Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

September 13, 2006

@ 6:00 p.m.

THE UNIVERSITY OF OKLAHOMA

THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Gorman, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – September 13, 2006**

DATE: September 6, 2006

NOTE: **THE DUR BOARD WILL MEET AT 6:00 P.M.**

Enclosed are the following items related to the September meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

Action Item – Approval of DUR Board Meeting Minutes – **See Appendix A.**

Update on DUR/MCAU Program – **See Appendix B.**

Action Item – Vote to Prior Authorize Pediculicides – **See Appendix C.**

Action Item – Vote to Prior Authorize Antiemetics – **See Appendix D.**

Action Item – Annual Review of Synagis® – **See Appendix E.**

30 Day Notice to Prior Authorize Zorbtive™ and Omnitrope™ – **See Appendix F.**

30 Day Notice to Prior Authorize Increlex™ and Iplex™ –**See Appendix G.**

30 Day Notice to Prior Authorize Exubera® – **See Appendix H.**

30 Day Notice to Prior Authorize Glumetza™ – **See Appendix I.**

30 Day Notice to Prior Authorize Zanaflex Capsules – **See Appendix J.**

New Products – **See Appendix K.**

FDA and DEA Updates – **See Appendix L.**

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – September 13, 2006 @ 6:00p.m.

Oklahoma Health Care Authority
4545 N. Lincoln Suite 124
Oklahoma City, Oklahoma 73105
Oklahoma Health Care Authority Board Room

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. McNeill, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. McNeill, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. McNeill, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.

A. July 12, 2006 DUR Minutes – Vote
B. July 12, 2006 DUR Recommendations Memorandum

Items to be presented by Dr. Flannigan, Dr. McNeill, Chairman:

4. Update on DUR/MCAU Program – See Appendix B.

A. Retrospective Drug Utilization Review for April 2006
B. Retrospective Drug Utilization Review Response for February 2006
C. Medication Coverage Activity Audit for July and August 2006
D. Help Desk Activity Audit for July and August 2006
E. Therapy Management Quarterly Report 4th Qtr FY06

Items to be presented by Dr. Patel, Dr. McNeill, Chairman:

5. Action Item – Vote to Prior Authorize Pediculicides – See Appendix C.

A. COP Recommendations

Items to be presented by Dr. Chonlahan, Dr. McNeill, Chairman

6. Action Item – Vote to Prior Authorize Antiemetics– See Appendix D.

A. COP Recommendations

Items to be presented by Dr. Moore, Dr. McNeill, Chairman:

7. Action Item – Annual Review of Synagis® – See Appendix E.

A. Current Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Moore, Dr. McNeill, Chairman

8. 30 Day Notice to Prior Authorize Zorbtive™ and Omnitrope™ – See Appendix F.

A. Product Summaries
B. COP Recommendations

Items to be presented by Dr. Moore, Dr. McNeill, Chairman:

9. 30 Day Notice to Prior Authorize Increlex™ and Iplex™ – See Appendix G.

A. Product Summaries
B. COP Recommendations

Items to be presented by Dr. Gorman, Dr. McNeill, Chairman

10. 30 Day Notice to Prior Authorize Exbuera® – See Appendix H.

A. Product Summary
B. Dosing and Price Comparison
C. COP Recommendations
D. Product Monograph
E. Clinical Trial Data

Items to be presented by Dr. Gorman, Dr. McNeill, Chairman:

11. 30 Day Notice to Prior Authorize Glumetza™ – See Appendix I.

A. Product Summary
B. Price Comparison
C. COP Recommendation

Items to be presented by Dr. Browning, Dr. McNeill, Chairman:

12. 30 Day Notice to Prior Authorize Zanaflex Capsules™ – See Appendix J.

A. Product Summary
B. Price Comparison
C. COP Recommendation

Items to be presented by Dr. Gorman, Dr. McNeill, Chairman:

13. New Product Reviews – See Appendix K.

14. FDA and DEA Updates – See Appendix L.

15. Future Business

A. Flu Medication Utilization Review
B. Hemophilia Utilization Review
C. Topical Products Utilization Review
D. Beta Blocker Utilization Review
E. Annual Reviews
F. New Product Reviews and 30 Day Notices

16. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JULY 12, 2006

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Mark Feightner, D.Ph.	X	
Dorothy Gourley, D.Ph.	X	
Anetta Harrell, D.Ph.	X	
Kyle Hrdlicka, D.O.	X	
Dan McNeill, Ph.D., PA-C; Chairman		X
Cliff Meece, D.Ph., Vice-Chairman	X	
John Muchmore, M.D.	X	
James Rhymer, D.Ph		X

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph./PA Coordinator	X	
Metha Chonlahan, D.Ph./Clinical Pharmacist	X	
Karen Egesdal, D.Ph./SMAC-ProDUR Coordinator/OHCA Liaison	X	
Kelly Flannigan, Pharm.D../Operations Manager	X	
Shellie Gorman, Pharm.D./DUR Manager	X	
Ronald Graham, D.Ph./Pharmacy Director	X	
Chris Le, Pharm.D., Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D., Clinical Pharmacist		X
Neeraj Patel, Pharm.D., Clinical Pharmacist		X
Lester A. Reinke, Ph.D.	X	
Visiting Pharmacy Students: Carol Sparks, Hneade Elliott	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A./ Pharmacy Operations Manager		X
Mike Fogarty, J.D., M.S.W./Chief Executive Officer		X
Lynn Mitchell, M.D., M.P.H/Director of Medical Services	X	
Nancy Nesser, Pharm.D., J.D./Pharmacy Director	X	
Howard Pallotta, J.D./Director of Legal Services	X	
Lynn Rambo-Jones, J.D./Deputy General Counsel III		X
Rodney Ramsey/Drug Reference Coordinator	X	
Jill Ratterman, D.Ph./Pharmacy Specialist	X	

OTHERS PRESENT:

Jim Goddard, Shire	Carlos Palasciano, Hawthorn	James McAdams, Daiichi-Sankyo
Richard Ponder, Johnson & Johnson	Steve Higgins, TAP Pharmaceuticals	Michael Wright, Roche
Fred Morse, BMS	Lance Stewart, Merck	Kay Ruble, FKG
Holly Jacques, Merck	Jim Dunlap, Lilly	Paul Sparks, Allergan
Toby Thompson, Pfizer	Greg Hoke, Wyeth	David Dude, BMS
Jay Dee Fredricksen, Tibotec Therapeutics		

PRESENT FOR PUBLIC COMMENT:

GUEST SPEAKER: Chris Rathbun, Pharm.D., OU College of Pharmacy
Agenda Item No. 5

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: Roll Call

Dr. Meece called the meeting to order. Roll call by Dr. Graham established the presence of a quorum.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

Guest Speaker: Chris Rathbun, Pharm.D.; OU College of Pharmacy - Agenda Item No. 5

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 3: **APPROVAL OF DUR BOARD MINUTES**

3A: June 14, 2006 DUR Minutes

Dr. Gourley moved to approve minutes as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 4: **UPDATE ON DUR/MCAU PROGRAM**

4A: Retrospective Drug Utilization Review Report: March 2006

4B: Retrospective Drug Utilization Review Response: January 2006

4C: Medication Coverage Activity Report: June 2006

4D: Help Desk Activity Report: June 2006

Reports included in agenda packet; presented by Dr. Flannigan.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **UTILIZATION REVIEW OF ANTIRETROVIRALS**

Guest Speaker, Dr. Chris Rathbun. Materials included in agenda packet; presented by Dr. Rathbun and Dr. Le.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 6: **OVERVIEW OF PHARMACY PROGRAM AND DUR**

Materials included in agenda packet; presented by Dr. Nesser.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE CHANTIX™**

Materials included in agenda packet; presented by Dr. Browning.

Dr. Bell moved to approve as submitted; seconded by Dr. Gourley.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **REVIEW OF ANTI-MIGRAINE UTILIZATION**

Materials included in agenda packet; presented by Dr. Flannigan.

Dr. Gourley moved to approve the quantity limit recommendations as submitted; seconded by Dr. Feightner.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **30-DAY NOTICE TO PRIOR AUTHORIZE ANTIEMETICS**

Materials included in agenda packet; presented by Dr. Chonlahan.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **30-DAY NOTICE TO PRIOR AUTHORIZE PEDICULICIDES**

Materials included in agenda packet; presented by Dr. Gorman.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **ADDITION OF OTC COUGH & COLD DRUGS TO CHILDREN'S PHARMACY BENEFIT PACKAGE**

Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 12: **NEW PRODUCT REVIEWS AND NOTICES**

Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 13: **FDA & DEA UPDATES**

Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 14: **FUTURE BUSINESS**

14A: **Beta-Blocker Utilization Review**
14B: **Antipsychotic Utilization Review**
14C: **Heart Failure Utilization Review**
14D: **Flu Medication Review**
14E: **Annual Reviews**
14F: **New Product Reviews and 30-Day Notices**

Materials included in agenda packet; submitted by Dr. Graham.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 15: **ADJOURNMENT**

The meeting was declared adjourned.

