayed-Release Capsules

I. Esomeprazole differs from omeprazole, and differs in hepatic metabolism. Esomeprazole is the optically pure S-enantiomer of omeprazole, which is a racemic mixture of S- and R- enantiomers. Two hepatic enzymes of the cytochrome P-450 family, CYP 2C19 and CYP 3A4, are primarily responsible for metabolism of these enantiomers. 2C19 is responsible for most of their metabolism, and has the faster and more variable metabolic rate. The metabolic profile of esomeprazole differs from that of the R-isomer in that a greater proportion of hepatic metabolism is shifted from 2C19 to the slower, less variable 3A4 enzyme.[1] Thus, the clearance of esomeprazole is significantly slower than that of omeprazole. This translates into a non-linear increase of bioavailability when omeprazole 20 mg is compared to esomeprazole 20 and 40 mg (AUCs of 2.3, 4.2, and 12.6 micromol*h/L, respectively).[2] The metabolism of esomeprazole is also more homogenous, resulting in less inter-patient variability in response.[3] Because of these differences in drug chemistry and pharmacology, and the polymorphic genetic heterogeneity in 2C19 of the population, no "equivalent" dose of esomeprazole can be defined for omeprazole across the population. In fact, when equal mg doses of esomeprazole and omeprazole are administered to volunteer subjects, significantly higher blood levels of esomeprazole are observed, as is greater gastric acid inhibition.[2,3,4]

II. Esomeprazole is pharmacodynamically more effective than other proton pump inhibitors (PPIs). PPIs suppress gastric acid secretion by inhibiting the H^+, K^+-ATPase in gastric parietal cells. The pharmacologic effects of acid-reducing drugs have been compared by measuring the percentage of a 24 hour period that intragastric pH is above 4.0 because healing of erosive esophagitis (EE) can be linked to this parameter.[5] The comparative performance of different PPIs in acid suppression may be important to prescribers when they need to make treatment decisions for patients whose demographic characteristics differ from those of the patients enrolled in comparative clinical efficacy studies (summarized in sections III-VI., below). In eleven different comparative pharmacodynamic studies conducted in healthy subjects or patients with symptoms of GERD, esomeprazole provided significantly greater intragastric acid control than lansoprazole, pantoprazole, rabeprazole and omeprazole delayed-release capsules (Prilosec®).[2,3,6,7,8,9,10,11] In one of these studies, Miner et al compared all branded PPIs in a 5-way crossover study and revealed that esomeprazole maintained intragastric pH above 4.0 for a significantly greater proportion of the 24 hours on day 5 compared to rabeprazole 20 mg, omeprazole 20 mg, lansoprazole 30 mg or pantoprazole 40 mg ($p \leq 0.0004$).[7,8] Esomeprazole 40 mg sustained intragastric pH >4.0 for a greater proportion of a 24 hour period on day 5 as compared to omeprazole 40 mg (16.4 vs 14.9 hours, respectively; $p<0.001$)[3] or lansoprazole 60 mg (14.7 vs. 12.4 hours respectively; $p<0.0001$).[11] Oral esomeprazole 40 mg also sustained intragastric pH > 3.0, 4.0, 5.0, and 6.0 for a greater proportion of the 24 hours on day 5 than intravenous pantoprazole 40 mg ($p < 0.001$ for comparisons at pH 3.0, 4.0, and 5.0; $p = 0.045$ for comparison at pH 6.0).[12] In addition, a comparison of intravenous esomeprazole 40 mg and intravenous pantoprazole 40 mg demonstrated faster and more effective intragastric acid control by esomeprazole on day 1 and day 5 at pH > 4, 5, and 6.[13]

III. Relationship between the percentage of time with pH > 4 and the healing of erosive esophagitis. In a multicenter, randomized, double-blind trial, Katz et al evaluated the relationship between the percentage of time with pH > 4 and the healing of EE and the symptomatic control of GERD with esomeprazole 10 mg or 40 mg once daily for 4 weeks in patients with LA grade C or D EE.[14] Complete healing of EE was demonstrated to be positively associated with greater percentage of time intragastric pH was > 4.

IV. Esomeprazole has greater efficacy in healing of erosive esophagitis (EE) than omeprazole, lansoprazole, and pantoprazole through 8 weeks. EE is estimated to be present in approximately 30% of all GERD sufferers[15,16,17,18] and the estimated prevalence of EE in the general population ranges from 2-7%.[16,18,19] Before the approval of esomeprazole, no other PPI was shown to have greater EE healing efficacy than the prototype PPI, omeprazole 20 mg.[20] Esomeprazole is the first PPI to demonstrate a statistically significant difference in the healing of EE when compared to another PPI. Several large, multicenter, randomized, double-blind, placebo controlled, head-to-head studies have examined the EE healing rates of esomeprazole versus omeprazole, lansoprazole, and pantoprazole. In Kahrilas et al, EE healing rates with esomeprazole 40 mg (n=654), esomeprazole 20 mg (n=656), and omeprazole 20 mg (n=650) were 94.1, 89.9, and 86.9%, respectively, at up to 8 weeks; healing rates with both doses of esomeprazole were statistically more effective than omeprazole ($p<0.001$).[21] In a study by Richter et al, EE healing rates with esomeprazole 40 mg (n=1216) and omeprazole 20 mg (n=1209) were 93.7 and 84.2%, respectively, at up to 8 weeks; the 9.5% difference favoring esomeprazole was statistically significant ($p<0.001$).[22] In a third study, EE healing rates with esomeprazole 40 mg (n=576) and omeprazole 20 mg (n=572) were 92.2 and 89.8%, respectively, at week 8 (p=NS).[23] In a fourth study, EE healing rates with esomeprazole 20 mg (n=588) and omeprazole 20 mg (n=588) were 90.6% and 88.3%, respectively, at week 8 (p = NS).[24] In Castell et al, EE healing rates with esomeprazole 40 mg and lansoprazole 30 mg were 92.6 and 88.8%, respectively, at week 8 ($p<0.0001$).[25] In an international, multicenter, randomized, double-blind trial, EE healing rates with esomeprazole 40mg and pantoprazole 40 mg were 95.5 and 92.0%, respectively, at week 8 ($p<0.001$).[26]