The University of Oklahoma College of Pharmacy

Pharmacy Management Consultants
ORI W-4403; PO Box 26901
Oklahoma City, OK 73190
(405)-271-9039

Memorandum

Date: July 13, 2006

To: Nancy Nesser, Pharm.D., J.D.
Pharmacy Director
Oklahoma Health Care Authority

From: Shellie Gorman, Pharm.D.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of July 12, 2006.

Recommendation 1: Vote to Prior Authorize Chantix™

MOTION CARRIED by majority approval.

The College of Pharmacy recommends Chantix™ be included with all other smoking cessation products.

- All smoking cessation products are covered, including OTC products.
- All smoking cessation products are covered without prior authorization for the first 90 days (claims should run without a PA).
- After 90 days of use in a 365 day period, further use of smoking cessation products requires prior authorization.
- Criterion for approval of PA after the first 90 days of use: petition must state that the patient is enrolled in a smoking cessation behavior modification program.
- Length of approval: PA can be approved for another 90 days.
- After the patient has had 180 days of treatment in a 365 day period, the patient must wait another 180 days before smoking cessation treatment will be covered again.
- Smoking cessation products do not count against the 6 prescription per month limit.

A quantity limit of 60 tablets for a 30 day supply will also be implemented.

Recommendation 2: New Quantity Limits for Anti-Migraine Products

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following quantity limits:

Ergotamine 2mg sublingual tab	25 tabs/30 days
Ergotamine/Caffeine 1-100mg tab	50 tabs/30 days
Ergotamine/Caffeine Supp 2-100mg	25 supp/30 days
Ergotamine/Belladonna/Phenobarb tab	60 tabs/30 days

APPENDIX B

Retrospective Drug Utilization Review Report

Claims Reviewed for April 2006

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	40,677	49,811	651,687	29,029
Limits which were applied	Established, Major, Males and Females, 43-65 years	Narcotics, Females, age 42-44 years	Contraindicated, Female Age 35-50 years, Pregnancy	High dose, Carbamates, Tingabine, Hydantoins, Oxazolidinedions, Succinimides, Valproic Acid, Misc. Anticonvulsants. Males and Females, Age 22-40
Total # of messages after limits were applied	72	291	155	128
Total # of members reviewed after limits were applied	171	206	101	113

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
223		181	

Retrospective Drug Utilization Review Report

Claims Reviewed for February 2006

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females Age 0-21	Narcotics, Females, Age 34-37	Contraindicated, Age 0-15, Pregnancy	High dose, Carbamates, Tingabine, Hydantoins, Oxazolidinediones, Succinimides, Valproic Acid, Miscellaneous Anticonvulsants, Males and Females, Age 0-15

Response Summary (Physician)
Letters Sent: 203
Response Forms Returned: 124

The response forms returned yielded the following results:

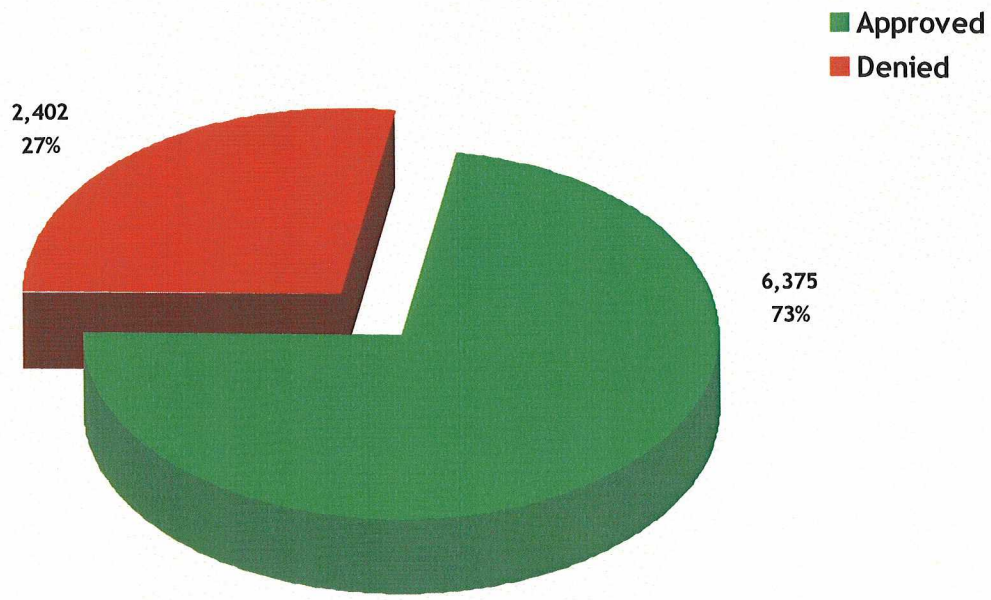
64 (52%)	*Record Error—Not my patient.*
9 (7%)	*No longer my patient.*
3 (2%)	*Medication has been changed prior to date of review letter.*
16 (13%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
16 (13%)	*I am aware of this situation and will plan to continue monitoring therapy.*
16 (13%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 160
Response Forms Returned: 143

The response forms returned yielded the following results:

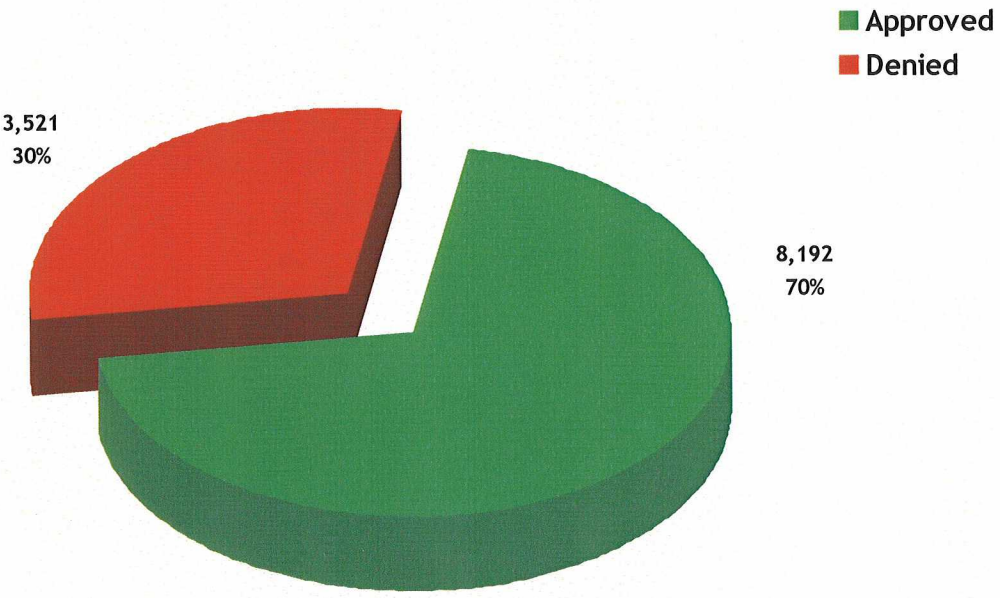
33 (23%)	*Record Error—Not my patient.*
15 (11%)	*No longer my patient.*
3 (2%)	*Medication has been changed prior to date of review letter.*
25 (17%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
57 (40%)	*I am aware of this situation and will plan to continue monitoring therapy.*
10 (7%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT
July 2006