V. Esomeprazole has greater efficacy in healing of more severe grades of EE than omeprazole, lansoprazole, and pantoprazole through 8 weeks. In all of these studies, esomeprazole 40 mg was found to have consistently higher healing rates across all baseline severity grades of EE compared with the other PPIs against which it was compared, and efficacy differences favoring esomeprazole were greater in the patients with more severe baseline grades of EE (LA grades C and D).[21,22,23,24,25,26,27] For example, when esomeprazole 40 mg was compared to lansoprazole 30 mg, the difference in healing of EE was greater in the patients with moderate to severe disease (86.6 vs. 73.9%, respectively).[25] In addition, in a multicenter, randomized, double-blind, double-dummy, parallel-group trial that compared esomeprazole 40 mg and lansoprazole 30 mg in patients with moderate to severe EE (LA grades C and D), healing rates with esomeprazole and lansoprazole were 82.4 and 77.5 %, respectively (p=0.007).[28] The clinical benefit of esomeprazole in the more severe cases of EE (about 25% of all patients with EE) cannot be overstated because such patients are otherwise predisposed to disease complications. In patients with GERD, symptom severity does not correlate with the presence or absence of erosions, or if erosions are present, their severity.[29] Therefore, because the presence or severity of erosive disease can only be determined through diagnostic testing, such as endoscopy, it is reasonable that a treatment that is reliable in healing all grades of erosive disease be considered in patients with clinical symptoms of GERD.

VI. Esomeprazole has greater efficacy in maintaining healing of EE than lansoprazole and pantoprazole through 6 months. The maintenance of healed erosions is important as GERD is a chronic disorder and up to 70% of patients who cease treatment are likely to relapse.[30,31] Esomeprazole 20 mg and lansoprazole 15 mg maintained healed EE and symptom control through 6 months in 83 and 74% of patients, respectively, ($p<0.0001$) across all baseline grades of esophagitis; in 85 and 77% of patients, respectively, ($p<0.01$) with mild baseline EE; and in 76 and 59% of patients, respectively, ($p<0.01$) with moderate to severe baseline EE.[32] In another study, esomeprazole 20 mg and lansoprazole 15 mg maintained healed EE and symptom control through 6 months in 84.8 and 75.9% of patients, respectively ($p =0.007$) across all baseline grades of esophagitis; in 87.2 and 78.7% of patients, respectively, with mild baseline EE; and in 77.6 and 68.4% of patients, respectively, with moderate to severe baseline EE.[33] Esomeprazole 20 mg and pantoprazole 20 mg maintained healed erosive esophagitis and symptom control through 6 months in 87.0% and 74.9% of patients, respectively ($p < 0.0001$).[34]

VII. Esomeprazole for the control of symptoms of patients with established GERD. In the above trials, esomeprazole 40 mg was more effective than omeprazole 20 mg at both day 1 heartburn resolution and the initial onset of sustained heartburn resolution.[21,22] Esomeprazole 40 mg also demonstrated better symptom control than lansoprazole 30 mg at 4 weeks, and faster onset of sustained heartburn resolution.[25] Suboptimal response of symptoms to PPI therapy may lead physicians to either double the PPI dose or switch to a different PPI. In fact, up to 30% of patients with GERD are being prescribed greater than a single daily PPI dose. Fass et al compared heartburn relief in patients taking esomeprazole 40 mg once daily as compared to lansoprazole 30 mg twice daily after they had failed once daily therapy with lansoprazole 30 mg.[35] This study demonstrated that switching patients with persistent heartburn on once daily lansoprazole 30 mg to esomeprazole 40 mg once daily was effective and clinically similar to increasing the lansoprazole dose to 30 mg twice daily, providing clinicians and patients with an effective, potentially less costly alternative to double dose PPI therapy.

VIII. Esomeprazole for the reduction in the occurrence of gastric ulcers associated with continuous NSAID therapy in patients at risk for developing gastric ulcers. Patients are considered to be at risk due to their age ($\geq$ 60) and/or documented history of gastric ulcers.[36] In two multicenter, double-blind, placebo-controlled studies conducted in patients (n=1429) at risk of developing gastric and/or duodenal ulcers associated with continuous use of non-selective and COX-2 selective NSAIDs, treatment with esomeprazole 20 mg or 40 mg once-a-day resulted in a significant reduction in gastric ulcer occurrences relative to placebo treatment at 26 weeks. No additional benefit was seen with esomeprazole 40 mg over esomeprazole 20 mg.[37] Controlled studies do not extend beyond 6 months.[36]

IX. Esomeprazole alternative administration options. For patients who have difficulty swallowing capsules, esomeprazole capsules may be opened, and their contents (pellets) given in applesauce.[36] The pellets are also stable in other media.[38] Esomeprazole pellets may also be suspended in water and administered via a nasogastric tube.[36] Furthermore, esomeprazole is now available as an intravenous formulation and is indicated for the short-term treatment (up to 10 days) of GERD patients with a history of erosive esophagitis as an alternative to oral therapy in patients when therapy with oral esomeprazole is not possible or appropriate.[39]

X. Esomeprazole use in adolescents (age 12 – 17 years). NEXIUM 20 mg or 40 mg once daily is approved for the short-term treatment of GERD for up to 8 weeks in adolescent patients aged 12 to 17 years.[36] Esomeprazole pharmacokinetics in adolescent patients were similar to those observed in adult patients with symptomatic GERD. In addition, no new safety concerns were identified in a study that evaluated the safety and tolerability of esomeprazole 20mg and 40 mg for up to 8 weeks in 149 adolescent patients with clinically diagnosed GERD.

References:

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ACIPHEX® (rabeprazole sodium) Executive Summary

Clinical Rationale:

- ACIPHEX® is a gastric proton-pump inhibitor which suppresses gastric acid secretion by inhibiting the gastric H^+, K^+ ATPase at the secretory surface of the gastric parietal cell.
- ACIPHEX® 's anti-secretory effect begins within one hour of administration of a 20mg tablet and lasts for a full 24 hours.
- ACIPHEX® has been shown to be safe and effective for the healing of erosive or ulcerative gastroesophageal reflux disease (GERD), maintenance of healing of erosive or ulcerative GERD, treatment of daytime and nighttime heartburn and other symptoms associated with GERD, and the healing of duodenal ulcers.
- ACIPHEX® is the only PPI (proton pump inhibitor) to have FDA approval as part of a 7-day regimen with amoxicillin and clarithromycin for the eradication of *H. pylori* to reduce the risk of duodenal ulcer recurrence.
- ACIPHEX® is also indicated for the treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome (ZES).

ACIPHEX® Efficacy Trials

In randomized, double-blind, placebo-controlled crossover studies, ACIPHEX® has been shown to be safe and effective for the healing of erosive or ulcerative gastroesophageal reflux disease (GERD), maintenance of healing of erosive or ulcerative GERD, treatment of symptomatic GERD, healing of duodenal ulcers (DU), and treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome (ZES). In addition, ACIPHEX® is the only PPI approved as part of a seven-day treatment regimen for the eradication of H. pylori which is known to be the most common cause of PUD.

The antisecretory effect of ACIPHEX® was evaluated in a randomized, double blind, placebo-controlled crossover trial. At Day 1, the median 24-hour intragastric acidity was significantly less for ACIPHEX® compared to both omeprazole and placebo, suggesting faster acid control. In addition, the percentage of time that gastric pH was >3 and > 4 was significantly longer for ACIPHEX® suggesting consistent 24-hour control. (Williams 1998)

At a pH of 1.2 and 5.1, ACIPHEX® had a faster activation rate than lansoprazole, omeprazole and pantoprazole (Kromer 1998). An in-vitro study on the rate and percent of H+/K+/ATPase inhibition by four PPIs (lansoprazole, omeprazole, rabeprazole sodium, and pantoprazole) demonstrated that rabeprazole sodium fully inhibited the enzyme after five minutes (Besancon 1997).

A randomized, double-blind, cross-over trial was conducted to compare the antisecretory activity and onset of action of single doses of ACIPHEX®, lansoprazole, pantoprazole, omeprazole capsule, omeprazole multiple unit pellet system table and placebo in health H.pylori-negative subjects. At day 1, ACIPHEX® had significantly higher median intragastric pH values during the post-dose period than lansoprazole, pantoprazole, omeprazole capsule and omeprazole MUPS tablet. ACIPHEX® also had significantly higher median pH values compared to the other PPIs.

Dean et al *(2004)* conducted an evidence-based review of RCT to evaluate the effectiveness of proton pump inhibitors on 8-week endoscopic healing rates and 1-year symptomatic recurrence rates in patients with erosive esophagitis. The systematic review was conducted using MEDLINE and HealthStar databases to search for published literature from 1985 – 2002 pertaining to PPI therapy in patients with erosive esophagitis. Randomized, placebo-controlled, head-to-head studies, available in English, reporting the effects of PPIs on endoscopic healing and symptomatic reoccurrence rates in patients with erosive esophagitis were identified. Data pertaining to patient population, endoscopic healing, symptomatic recurrence were abstracted. Healing rates were derived from studies with endoscopically confirmed healing of erosions after 8 weeks of acute therapy. One year symptomatic recurrence rates were calculated as the proportion of erosive esophagitis patients who, after having been previously healed, failed one of three symptomatic recurrence criteria at the end of one year: had relief of GERD symptoms, had complete absence of heartburn, or had absence of daytime heartburn symptoms. There were a total of nine studies identified for the 8 week endoscopic healing rates post PPI therapy, and thirteen studies identified for the 1-year symptomatic recurrence rates. The odds ratios for healing in PPI treated patients versus placebo treated patients ranged from 5.90 – 18.53 for each pooled PPI regimen. Pooled healing rates were greater than 85% for all PPI therapies when adjusted for the overall pooled placebo rate.

Cost Effectiveness Data
ACIPHEX® has been shown to be cost-effective and has demonstrated cost savings to formulary decision makers. In addition, HRQOL improvements in patients receiving ACIPHEX® have been documented. Retrospective database studies as well as decision analytic models have demonstrated the economic benefits of ACIPHEX®.

In a study published by Hall et al, the investigators found that ACIPHEX® patients had lower GERD-related pharmacy and total costs, lower DACON and less dose escalation compared to lansoprazole and omeprazole patients. Total costs for lansoprazole, omeprazole, and rabeprazole sodium were $751, $787, and $616 respectively. ACIPHEX®'s average DACON was significantly lower that omeprazole average DACON during initial treatment. Only 3.5% of ACIPHEX® patients escalated their dose vs. 5.5% of omeprazole and 9.3% of lansoprazole patients. (Hall, 2002)

Assessment of four therapeutic interchange programs demonstrated cost savings after implementation of ACIPHEX®. In a VA population, Gordon et al, found that implementation of a therapeutic interchange program saved more than one half million US dollars in pharmacy acquisition costs despite a 32% increase in PPI usage after utilizing ACIPHEX® vs. lansoprazole and omeprazole (Gordon 2002). In another VA setting, Farrell et al concluded that ACIPHEX® would have a projected $43,195 cost savings per year if half of the patients switched from lansoprazole 30mg twice daily to ACIPHEX®20mg daily. In a managed care setting, Kipley el al showed a cost savings when patients were converted from lansoprazole to ACIPHEX®. (Kipley 2002). In a managed care setting, Guenette et al showed that a cost savings of $74,418.80 from May 2000 to December 2000 could be realized by using ACIPHEX® as the formulary PPI (Guenette 2001).

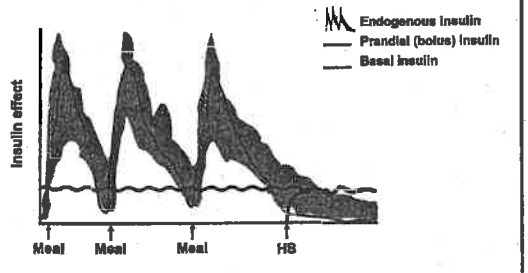
Summary for ACIPHEX®®
ACIPHEX® has been shown to be safe and effective for the healing of erosive or ulcerative gastroesophageal reflux disease (GERD), maintenance of healing of erosive or ulcerative GERD, treatment of symptomatic GERD, healing of duodenal ulcers (DU), and treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome (ZES). In addition, ACIPHEX® is the only PPI approved as part of a seven-day treatment regimen for the eradication of H. pylori which is known to be the most common cause of PUD.