PHARMACY Management Consultants

PRIOR AUTHORIZATION ACTIVITY REPORT
August 2006



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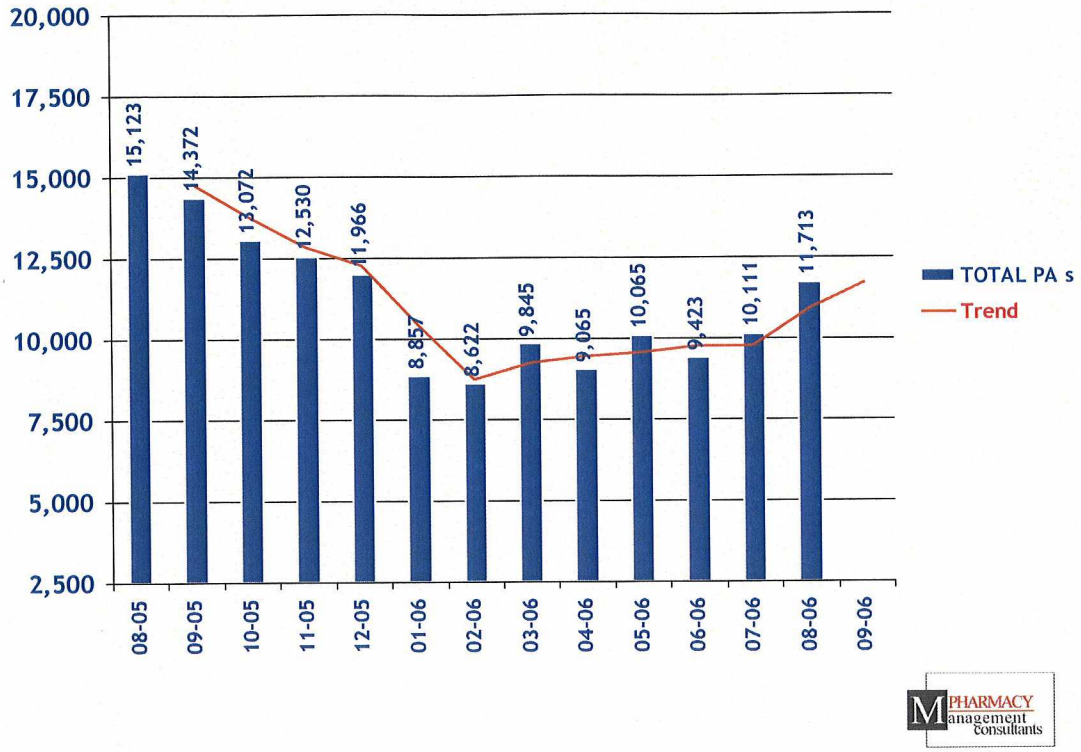
PRIOR AUTHORIZATION REPORT
August 2005 - August 2006



PHARMACY management consultants

Date Processed: August 01, 2006

Activity Audit for

July 01 2006 Through July 31 2006

Date	Antiulcers app.	Antiulcers den.	Anxiolytic app.	Anxiolytic den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	ARB app.	ARB den.	Anti-depressants app.	Anti-depressants den.	Daily Total
App.	20		3182		930		25		583		34		11		4		17		135		0		136		
Den.		4		418		452		1		189		124		18		0		76		20		1		164	
Average Length of Approvals in Days	13		94		97		148		210		317		140		100		290		356		0		193		

Changes to existing PA's	652
Total (Previous Year)	13527

* Denial Codes	
762 = Lack of clinical information	36.39%
763 = Medication not eligible	0.87%
764 = Existing PA	3.46%
772 = Not qualified for requested Tier 2	3.91%
773 = Requested override not approved	13.07%

SUPER PA's	
Admitted to Nursing Home	18
Early Refill Attempts	22453
Dosing Change	310
High Dose	13
Lost/Broken Rx	79
Stolen	8
Other	35
Wrong D.S. on Previous Rx	6
Quantity vs. Days Supply	784
Brand	50
-- Approved	18
-- Denied	19

Monthly Totals

	Number	Percent of Total
Approved	6284	62.15%
Additional PA's	88	0.87%
Emergency PA's	3	0.03%
Duplicates	425	4.20%
Incompletes	909	8.99%
Denied *	2402	23.76%
Total	10111	100.00%

Daily Average of 404.44 for 25 Days

Changes to existing PA's: Backdates, changing units, end dates, etc.

Additional PA's: Done by the help desk (doctor letter responses, PA ran for the wrong person)

Incompletes: Missing necessary information (NDC, SIG, Diagnosis, etc.)

Activity Audit for
August 01, 2006 Through August 31, 2006

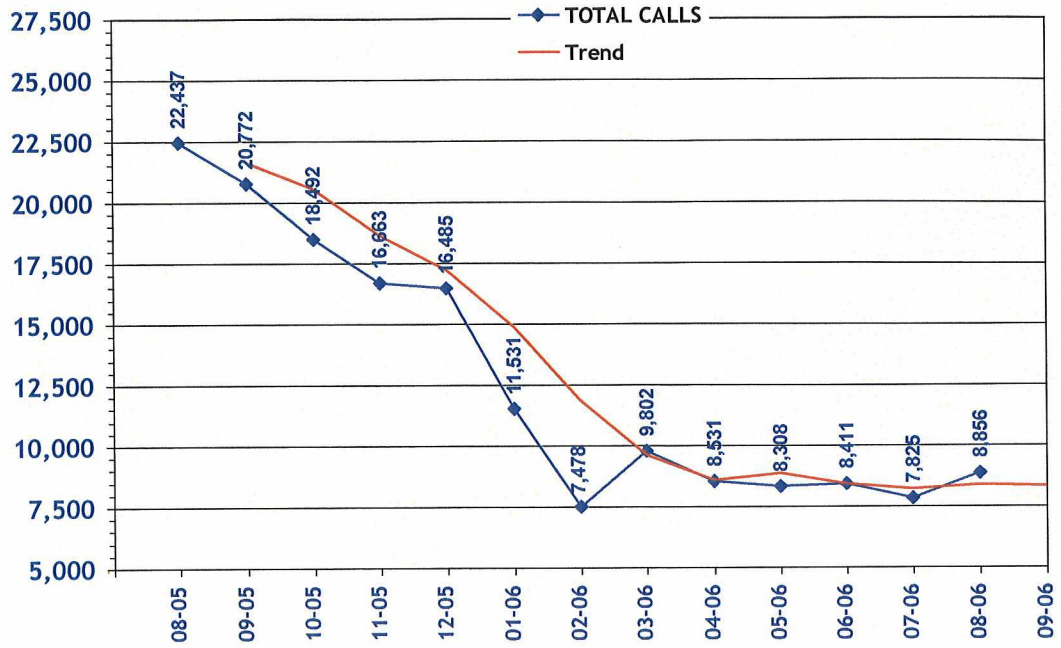
	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	365	6	23	29
Antidepressant	298	50	173	223
Antihistamine	98	1156	689	1845
Antiulcers	0	0	5	5
Anxiolytic	93	3700	552	4252
Calcium Channel Blockers	310	16	70	86
Growth Hormones	166	48	4	52
HTN Combos	0	0	2	2
Hypnotics	92	679	205	884
Nsaids	325	29	121	150
Plavix	359	208	28	236
Stimulant	202	740	263	1003
Others	78	831	1063	1894
Emergency PAs		12	0	12
Overrides				
Brand	279	18	10	28
Dosage Change	12	291	30	321
High Dose	3	1	0	1
Lost/Broken Rx	13	72	17	89
Nursing Home Issue	10	40	1	41
Other	27	28	18	46
Quantity vs. Days Supply	205	258	234	492
Stolen	15	7	3	10
Wrong D.S. on Previous Rx	2	2	10	12
Total		8,192	3,521	11,713

Denial Reasons

Lack of required information to process authorization request.	2605
Antihistamine diagnosis of allergy with no previous OTC trial.	394
Requested override not approved.	382
Denied, unable to verify required trials.	170
Denied, member has an active PA for the requested medication.	165
Denied, this is not an FDA approved indication/diagnosis for this medication.	159
Antiulcer medication does not meet established criteria.	138
Medication considered duplicate therapy. Member has a prior authorization for a medication with equivalent activity.	128
SSRI denied due to lack of tier 1 trial.	84
Denied, the requested dose of this medication exceeds the FDA recommended maximum dose.	82
Request submitted on incorrect form.	64
Requested medication requires trials of other stimulants.	63
NSAID therapy without prior use of at least two tier 1 trials.	62
CCB denied due to lack of tier-1 CCB trial.	34
Medication not covered as a pharmacy benefit.	22
Smoking cessation denied, no proof of enrollment in a behavior modification program.	22
Denied, information provided does not meet established criteria.	21
ACE or ARB denied due to lack of tier-1 ACE trial.	15
Antihistamines are only covered for chronic allergic conditions.	7
Statin denied due to lack of tier-1 trial.	6
Incorrect/invalid provider prescriber number.	3
Growth hormone therapy-considered non-medically necessary.	1
Duplicate Requests	689
* Changes to existing	921

** Changes to existing PA's: Backdates, changing units, end dates, etc.*

CALL VOLUME MONTHLY REPORT
August 2005 - August 2006



PHARMACY Management Consultants

Pharmacotherapy Management Program
Quarterly Report FY'06
July 2005 – June 2006
Oklahoma Health Care Authority

	MEMBER PROFILES REVIEWED		PRIOR AUTHORIZATIONS				COMMUNICATIONS	
Month	New Members	Established Members	Total	Approved	Denied	Incomplete	Letters	Calls
July 2005	94	47	818	540	44	234	357	29
Aug 2005	103	73	830	585	38	257	482	45
Sept 2005	73	32	962	643	45	274	230	37
Oct 2005	25	28	805	561	53	191	152	37
Nov 2005	28	66	848	634	29	185	236	47
Dec 2005	31	52	861	648	39	550	156	29
Jan 2006	23	76	299	190	22	87	229	22
Feb 2006	17	47	158	94	5	59	136	28
March 2006	29	51	271	177	32	62	174	38
April 2006	17	6	265	135	40	90	86	31
May 2006	28	40	238	138	23	77	163	27
June 2006	17	16	276	164	41	71	69	33
Totals	485	534	6,681	4,509	411	1,761	2,470	403
1st Quarter	270	152	2,660	1,768	127	765	1,069	111
2nd Quarter	84	146	2,514	1,843	121	550	554	113
3rd Quarter	69	174	728	461	59	208	539	88
4th Quarter	62	62	779	437	104	238	318	91
Totals	485	534	6,681	4,509	411	1,761	2,470	403

APPENDIX C

Vote to Prior Authorize Pediculicides

Oklahoma Health Care Authority
September 2006

Recommendations:

The College of Pharmacy recommends:

1. Coverage of OTC Permethrin and Pyrethrin products (will include kits containing lotion, shampoos and creams, but not coverage of individual combs, sprays etc.) will require a prescription (written or called in). A quantity limit will be placed based on the package size of the OTC product.

2. Lindane lotion and shampoo will be available only after first-line treatment with OTC permethrin or pyrethrin products has failed. At point-of-sale the pharmacy clinical edit will search history for paid claims to identify the following criteria:
   - Member must be ≥13 years old (clinical exception if less than 13 years old and weighs ≥110lbs)
   - Must have trial of OTC Permethrin or Pyrethrin
   - Quantity limit of 60ml for 7 days (claim will deny if there is a Lindane prescription in history during the previous 30 days)

3. Ovide® lotion available only after treatment with an OTC product and Lindane have failed. Clinical exception to the use Lindane if member is between the ages of 6 and 13 or weighs less than 110lbs. At point-of-sale the pharmacy clinical edit will search history for paid claims to identify the following criteria:
   - Member must be ≥ 6 years old
   - Quantity limit of 60ml for 7 days; may be repeated once if needed for current infestation after 7 days of date of service of the original fill.

4. Prior authorization required for Eurax
   - Must have a trial of Permethrin 1% or 5%
   - Quantity Limit of 60 grams/mls for 30 days

5. Clinical exception if known resistance to OTC Permethrin and Pyrethrin.

APPENDIX D

Vote to Prior Authorize Antiemetics

Oklahoma Health Care Authority
September 2006

Recommendations

The College of Pharmacy recommends consideration of prior authorization for 5HT3 antagonists, substance P antagonists, and cannabinoids to ensure appropriate utilization. Quantity limits already established will remain in effect.

Purpose: Ensure appropriate utilization of antiemetic medication.

Criteria for Approval:

1. *FDA approved diagnosis.*
2. *Clinical supporting information on failure or contraindication with conventional antiemetic drug therapies at maximum FDA approved daily dose with dates and dosages.*

Clinical Exceptions:

1. *Approval granted through the Point-of-Sale system for members undergoing chemotherapy, radiation therapy or surgery for cancer related diagnosis or prescriptions written by an oncologist or radiology oncologist.*
2. *Documented adverse effect, drug interaction, or contraindication to tier-1 products.*
3. *Approval granted for hyperemesis gravidarum with supporting documentation listing*
    a. *week of gestation,*
    b. *presence of weight loss (loss of ≥ 5% pre-pregnancy body weight)*
    c. *recent hospitalizations or emergency room visits due to hyperemesis, or*
    d. *history of hyperemesis gravidarum with previous pregnancies.*
4. *Approval granted if there is a unique FDA-approved indication not covered by any other products.*

No PA	PA Required
Corticosteroids	**5HT3 Antagonist**
Dexamethasone, methylprednisolone, cortisone, prednisone, prednisolone	Dolasetron Ondansetron
Antidopaminergic	
Thiethylperazine	Granisetron
Antihistaminic	
Meclizine, hydroxyzine	Palonosetron
Cyclizine	
Promethazine	
Anticholinergic	
Scopolamine, trimethobenzamide,	
Prokinetic	**Substance P/Neurokinin Antagonist**
Metoclopramide	Aprepitant (In combination with corticosteroid or 5HT3 antagonist)
Antipsychotic	**Cannabinoids**
Droperidol	Nabilone
Chlorpromazine	Dronabinol
Prochlorperazine	
Perphenazine, prochlorperazine, fluphenazine, mesoridazine, thioridazine, trifluoperazine	

APPENDIX E

Prior Authorization Annual Review - Fiscal Year 2005

Synagis®

Oklahoma Health Care Authority
September 2006

Definition of Prior Authorization Category for FY '06

Prior authorization is required for all members who receive Synagis® in an outpatient setting. Synagis® is approved for members who meet the established criteria based on the 2003 American Academy of Pediatrics (AAP) guidelines.

Current Criteria for Prior Authorization of Synagis

A. Member Selection. Members must be included in one of the following age groups at the beginning of the RSV season:*

1) Infants and children less than 24 months old with Chronic Lung Disease (CLD) who have required medical treatment (O_2, bronchodilator, corticosteroid, or diuretic therapy) for CLD in the 6 months prior to RSV season
2) Infants less than 12 months of age, born at 28 weeks gestation or earlier
3) Infants less than 6 months of age, born at 29-32 weeks gestation.
4) Infants, up to 6 months old at the start of RSV season, born at 32-36 weeks gestation, who have 2 or more of the following risk factors:
    a. Child care attendance
    b. School-aged siblings
    c. Exposure to environmental air pollutants (Tobacco smoke exposure can be controlled by the family, therefore not a risk factor for Synagis prophylaxis)
    d. Congenital abnormalities of the airway
    e. Severe neuromuscular disease
5) Children up to 24 months old with hemodynamically significant cyanotic and acyanotic congenital heart disease.
6) Infants up to 12 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure.

* Treatment should continue through the entire RSV season.

B. Length of treatment. Synagis® is approved for use only during RSV season, which is generally November 1 through April 30, as determined by Oklahoma State Dept. of Health.

C. Units authorized. The number of units authorized is calculated as the closest number of full vials necessary to provide the dose based on 15mg/kg per month.

D. Dose-pooling. To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Utilization

For the period of October 1, 2005 through May 15, 2006, a total of 885 members received Synagis® through the Medicaid fee-for-service program from a pharmacy provider or a physician's office.

Total Cost - RSV Season 05-06	**$7,540,989.18**	**4.5%↑**
Total Cost RSV Season 04-05	***$7,216,652.71***	
Total Claims- RSV Season 05-06	**5,670**	**3.3%↓**
Total Claims RSV Season 04-05	***5,864***	
Total Members - RSV Season 05-06	**885****	**8.1%↓**
Total Members RSV Season 04-05	***963***	

**Four members have claims for both pharmacy and physician office

RSV Season	2004-2005	2005-2006	%↑/↓
Cost/claim	$1230.67	$1329.98	8.1%↑
Claims/member	6.1	6.4	4.9%↑
Cost/member	$7493.93	$8520.89	13.7%↑

Pharmacy Claims:

Product	# of Claims	Total Units	Total Days	Total Cost	Total Clients
Synagis® 50 mg/0.5 ml vial	2,733	3,061	67,861	$4,098,994.40	706
Synagis® 100 mg/ml vial	1,541	903	38,827	$1,278,494.44	568
Synagis® 50 mg vial	466	816	12,444	$578,510.86	217
Synagis® 100 mg vial	639	754	15,357	$1,007,346.56	343
Total	**5,379**	**5,533**	**134,489**	**$6,963,349.26**	**823***

Physician Office Claims – CPT code 90378

Product	# of Claims	Total Units	Total Days	Total Cost	Total Clients
Synagis® 50 mg increments	291	859	8,148	$577,639.92	66*

*Total unduplicated members for 05-06

Total petitions - RSV Season 05-06

A total of 1,914 petitions were submitted for consideration of Synagis®. Of the 879 petitions that were initially denied or incomplete, petitions for 290 clients were subsequently approved.