ACIPHEX® is not only a safe and effective medication, but has been demonstrated to be cost-effective when compared to other PPI agents from a managed care perspective. Additionally, ACIPHEX® provides patient benefits in terms of improvements in HRQOL. Considering the aforementioned benefits, ACIPHEX® is a favorable candidate for formulary inclusion in the treatment of acid-related disorders.

References

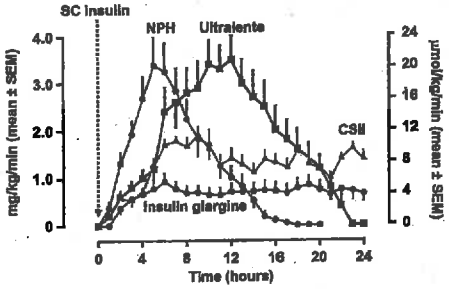
- ACIPHEX®® (package insert) Janssen Pharmaceutica Products, L.P. and Eisai Inc; 2003.
- Besancon M, Simon A, Sachs G, Shin JM. Sites of reaction of the gastric H-K-ATPase with extracytoplasmic thiol reagents. J Biol Chem 1997;272(36):22438-46.
- Dean B, Gano A, Dodd S, Ofman JJ. Proton Pump Inhibitors: An evidence-based review of endoscopic healing and symptomatic healing rates in patients diagnosed with erosive esophagitis. [Poster] Presented at: 38th American Society of Health Systems Pharmacists Midyear Clinical Meeting: December 7, 2004
- Hall J, Dodd S, Durkin M, Sloan S. Impact o proton pump inhibitor utilization patterns on gastroesophageal relux disease-related costs. *Managed Care* 2002;11(7):14-18.
- Guenette AJ, Plank GS, Kolstad C, Lee JD. Comprehensive communication program to facilitate therapeutic interchange: expericence with proton-pump inhibitors. *J Managed Care Pharm.* 2001;7(5):360-361
- Gordon M. Outcomes analysis of rabeprazole (ACIPHEX®) sue at a Verterans Affairs medical center (Abstract) Value in Health. 2002;5(6):503-504. Abstract PG59
- Kipley La, Browne B, Tabor P, et al. Impact on proton pump inhibitor utilization and costs following a pharmacy preference change and conversion. Am J Gastroenterol. 2002;97(9):A698.
- Kromer W, Kruger U, Huber R, et al. Differences in pH-dependent activation rates of substituted benzimidazoles and biological in-vitro correlates. Pharmacology. 1998;56(2):57-70.
- Williams MP, Sercombe J, Hamilton MI, Pounder RE. A placebo-controlled trial to assess the effects of 8 days of dosing with rabeprazole verss omeprazole on 24-h intragastric acidity and plasma gastrin concentrations in young healthy male subjects. *Aliment Pharmacol Ther.* 1998;12(11):1079-1089.

Mimicking Nature: The Basal-prandial (bolus) Insulin Concept



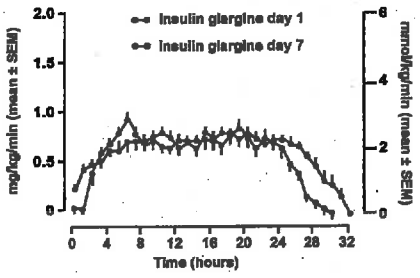
Adapted with permission from McCall A. In: *Insulin Therapy*. Leahy J, Cefalu W, eds. New York, NY: Marcel Dekker, Inc; 2002:193.

Results: Glucose Infusion Rate (GIR)



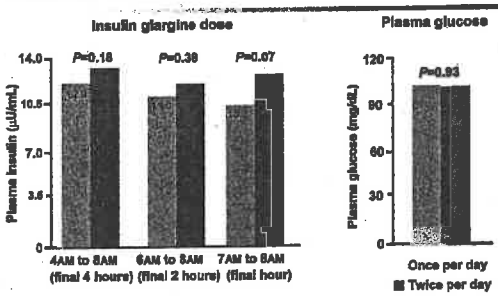
Adapted with permission from Lepore M et al. *Diabetes*. 2000;49:2142-2148.

Results: Glucose Infusion Rate (GIR)



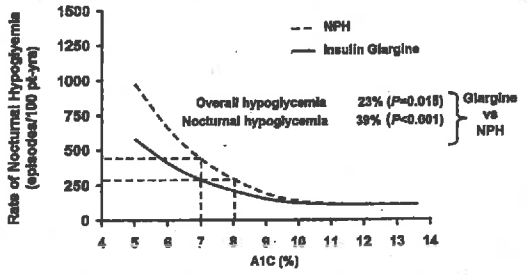
Fanelli CG et al. *Diabetologia*. 2002;45(Suppl 2). Abstract 502.

Results: Insulin Concentrations and Plasma Glucose Levels



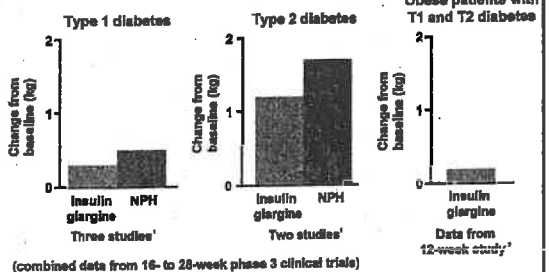
Burge M et al. *Diabetes*. 2004;53(Suppl 2):A130.

Results: Better Glycemic Control at Equivalent Hypoglycemia Rates: Meta-Regression Analysis of All Glargine vs NPH Trials



Yki-Järvinen H et al. *Diabetes*. 2003;52(6):A148.