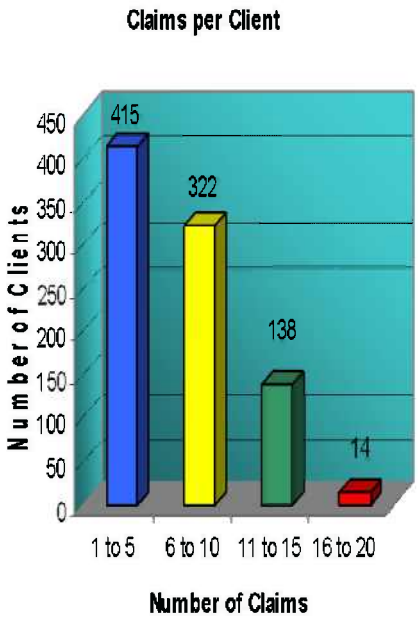
	PAs	Members
Approved	1035	954
Denied	408	352
Incomplete	471	377

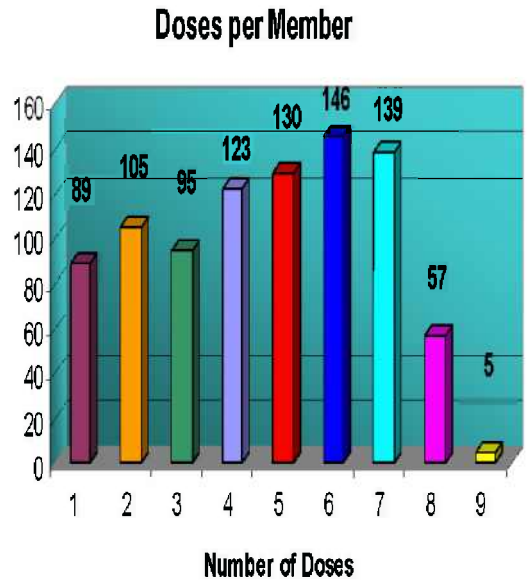
Age	Female	Male	Totals
0 to 1	366	393	759
1 to 2	52	74	126
Totals	**418**	**467**	**885**

Claims were reviewed to determine the age/gender of the clients.

Claims Data

- Because two sizes of vials can be used per patient and each vial size must be submitted as a separate pharmacy claim, the number of claims appears to be excessive. A total of 4,076 doses were given through the season. The average cost per dose was $1,850. Some of the members had excessive dosing, but most were as expected.





Hospitalization

Medical/Hospital claims submitted only during the 2005-06 RSV season were evaluated to determine the incidence of RSV or similar lower respiratory infection (LRI) requiring medical intervention (hospitalization, emergency room visit, or office visit). Claims were selected using RSV-specific ICD-9 codes (480.1, 079.6, and 466.11) as well as unspecific bronchiolitis and viral pneumonia codes (480.9, 466.1, and 466.19). These claims were compared with prior authorization approval and denial data for Synagis® for the same time period.

Treatment was sought for 44 of the 223 members (19.7%) whose petitions were denied. There were 80 encounters of medical care, including 9 hospitalizations, 14 emergency room visits, and 6 outpatient clinic visits The remaining claims were for office visits or treatment associated with the aforementioned incidences.

In comparison, 240 of the 954 members (25.2%) who had approval for Synagis® and received the monthly injections sought treatment for RSV or a similar respiratory illness. Of the 464 encounters, there were 84 hospitalizations, 43 emergency room visits, 17 outpatient clinic visits, and 41 home health care visits.

	Approved (N=954)	Denied (N=223)
Hospitalization	80 (8.4%)	9 (4.0%)
Emergency Room	43 (4.5%)	14 (6.2%)
Outpatient Visit	17 (1.8%)	6 (2.7%)

Discussion

- The new liquid formulation of Synagis® became available in mid-November and though some powder product use was seen into April, the vast majority had been replaced with the liquid product by December 1st.
- The season was extended to May 15, 2006 due to an increased incidence of RSV in the last week of April, as is shown in the graph that follows.
- Occasionally a pharmacy would request additional units on an existing PA, providing the child's current weight to support the request. Sometimes the pharmacy would use the next available vial size, even if it was less than 0.1 ml of the additional vial, rather than use the overfill, regardless of whether it was a 50 mg or a 100 mg vial. Because we don't allow dose pooling, the remainder of the vial is discarded.
- Synagis is requested for patients with some type of lung disease such as asthma or respiratory distress syndrome of newborn. The guidelines specify Chronic Lung Disease, which was formerly called bronchopulmonary dysplasia. Other lung diseases are not included in the guidelines.

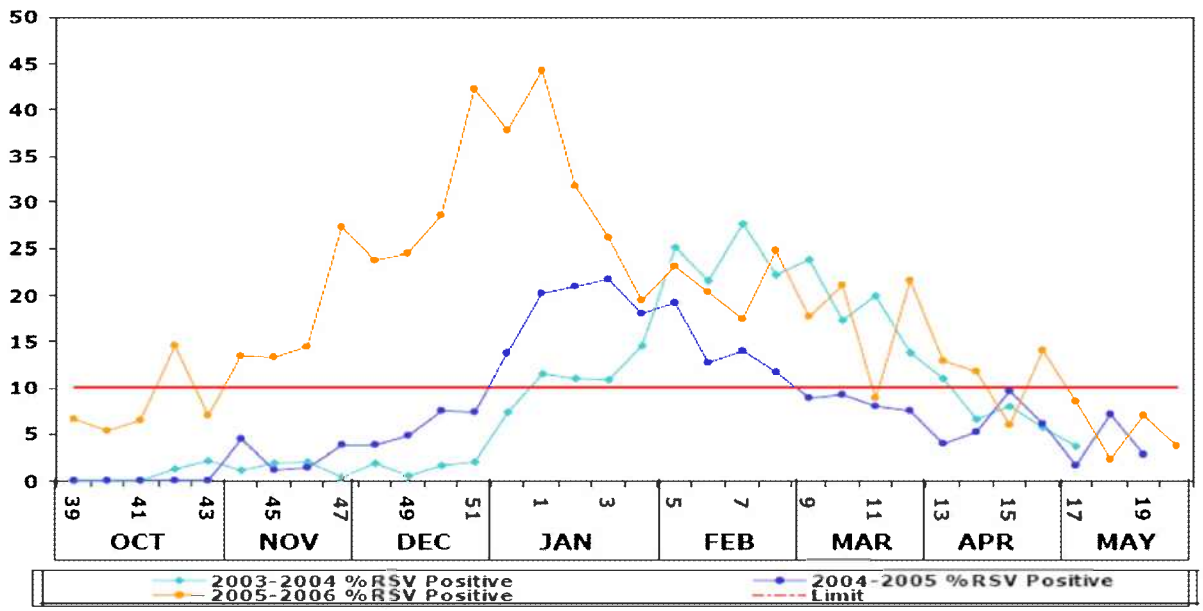
Recommendations

The College of Pharmacy recommends the following:

- Limit to six (6) doses, to be given one every 30 days. Additional doses will be reviewed and authorized by a clinical pharmacist on an individual basis.
- Change the start date of authorization from October 1st to October 15th.
- Change the end date of authorization from May 1st to March 31st.
- Define Chronic Lung Disease as "formerly bronchopulmonary dysplasia" on the criteria and on the petition form.
- Set dosing range of vial size + 10% to avoid the use of additional or larger vials. (e.g. 1 to 55 mg = 50 mg vial x1, 56-110 mg = 100 mg vial x1 ..etc)

Weekly Percent Positivity RSV Based on Total Tests from Sentinel Providers for Oklahoma 2005-06 and Previous Two Seasons

Week Ending May 20, 2006



*The 2003-2004 & 2004-2005 RSV surveillance stopped at week 17 & 19 due to continued low activity.