Results: Weight Profiles in Patients With Type 1 and Type 2 Diabetes



(combined data from 16- to 28-week phase 3 clinical trials)

1. Data on file. sanofi-aventis.
2. Strojek-Kaminska D et al. *Diabetes*. 2002;51(2):A114.

South Carolina Medicaid Pharmacy and Therapeutics Committee

Location: South Carolina Pharmacy Association (SCPhA) Office*

1350 Browning Road, Columbia, SC 29210

Wednesday, August 2, 2006, 4:00 P.M.

AGENDA

I. **Welcome**.....Dr. LaCroix, Chairperson

Freedom of Information Act/Americans With Disabilities Act Compliance Pledge – This body's official minutes will indicate that this meeting is in compliance with the Freedom of Information Act's mandate that the public be notified when the public's business is being done, and that furthermore, the public has been notified that this facility is accessible to individuals with disabilities, and special accommodations could have been provided if requested in advance.

II. **Approval of Minutes from the May 3, 2006 meeting**.....P&T Committee

III. **Old Business**

a. **Disclosure Declaration Forms for Speakers**.....DHHS

IV. **New Business** - *No PDL drug classes are scheduled for review and recommendation by the P&T Committee*

a. **New Insulins In The Treatment of Diabetes**.....Ali A. Rizvi, M.D.
Div. of Endocrinology, Diabetes, & Metabolism
Department of Internal Medicine
USC School of Medicine

b. **Impact - Medicare Part D on Medicaid**.....DHHS and First Health

c. **Impact – PDL on Medicaid Expenditures**.....DHHS and First Health

d. **Next P&T Meeting (Wednesday, November 1, 2006)**

V. **Adjournment**

*** Directions to SCPhA Office**
Exit I-20 onto I-26 (toward Spartanburg). Stay in right lane. Exit at first St. Andrew's Rd. exit (Exit 106B). Once on off ramp, veer right for Browning/Burning Tree Rd. Turn right at stop sign onto Browning/Burning Tree Rd. and follow for about one mile. Building is on left just past Center Point business area.

From I-26 (from Spartanburg). Exit at St. Andrew's Road. Take a left off of ramp onto St. Andrew's Rd. Get into the right lane and take a right at the first stop light onto Browning/Burning Tree Rd. The SCPhA building is on left just past Center Point business area.

No Voluntarily Submitted Handouts at the August 2, 2007 Pharmacy and Therapeutics Committee Meeting.

South Carolina Medicaid Pharmacy and Therapeutics Committee

Location: South Carolina Pharmacy Association (SCPhA) Office*
1350 Browning Road, Columbia, SC 29210

Wednesday, May 3, 2006, 4:00 P.M.

AGENDA

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II. **Approval of Minutes from the February 1, 2006 meeting**.....P&T Committee

III. **Public Comment On Drug Classes Opened for Re-Review from PDL Phases I, II, and III**

Presenters must pre-register with DHHS no less than seven days in advance of the meeting. Testimony will be limited to three minutes and there will be only one speaker per pharmaceutical agent under consideration. P&T Committee members may use an additional two minutes to ask the speaker questions if warranted.
Criteria for Re-Reviews: Previously reviewed therapeutic classes from PDL phases subject to re-review may be opened for re-review if one or more of the following has occurred: a) a new drug in the therapeutic class, b) a new indication for an existing drug in the therapeutic class, c) a new study recognized and generally accepted by the medical community or three peer-reviewed studies for a drug in the therapeutic class.

Drug Classes Opened for Re-Review..... Public Comment

- Sedative Hypnotics
- Inhaled Corticosteroids-Oral Inhalation Devices

IV. **Validation of Previous Decisions from Phases I, II, and III** P&T Committee
PDL Therapeutic Classes (Not Subject to Re-Review).....DHHS and First Health Staff

- Antihistamines: Second Generation
- Antihistamines: 2nd Generation Decongestant Combinations
- Angiotensin Receptor Blockers
- Angiotensin Receptor Blocker/Diuretic Combinations
- Short Acting Beta Adrenergic Inhalation Devices
- Antihyperkinesis Agents
- ACE Inhibitors
- ACE Inhibitor/Diuretic Combination
- ACE Calcium Channel Blocker Combination Agents
- Beta Blockers
- Beta Adrenergic Long Acting Inhalers
- Beta Adrenergic Nebulizers
- Beta Adrenergic/Corticosteroid Combinations
- Cephalosporins – Second Generation
- Cephalosporins - Third Generation
- Calcium Channel Blockers - Dihydropyridines
- Calcium Channel Blockers - Non-Dihydropyridines
- Histamine-2 Receptor Blockers
- Leukotriene Modifiers
- Nasal Steroids
- Non-Steroidal Anti-Inflammatory Agents
- Osteoporosis
- Proton Pump Inhibitors
- Serotonin Receptor Agonists-Migraine Therapy

V. **Old Business**

a. Review and approval of P&T Committee draft policy regarding P&T members' interaction with pharmaceutical manufacturers.....P&T Committee

VII. **New Business**

a. Information on impact of Medicare Part D on S. C. Medicaid expenditures and utilization.....DHHS and First Health Staff

b. Next P&T Meeting (August 2, 2006)

VIII. **Adjournment**

*** Directions to SCPhA Office**

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Pulmicort Turbuhaler™ 200 µg (budesonide inhalation powder)
200 inhalations per inhaler

Indication: Maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients 6 years of age and older.

- ❖ Monotherapy with inhaled corticosteroids (ICS) is first-line therapy for children ≥ 6 years of age and adults with mild asthma.[1]
- ❖ Pulmicort Turbuhaler™, along with Pulmicort Respules™
  - o ***is the only ICS with FDA Category B Pregnancy rating; all other ICS are Category C***
  - o ***is the only ICS FDA approved for QD dosing***
  - Proven safety profile
  - Flexible dosing
  - No taste, no feel
  - Convenient dose indicator
  - Continuity of care with Pulmicort Respules™
- ❖ Dosing from one Turbuhaler
  - o 200 µg QD = 6 months of therapy
  - o 400 µg QD = 3 months of therapy

- ❖ Budesonide is most studied ICS with over 20 years experience worldwide, and the ***only ICS with long-term efficacy, safety and health outcomes data.***

1. **CAMP** – Childhood Asthma Management Program (NHLBI funded program)[2]
   - 1041 children, 5-12 years old with mild asthma; duration of trial: 4.3 years
   - Randomized, double-masked, placebo controlled
     - budesonide, 200 µg twice daily (n = 311); nedocromil sodium, 8 mg twice daily (n = 312); placebo (n = 418)

	Budesonide	***Nedocromil***	***Placebo***
Urgent care visits #/100 person-year	12**	16*	22
Hospitalizations #/100 person-year	2.5**	4.3	4.5
% predicted FEV_1 before bronchodilator	2.9%***	0.4%	0.9%
% predicted FEV_1 post bronchodilator	0.6%	- 0.5%	- 0.1%
Final predicted height (cm)	174.8	174.8	174.8

*p<0.05 vs. placebo; **p<0.001 vs. placebo, ***p<0.02 vs. placebo

2. **START** – Inhaled Steroid Treatment as Regular Treatment in Early Asthma[3]
   - 7241 patients (5155 completed), 5-66 years old (~2000 children 5-10 years of age) with mild asthma diagnosed < 2 years; duration of trial 3 years
   - Randomized, double-masked, placebo controlled trial
     - budesonide 200-400 µg QD vs. placebo (including regular asthma therapy)
   - Primary Outcome Variable: time to first serious adverse related event (SARE)
     - Hospitalization or emergency treatment for asthma or death
   - Results: 44% reduction risk of first SARE (p<.0001)
   - Other outcomes: reduced need for oral steroids and more symptom free days with budesonide treated group
   - HECON outcomes: fewer hospital days (69%, p<.001) and ER visits (67%, p<.05) and lower absences from school and work

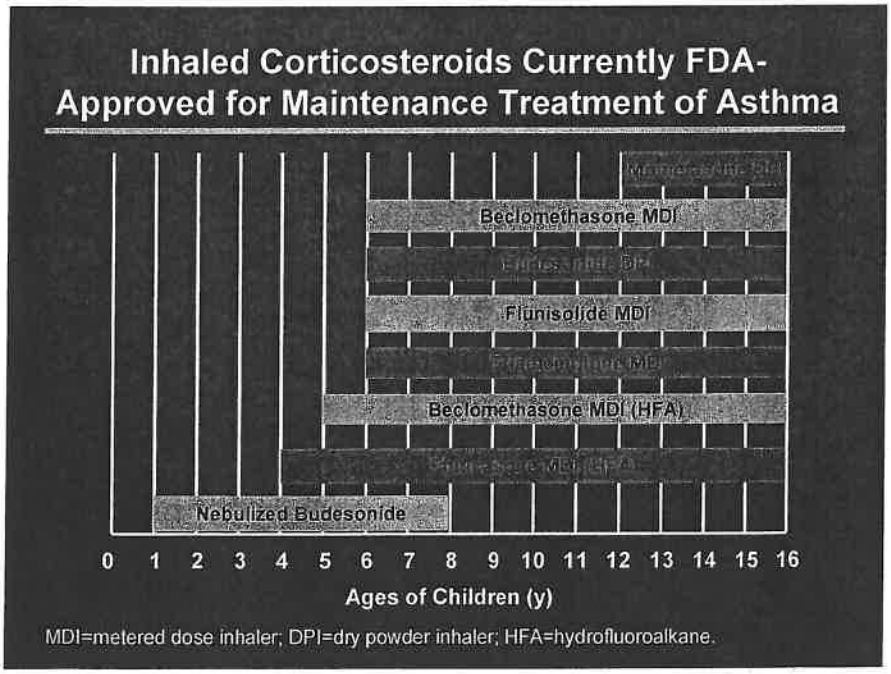
3. **Long-term Final Height**[4]
    - Children treated for an average of 9.3 years reached projected final height, with no difference from control group
    - A small, but statistically significant decrease in growth rate occurred during the first year

[1]NAEPP. Guidelines Update 2002. J Allergy Clin Immunol. 2002;110(pt 2):S141-219; [2]Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. N Engl J Med 2000;343:1054-63; [3]Pauwels et al. Early intervention with budesonide in mild persistent asthma: a randomized double blind trial. Lancet 2003;361:1071-76; Effect of long-term treatment of inhaled budesonide on adult height in children treated with asthma. N Engl J Med 2000;343:1064-9.

Pulmicort Respules™ (budesonide inhalation suspension 0.25 mg and 0.5 mg)
30 Respules per box

Indications: maintenance treatment of asthma and as prophylactic therapy of children with asthma 12 months – 8 years old.

- ❖ Monotherapy with low dose inhaled corticosteroids (ICS) is first-line therapy for asthma in children < 5 years old. [1]
- ❖ Pulmicort Respules™ is the only ICS FDA approved and marketed product for children < 5 years old.
- ❖ Pulmicort Respules™ is the only nebulizable corticosteroid.



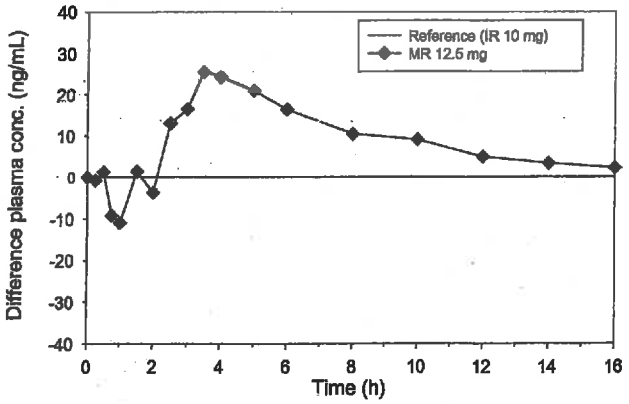
- ❖ Proven safe and effective, with over 12 years experience world-wide
    - o Improved nighttime and daytime asthma symptom scores
    - o Reduced need for daily bronchodilator treatment
    - o Improved lung function
    - o No effect on HPA-axis
- ❖ FDA approved QD dosing
- ❖ FDA labeled Category B for pregnancy
- ❖ Reimbursed by Medicare
- ❖ FDA approved with any nebulizer and compressor combination