From the Oklahoma State Health Department website: http://www.health.state.ok.us/program/cdd/flu

APPENDIX F

30 Day Notice to Prior Authorize New Growth Hormone Products
Zorbtive ™ and Omnitrope™ [somatropin (rDNA origin) for injection]
Oklahoma Health Care Authority
September 2006

	Zorbtive™ Serono, Inc	Omnitrope™ Sandoz, Inc
Summary	Zorbtive™ is a recombinant human growth hormone (hGH) approved for treatment of Short Bowel Syndrome. It acts on receptors in the small intestines, enhancing the transport of water, electrolytes, and nutrients across the intestinal mucosa. It is available in 8.8 mg multidose vials to be reconstituted.	Omnitrope™ is a recombinant human growth hormone approved for treatment of pediatric and adult growth hormone deficiency (GHD). It is available as lyophilized powder for reconstitution in 1.5 mg single use and 5.8 mg multidose vials
Clinical Trials	In randomized, double-blind, controlled, parallel-group study using hGH placebo with an oral dietary supplement containing glutamine or hGH plus the dietary supplement with or without glutamine, statistically significant reductions in parenteral nutrition requirements were seen with hGH arms	In a 9-month randomized study comparing Omnitrope™ with another somatropin approved for pediatric GHD, both products had similar effects on growth. Randomized, placebo-controlled trials over 6 months in adult GHD patients showed positive effect on body composition
Indications	Short Bowel Syndrome (SBS) in patient receiving specialized nutritional support. To be used in conjunction with optimal management of SBS.	Pediatric growth failure due to endogenous GHD; Adult GHD of childhood or adult onset.
Price (EAC)	$704/vial (8.8 mg) = $80/mg	Not available
Bioavailability/pharmacokinetics		
Absorption	Bioavailability after subcutaneous injection is 70-90%.	The AUC after a 5 mg injection was 291 hr. µg/L and Cmax was 37µg/L.
Distribution	Steady-state volume of distribution is 12.0 ± 1.08L	Mean volume of distribution estimated at 1.4 L/kg.
Metabolism	Though the liver plays a role, growth hormone, including Zorbtive™, is presumed to undergo primary cleavage and glomerular filtration in the kidneys before amino acids and peptides return to systemic circulation.	As with endogenous growth hormone, Omnitrope™ is presumed to undergo classical protein catabolism in the liver and kidneys before amino acids and peptides return to systemic circulation.
Elimination	$T_{1/2}$ was 4.28 ± 2.14 hrs.	$T_{1/2}$ is 2.4 hrs
Clinical Information		
Dosage range	Dose of 0.1 mg/kg/day for four weeks. Maximum of 8 mg/day. Dosing for more than 4 weeks has not been studied	Pediatrics: 0.16 to 0.24 mg/kg/week Adults: 0.04 mg/kg/week to maximum of 0.08 mg/kg/wk, based on tolerance to treatment

	Zorbtive™ Serono, Inc	Omnitrope™ Sandoz, Inc
Known adverse effects/ toxicities	Peripheral edema, facial edema, arthralgia, injection site reaction, flatulence, abdominal pain, vomiting, malaise, nausea, diaphoresis, rhinitis, dizziness, carpal tunnel syndrome	Pediatrics: Hypothyroidism elevated HbA1c, eosinophilia, hematoma, headache, hypertriglyceridemia, leg pain. Adults: peripheral edema, fluid retention, arthralgia, myalgia, paresthesia, injection site reaction
Special precautions	Caution in patients with diabetes or with risk factors for glucose intolerance since hGH can induce a state insulin resistance, ketoacidosis, and diabetic coma. Observe for acute pancreatitis, intracranial hypertension, increased skin turgor, musculoskeletal discomfort, carpal tunnel syndrome.	Caution in patients with diabetes or with risk factors for glucose intolerance since hGH can induce a state insulin resistance. Observe for recurrent neoplastic activity, slipped capital femoral epiphyses, intracranial hypertension, hypothyroidism, progression of existing scoliosis. Omnitrope™ 5.8 mg contains benzyl alcohol as a preservative and should not be used in newborns.
Contraindications	Contraindicated in patients with active neoplasia, new or recurrent, acute critical illness due to complications following open heart or abdominal surgery multiple accidental trauma or acute respiratory failure, known hypersensitivity to growth hormone,	Contraindicated when there is evidence of neoplastic activity, contraindicated in pediatric patients with fused epiphyses, patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment, patients with acute critical illness due to complications following open heart or abdominal surgery multiple accidental trauma or acute respiratory failure, or known hypersensitivity to somatropin or any of the excipients.
Drug interactions	Studies have not been conducted	Glucocorticoids may inhibit the growth promoting effect of growth hormone. Limited data suggests that hGH may increase clearance of compounds know to be metabolized by cytochrome P450 liver enzymes (corticosteroids, sex steroids, anticonvulsants, cyclosporine)
Patient monitoring guidelines	Reconstituted Zorbtive™ can be refrigerated for up to 14 days. Zorbtive™ should be administered using sterile, insulin-type subcutaneous syringe, rotating injection sites to avoid local tissue atrophy. After reconstitution, vial should be gently swirled to mix and inspected for cloudiness. Cloudy solution must not be used.	After reconstitution, Omnitrope™ 5.8 mg can be refrigerated for up to 3 weeks, Omnitrope™ 1.5 mg for up to 24 hours. The site of subcutaneous injections should be rotated daily to help prevent lipoatrophy. After reconstitution, vial should be gently swirled to mix and inspected for cloudiness. Cloudy solution must not be used.

Cost Comparison

Omnitrope is not available yet, so pricing has not been set. This is a comparison of Zorbtive™ and most of the more utilized growth hormone products in the SoonerCare population.

Product	Sizes	Cost/units (EAC)
Zorbtive™ vial	8.8 mg	$80/mg
Humatrope® cartridges	6 mg, 12 mg, 18 mg,	$54.63/mg
Humatrope® vial	5 mg	$54.63/mg
Genotropin® prefilled syringes	0.2 mg, 0.4 mg, 0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, 1.6 mg, 1.8 mg, 2.0 mg	$50.93/mg
Genotropin® cartridge	5.8 mg	$43.91/mg
Genotropin® cartridge	13.8 mg	$44.29/mg
Nutropin® vial	10 mg/ml	$54.63/mg
Nutropin AQ® cartridge	10 mg/2ml	$54.63/mg
Norditropin Nordiflex® pen injector	10 mg/1.5 ml	$54.61/mg
Norditropin® vial	4 mg vial	$44.32/mg
Nortitropin® cartridge	15 mg/1.5 ml	$54.63/mg
Tev-Tropin vial	5 mg	$36.13/mg

Recommendations

As with all other growth hormones, the College of Pharmacy recommends prior authorization of these two drugs. The criteria are based on the specific indications of each drug.

Omnitrope™

- Criteria established for Classic hGH deficiency for pediatric and adult members

Zorbtive™

- Diagnosis of Short Bowel Syndrome
- Under the care of gastroenterologist
- Documentation of specialized nutritional support (may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences. Nutritional supplements may be added according to the discretion of the treating physician.)
- Used in conjunction with optimal management of SBS may include dietary adjustments, enteral feedings, parenteral nutrition, fluids, and micronutrient supplements as needed.
- Daily dose not to exceed 8 mg
- Approval for 4 weeks of treatment (administration for greater than 4 weeks has not been adequately studied)

APPENDIX G

30 Day Notice to Prior Authorize IGF-1 Analog Products
Increlex™ and Iplex™ (mecasermin rinfabate [rDNA origin])
Oklahoma Health Care Authority
September 2006

Introduction[1]

Insulin-like growth factor-1 (IGF-1) is the primary hormonal mediator of statural growth. Growth hormone (GH) binds to receptors in the liver and other tissues, where it stimulates the synthesis and release of IGF-1. IGF-1, along with GH, controls production of chondrocytes, which are components of new growth at the epiphyses of bones. IGF-1 also stimulates cell and organ growth through mitogenic activity. IGF-1 also suppresses hepatic glucose production, stimulates peripheral glucose utilization, and inhibits insulin secretion, thus it has the potential to cause hypoglycemia. Though it has no effect on linear growth, insulin-like growth factor binding protein-3 (IGFBP-3) binds to IGF-1 along with an acid-labile subunit, providing a physiological reservoir for IGF-1.