Ambien CR™ (Zolpidem tartrate extended release) C_{IV} A New Pharmacotherapy for Insomnia

Jeffrey Harless, PhD
Regional Medical Liaison
US Medical Affairs
May 3, 2006

Study 4624 - Zolpidem MR Pharmacokinetic Properties

Difference of plasma concentrations between MR and IR formulations



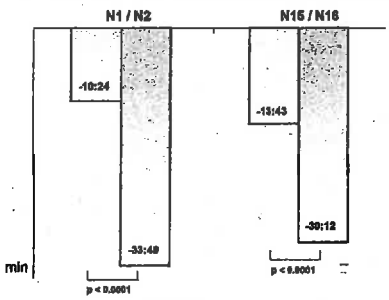
Studies EFC4529 and EFC4530 – Zolpidem MR Maintains Sleep by Reducing PSG WASO (1-6 h)

EFC4529

- Mean PSG WASO (1-6 h) at baseline (min)

	placebo	Zolpidem MR 12.5 mg
Baseline (mean SN1/SN2)	59:13	48:24

- Adjusted mean change from baseline for WASO 1-6 h at N1/N2 and N15/N16 (min)

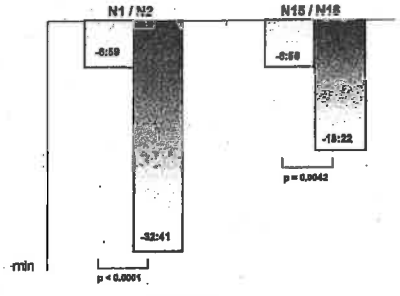


EFC4530

- Mean PSG WASO (1-6 h) at baseline (min)

	placebo	Zolpidem MR 6.25 mg
Baseline (mean SN1/SN2)	70:15	67:16

- Adjusted mean change from baseline for WASO at N1/N2 and N15/N16 (min)



ITT POPULATION – ANCOVA

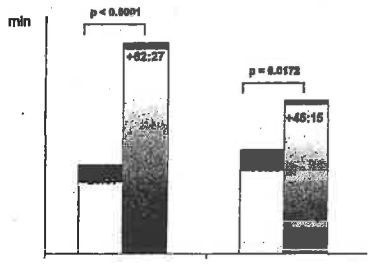
Studies EFC4529 and EFC4530 – Zolpidem MR 12.5 mg and 6.25 mg Increase the Duration of Sleep in Adult and Elderly Patients with Primary Insomnia

EFC4529

- Mean PSG TST at baseline

	placebo	Zolpidem MR 12.5 mg
Baseline (mean SN1/SN2)	348:05	361:50

- Adjusted mean change from baseline for PSG TST at N1/N2 and N15/N16

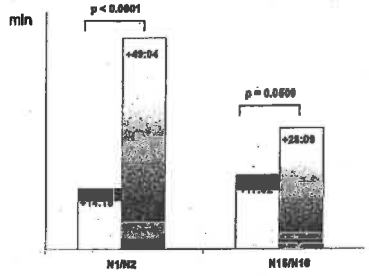


EFC4530

- Mean PSG TST at baseline

	placebo	Zolpidem MR 6.25 mg
Baseline (mean SN1/SN2)	335:13	338:21

- Adjusted mean change from baseline for PSG TST at N1/N2 and N15/N16



ITT POPULATION – ANCOVA

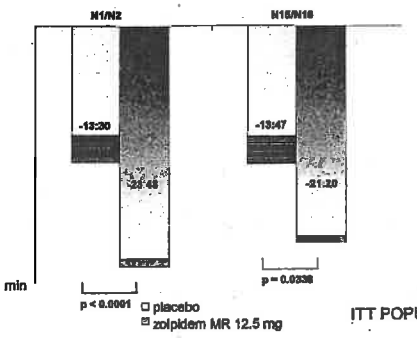
Studies EFC4529 and EFC4530 – Zolpidem MR 12.5 mg and 6.25 mg induce sleep by decreasing PSG LPS in Adult and Elderly Patients with primary insomnia