	Increlex™ Tercica, Inc	**IPlex™ Insmed, Inc**
Summary	Increlex™ is an aqueous solution for injection containing recombinant human IGF-1, approved for treatment of Primary IGF-1 deficiency (IGFD). It is available in 10 mg/ml multidose vials containing 4 ml.	IPlex™, an aqueous solution for injection containing a protein complex of recombinant human IGF-1 and human IGFBP-3, is approved for treatment of Primary IGFD. It is available as 36 mg/0.6 ml single dose vials
Clinical Trials	In five pooled studies (one double-blind, placebo-controlled and four open-label) lasting up to 8 years (mean duration of 3.9 years), subjects saw statistically significant increases in height velocity and SD change from the mean for height for years 1-6.	In a one-year, prospective, open label study evaluating safety and efficacy subjects saw significant increases in height velocity with doses ranging from 0.5 to 2.0 mg/kg/day.
Indication	Primary IGF-1 deficiency GH gene deletion w/ neutralizing antibodies to GH	Primary IGF-1 deficiency GH gene deletion w/ neutralizing antibodies to GH
EAC	$123.75/ml (4 ml vial) = $12.37/mg	$132/ml (0.6 ml vial) = $2.20/mg
Bioavailability/pharmacokinetics		
Absorption	Cmax after a 0.12 mg/kg injection was 234 ng/ml, AUC for IGF-1 was 2,932 ng*h/ml.	Cmax after a 1mg/kg injection was 133 ng/ml for IGF-1 and 1,574 ng/ml for IGFBP-3. AUC for IGF-1 was 2,654 ng*h/ml, 62,535 ng*h/ml for IGFBP-3.
Distribution	Vol. of distribution is 0.257 ± 0.073 L/kg Protein binding: >80% bound to IGFBP-3 and an acid-labile subunit (IGFBP-3 reduced with severe primary IGFD)	Vol. of distribution - 0.184-0.33 L/kg Protein binding: >80% bound to IGFBP-3 and an acid-labile subunit (IGFBP-3 reduced with severe primary IGFD)
Metabolism[2]	Hepatic and renal	Hepatic and renal
Elimination	$T_{1/2}$ was 5.8 hours	$T_{1/2}$ was >12 hours

	Increlex™ Tercica, Inc	IPlex™ Insmed, Inc
Clinical Information		
Dosage range	Initial dose of 0.04-0.08 mg/kg bid, SC, titrate to max dose of 0.12 mg/kg BID. Doses of more than max has not been studied and should not be used due to potential for hypoglycemia. Not approved for use in children under the age of 2 years.	Initial dose of 0.5 mg/kg/d, SC, titrate to max dose of 2 mg/kg/d. Not approved for use in children under the age of 3 years.
Known adverse effects/ toxicities	Hypoglycemia, headache, tonsillar hypertrophy, bone pain, arthralgia, increased transaminases, serous otitis media, injection site reaction, elevations in cholesterol and triglycerides	Hypoglycemia, headache, tonsillar and/or adenoid hypertrophy, bone pain, arthralgia, increased transaminases, iron deficiency anemia, injection site reaction, ovarian cysts
Special precautions	Observe for recurrent adenotonsillar enlargement, slipped capital femoral epiphyses, intracranial hypertension, progression of existing scoliosis. Because of potential for hypoglycemia, high-risk activities within 2-3 hours of dose should be avoided until well-tolerated dose has been established.	Because of potential hypoglycemic effects, avoid missing meals or take on days when cannot or will not eat. Observe for recurrent adenotonsillar enlargement, slipped capital femoral epiphyses, intracranial hypertension, progression of existing scoliosis.
Contraindications	Contraindicated when there is evidence of neoplastic activity, contraindicated in pediatric patients with fused epiphyses, or known hypersensitivity to mecasermin or any of the excipients. Not for IV administration	Contraindicated when there is evidence of neoplastic activity, contraindicated in pediatric patients with fused epiphyses, or known hypersensitivity to mecasermin rinfabate or any of the excipients. Not for IV administration
Drug interactions	Studies have not been conducted	Studies have not been conducted
Patient monitoring guidelines	Dose adjustment based on IGF-1 levels. Dose should be given just before or after meal due to hypoglycemic effect. Monitor glucose at initiation of therapy or dosage increase. Increlex™ should be administered using sterile, insulin-type subcutaneous syringe, rotating injection sites to avoid local tissue atrophy. Vials are stable for 30 days in refrigerator after initial vial entry. Cloudy solution must not be used.	Growth velocity should increase by 2 cm/yr in the first year. Failure should be assessed for compliance or other cause. Dosage is based on IGF-1 levels. Monitor glucose at initiation of therapy or dosage increase. Rotate injection site. Vials must remain frozen until prior to use. Bring to room temperature. Cloudy solution must not be used. Discard any unused portion. Administer dose with sterile disposable syringes and needles.

Recommendations

The College of Pharmacy recommends prior authorization with the criteria based on the following FDA approved indications for use as listed below.

- Initiation of therapy
  - Member is under the care of an endocrinologist
  - Diagnosis of Primary IGF-1 Deficiency with all of the following:
    - Height >3 SD below the mean
    - Basal IGF-1 >3 SD below the mean
    - Normal or elevated GH
  - Documentation of mutation in GH receptor (GHR) or mutation in post-GHR signaling pathway or IGF-1 gene defects (Laron Syndrome)
  - Not approved for use in secondary IGF-1 deficiencies related to GH deficiency, malnutrition, hypothyroidism, or chronic steroid therapy.

- Discontinue therapy
  - Epiphyses closed
  - Target height (165.1 cm. in males, 152.4 cm in females) is reached
  - Sensitivity to mecasermin
  - Member is noncompliant

1. Mosby's Drug Consult, 2006, Available at http://home.mdconsult.com/das/drug/view
2. Mecasermin. Lexi-Comp™Online. *Copyright © 1978-2006 Lexi-Comp Inc.*

APPENDIX H

30 Day Notice to Prior Authorize Exubera® (insulin human [rDNA origin]) Inhalation Powder

Oklahoma Health Care Authority
September 2006

Manufacturer Pfizer Inc.
Classification FDA classification: Human Insulin Inhalation Powder
Status: prescription only

Summary
Exubera® is an inhaled powder form of recombinant human insulin. It has FDA approval for treatment of adults with type 1 and type 2 diabetes. Efficacy is comparable to subcutaneously injected regular insulin. Onset of action is similar to rapid-acting analogs, however duration of action is the same as regular insulin. Because of this, Exubera® should be given within 10 minutes of a meal. Exubera® is not indicated for monotherapy and does not eliminate the need for longer-acting insulin in patients with type 1 diabetes.

Exubera® is contraindicated in smokers or patients who have discontinued smoking in the past 6 months, or in patients with unstable or poorly controlled lung disease. Pulmonary function should be assessed prior to initiating therapy. Exubera® will be available in 1 mg and 3 mg blisters. Dosing of three 1 mg blisters does not equal a single 3 mg blister (also see equivalent dosing chart below). The Exubera® release unit must be replaced every 2 weeks. Each blister must be administerd as a separate inhalation.

Because Exubera® does not require a self-injection, its proposed place in therapy is for patients who delay initiation of insulin therapy due to fear of self-injection. Earlier initiation of insulin therapy could have a positive impact on long-term outcomes. Packaging is based on average dosing of 12 or 15 mgs daily. Variation in dosing may cause issues with wasting or unnecessary purchasing of both strengths.

Approximate guidelines for Initial, Pre-Meal Exubera® Weight-Based Dose

Patient Wt (lb)	Initial Dose per Meal	Number of 1 mg Exubera® Blisters PER Dose	Number of 3 mg Exubera® Blisters PER Dose
66 – 87 lb	1 mg per meal	1	-
88 – 132 lb	2 mg per meal	2	-
133 – 176 lb	3 mg per meal	-	1
177 – 220 lb	**4 mg per meal**	**1**	**1**
221 – 264 lb	**5 mg per meal**	**2**	**1**
265 – 308 lb	6 mg per meal	-	2

Adapted from Exubera® Inhaler Product Dossier, June 2006.

Approximate Equivalent IU Dose of Regular Insulin

Dose (mg)	Approximate Regular Insulin SC Dose (IU)	Number of 1 mg Exubera® Blisters PER Dose	Number of 3 mg Exubera® Blisters PER Dose
1 mg	3	1	-
2 mg	6	2	-
3 mg	8	-	1
4 mg	**11**	**1**	**1**
5 mg	**14**	**2**	**1**
6 mg	16	-	2

Adapted from Exubera® Inhaler Product Dossier, June 2006.