EFC4529

- Mean PSG LPS at baseline

	placebo	Zolpidem MR 12.5 mg
Baseline (mean SN1/SN2)	43:47	41:41

- Adjusted mean change from baseline at N1/N2 and N15/N16



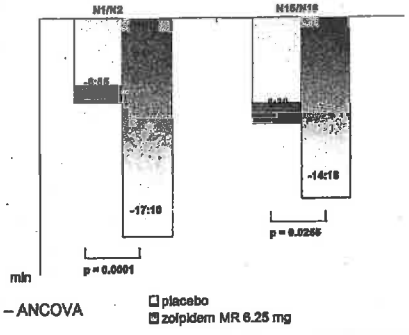
ITT POPULATION – ANCOVA

EFC4530

- Mean PSG LPS at baseline

	placebo	Zolpidem MR 6.25 mg
Baseline (mean SN1/SN2)	38:43	38:52

- Adjusted mean change from baseline at N1/N2 and N15/N16

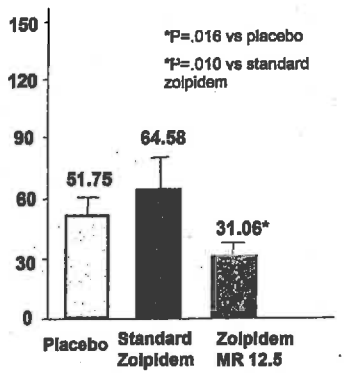


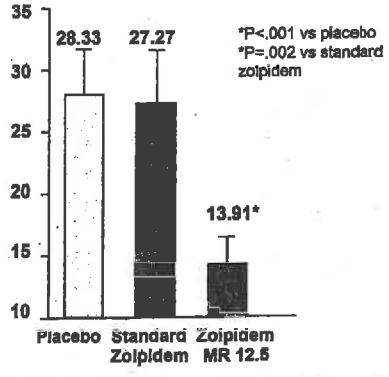
Study PDY 4054: Results

Number of Arousals (<10 seconds) Through Whole Night

Number of Awakenings After Sleep Onset

Mean (+ SEM) presented per treatment





I. Hindmarch, PhD, et al. ASCPT, Orlando, March 2005. Abstract #PI-68.

Safety of Zolpidem MR – Next-day Residual Effects in Healthy Volunteers

Study		PDY4054	PDY5036		PDY5035		
Population		Young HV	Young HV		Elderly HV		
Study drugs		Zolpidem MR 12.5 mg vs pbo	Zolpidem MR 12.5 mg vs pbo	FLURAZEPAM 30 mg vs pbo	Zolpidem MR 6.25 mg vs pbo	Zolpidem MR 12.5 mg vs pbo	FLURAZEPAM 30 mg vs pbo
Time of evaluation		8 hours	8 hours	8 hours	8 hours	8 hours	8 hours
Psychometric tests – Vigilance	CFF	-	-	↓	-	-	↓
	DSST	-	-	-	-	-	-
Motor function	CRT Recognition reaction time	-	-	↑	-	-	↑
	CRT Motor reaction time	-	-	↑	-	-	↑
	CRT Total reaction time	-	-	↑	-	-	↑
	CTT Mean deviation	-	-	↑	-	-	-
	CTT Mean response time	-	↑	↑	-	-	↑
Memory	IWR	-	-	↓	-	-	↓
	DWR	-	-	↓	-	-	↓
Subjective scales	Awakening from sleep	-	-	↓ (impaired)	-	-	-
	Behaviour following awakening	-	-	↓ (impaired)	↑ (improved)	-	-
	Alertness	NP	-	↑ (impaired)	NP	NP	NP

-: no statistical difference; ↓: significant decrease; ↑: significant increase; NP: not performed
for psychometric tests only: both ↓ and ↑ = impaired reaction;

N. Stanley, et al. APSS, Denver, June 2005. Poster # 0729 and 733.

Zolpidem MR Adverse Event Profile

Zoladult

MOST FREQUENT TEAE

	Placebo (N=110)		Zolpidem MR 12.5 mg (N=102)	
	N	(%)	N	(%)
Headache	18	(16.4%)	19	(18.6%)
Somnolence	2	(1.8%)	15	(14.7%)
Dizziness	6	(5.5%)	12	(11.8%)
Nausea	4	(3.6%)	7	(6.9%)

Zolelderly

MOST FREQUENT TEAE

	Placebo (N=106)		Zolpidem MR 6.25 mg (N=99)	
	N	(%)	N	(%)
Headache	12	(11.3%)	14	(14.1%)
Dizziness	3	(2.8%)	8	(8.1%)
Nausea	6	(5.7%)	6	(6.1%)
Somnolence	5	(4.7%)	6	(6.1%)
Nasopharyngitis	4	(3.8%)	6	(6.1%)

T. Roehrs, PhD, et al. APSS, Denver, June 2005. Poster # 0725
C. Soubrane, MD, et al APSS, Denver, June 2005. Poster # 0726

Zolpidem MR – Conclusions

- Zolpidem MR induces sleep, improves sleep maintenance, and increases sleep duration.
- Zolpidem MR does not produce residual effects 8 hours post dose.
- Zolpidem MR has greater effects from 3 to 6 hours post dose than zolpidem, based on pharmacodynamic models of sleep maintenance and sedation.
- Zolpidem MR 12.5 mg and 6.25 mg were well tolerated in comparison to placebo
- As of 4-17-06 Ambien CR available unrestricted (Tier 1) in 50% of all State Medicaid Programs

Rozerem™

ramelteon 8–mg tablets

- ❒ ***First and Only*** **Non-Scheduled prescription insomnia agent…NOT a controlled substance and approved for long-term use**

- ❒ ***First and Only*** **prescription insomnia agent with no evidence of abuse or addiction potential**

- ❒ ***First and Only*** **insomnia agent that does not act by CNS depression or target the GABA receptors. Completely different MOA than other prescription insomnia agents. Safe to use in patients with mild to moderate COPD and sleep apnea**

- ❒ **Proven efficacy and indicated by the FDA to treat chronic insomnia, transient insomnia and in elderly patients (65 years+)**

- ❒ **Clean safety profile**

Presented by:

Ricardo Fermo, M.D.
Assistant Professor
MUSC
Charleston, SC 29407

South Carolina Medicaid Pharmacy and Therapeutics Committee

Wednesday, February 1, 2006, 4:00 P.M.

South Carolina Pharmacy Association Office*

1350 Browning Road, Columbia, SC 29210

AGENDA

I- Welcome.....Dr. LaCroix, Chairperson

Freedom of Information Act/Americans With Disabilities Act Compliance Pledge
This body's official minutes will indicate that this meeting is in compliance with the Freedom of Information Act's mandate that the public be notified when the public's business is being done, and that furthermore, the public has been notified that this facility is accessible to individuals with disabilities, and special accommodations could have been provided if requested in advance.

II- Approval of Minutes from the November 2, 2005 meeting

III- New Business

a) Drug Class for P&T Committee Review.....P&T Committee
DHHS Staff
First Health Staff

Quinolones – Systemic *(No other drug class will be reviewed)*

b) Other Discussion Items - To Be Determined

c) Next P&T Meeting (May 3, 2006)

IV- Old Business

V- Adjournment

*** Directions to SCPhA Office**
Exit I-20 onto I-26 (toward Spartanburg). Stay in right lane. Exit at first St. Andrew's Rd. exit (Exit 106B). Once on off ramp, veer right for Browning/Burning Tree Rd. Turn right at stop sign onto Browning/Burning Tree Rd. and follow for about one mile. Building is on left just past Center Point business area.

From I-26 (from Spartanburg). Exit at St. Andrew's Road. Take a left off of ramp onto St. Andrew's Rd. Get into right lane and take a right at the first stop light onto Browning/Burning Tree Rd. The SCPhA building is on left just past Center Point business area.

No Voluntarily Submitted Handouts at the February 1, 2007 Pharmacy and Therapeutics Committee Meeting.