Cost Comparison

	EAC or Fee/ bill unit	SMAC / unit	Average Daily Dose[2]	$ / Month (30 day supply)
Exubera® Kit (1 Inh, 1 Replacement Chamber, 1mg X 180, 3mg X 90, 2 RUs[1]) (Each)	$ 0.61		5 mg TID	$ 164.70
Exubera® Combo Pack 12 (1mg X 90, 3mg X 90, 2 RUs) (Each)	$ 0.68		4 mg TID	$ 122.40
Exubera® Combo Pack 15 (1mg X 180, 3mg X 90, 2 RUs) (Each)	$ 0.57		5 mg TID	$ 153.90
Exubera® Release Units (2 Each)	$ 2.75			$ 5.50
Spirometry[3]	$ 34.27			
Regular Insulin 10 ml	$ 3.32		14 IU TID	$ 41.83
Humalog® 10 ml	$ 7.37		14 U TID	$ 92.86
Humalog® 3 ml Disposable Device	$ 9.49		14 U TID	$ 119.57
Humalog® 3 ml Cartridges	$ 9.55		14 U TID	$ 120.33
Syringes 100 count	$ 0.29			$ 29.00
Pen Needles 100 count	$ 0.89			$ 89.00
Alchohol Swabs 1 box	$ 2.50			$ 2.50
Byetta® 10 mg (2.4 ml)	$ 83.81		10 mg BID	$ 201.14
Avandia® 8 mg (tablet)	$ 5.77		8 mg QD	$ 173.10
Metformin (tablet) 1000 mg	N/A	$ 0.12	1000 mg BID	$ 7.20
Metformin ER (tablet) 500 mg	N/A	$ 0.23	1000 mg QD	$ 13.80

[1]RUs = Release Units
[2]Insulin dosing based on equivalent inhaled dosing of 15 mg.
[3]Average Payment

Recommendations
The College of Pharmacy has the following recommendations for Exubera®:

PRODUR EDITS

1. A quantity limit based on the manufacturer's packaging per 30 days.
2. Members must be 18 years of age or older.

PRIOR AUTHORIZATION

Prior Authorization with criteria as outlined below or as determined by the DUR Board:

Type II Diabetics:

1. Inability to maintain HbA1c levels at or below 7% after a minimum of six months of combined oral therapy at maximal doses. (Example: metforrmin and sulfonylurea.), *and*
2. Diagnosis of injection-phobia, provided no additional injectable medications (including other forms of insulin) are being utilized.
3. *Or* member currently using injectable insulin and experiencing severe persistent problems with injection sites, such as lipohypertrophy.

Type I Diabetics:

1. Currently using injectable insulin and experiencing severe persistent problems with injection sites, such as lipohypertrophy. (Exubera® is not approved as monotherapy in type 1 diabetics.)

For both types:
Patients must not be smokers or have discontinued smoking in the past 6 months, or have unstable or poorly controlled lung disease (asthma, COPD, etc). Pulmonary function should be assessed prior to initiating therapy.

Approval for 6 months with a follow up HbA1c. If HbA1c has not decreased by a minimum of 1% or if not at or below 7%, further renewal will not be granted without supporting information for continued use of the product.

All members who are approved for Exubera® will be enrolled in the Diabetes Disease Management Program, if not already participating.

Pharmacological data
The primary activity of insulin is regulation of glucose metabolism. Insulin lowers blood glucose concentrations by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis, and enhances protein synthesis.

Therapeutic indications
Exubera® is indicated for the treatment of adult patients with diabetes mellitus for the control of hyperglycemia. Exubera® has an onset of action similar to rapid-acting insulin analogs and has a duration of glucose-lowering activity comparable to subcutaneously administered regular human insulin. In patients with type 1 diabetes, Exubera® should be used in regimens that include a longer-acting insulin. In patients with type 2 diabetes, Exubera® can be used as monotherapy or in combination with oral agents or longer-acting insulins.

Bioavailability/pharmacokinetics
Absorption
- Human insulin given by inhalation is absorbed as fast as rapid acting insulin and faster than regular insulin given by subcutaneous route.

Distribution
- The distribution of inhaled insulin has not been studied but is expected to be the same as endogenous insulin, with no protein binding and distribution in the extracellular space.

Metabolism
- Liver 50%
- Kidney 30%
- Adipose Tissue/Muscle 20%

Elimination
- The elimination half-life has not been studied but is expected to be the same as endogenous insulin.

Dosage forms
Oral
- Inhalation form

Dosage range
1mg to 6mg preprandially based on weight and should be titrated based on glucose levels.

Known adverse effects/toxicities
- Cardiovascular—chest pain
- Hypoglycemia
- Dry mouth
- Insulin antibodies are formed
- Allergic reactions

- Ear—disorders, pain, and otitis media
- Pulmonary—cough, dyspnea, pharyngitis, and respiratory tract infection

Special precautions

- Changes in patients' physical activity or usual meal plan may require adjustment of dosage.
- Hyperglycemia may occur; if sustained, it may result in diabetic coma or death.
- Hypoglycemia commonly occurs and timing may differ among the various insulin formulations.
- Hypoglycemic signs and symptoms may be masked under conditions such as long duration of diabetes, diabetic nerve disease, use of medications such as beta-blockers, or intensified diabetes control.
- Hypokalemia may occur, especially when insulin is given intravenously; if left untreated, respiratory paralysis, ventricular arrhythmias, and death may occur.
- Type 1 diabetics will also require a longer-acting insulin.
- Safety and efficacy in patients with Underlying lung disease (asthma, COPD) has not been established.

Contraindications

- Episodes of hypoglycemia
- Hypersensitivity to insulin or any other ingredient in the product
- Patients who currently smoke or stopped smoking within last 6 months
- Unstable or poorly controlled lung disease

Drug interactions (major)

- Fluroquinolones (major interaction)—changes in blood glucose and increased risk of hypoglycemia or hyperglycemia
- Beta blockers (moderately severe)—hypoglycemia, hyperglycemia, or hypertension
- St. John's Wort (moderately severe)—hypoglycemia
- Ginseng and Ginkgo (moderately severe)—hypoglycemia
- Licorice (moderately severe)—hypokalemia and sodium retention
- Lithium (moderately severe)—hypoglycemia or hyperglycemia

Patient monitoring guidelines

Laboratory Monitoring

- Fasting blood glucose between 80 and 120 mg/dL.
- Bedtime glucose between 100 to 140 mg/dL.
- Glycosylated hemoglobin less than 7%.

Signs and Symptoms of Hypoglycemia—sweating, trembling, tachycardia, hunger, anxiety, dizziness, headache, clouding of vision, loss of fine motor skills, combativeness, seizures, mental confusion, and loss of consciousness

Patient information

Patients should be instructed on self-management procedures including glucose monitoring; proper Exubera® inhalation technique; and hypoglycemia and hyperglycemia management. Patients must be instructed on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, or skipped meals. Refer patients to the Exubera® Patient Medication Guide for additional information.

Patients should be informed that in clinical studies, treatment with Exubera® was associated with small, non-progressive mean declines in pulmonary function relative to comparator treatments. Because of the effect of Exubera® on pulmonary function, pulmonary function tests are recommended prior to initiating treatment with Exubera®. Following initiation of therapy, periodic pulmonary function tests are recommended (see PRECAUTIONS, Respiratory, Pulmonary Function).

Patients should inform their physician if they have a history of lung disease, because the use of Exubera® is not recommended in patients with underlying lung disease (e.g., asthma or COPD), and is contraindicated in patients with poorly controlled lung disease. Women with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy.

Clinical Trials Data Summary

Results of two 24-Week, Active-Control, Open-Label Trials in Patients with Type 1 Diabetes				
	Study A		Study B	
	EXU[1] (TID) + UL[2] (QD)	SC R[3] (BID) + NPH (BID)	EXU (TID) + NPH (BID)	SC R (TID) + NPH (BID)
Sample Size	136	132	103	103
HbA1c				
Baseline Mean	7.9	8.0	7.8	7.8
Adj. Mean Change	-0.2	-0.4	-0.3	-0.2
EXU-SC R	0.14		-0.11	
95% CI	(-0.03, 0.32)		(-0.30, 0.08)	
% with HbA1c < 8% at end	64.0 %	68.2 %	74.8 %	66.0 %
% with HbA1c < 7% at end	16.9 %	19.7 %	28.2 %	30.1 %

Adapted from Exubera® Inhaler Product Dossier, June 2006.
[1]EXU = Exubera Inhalation Powder
[2]SC R = Subcutaneous Regular Insulin [3]UL = Humulin® U Ultralente

Results of a 12-Week, Active-Control, Open-Label Trial in Patients With Type 2 Diabetes Not Optimally Controlled with Dual Oral Agent Therapy (Study D)			
	EXU Mono	OAs[1]	EXU + OAs
Sample Size	102	96	100
HbA1c			
Baseline Mean	9.3	9.3	9.2
Adj. Mean Change	-1.4	-0.2	-1.9
EXU-OAs	-1.18		-1.67
95% CI	(-1.41, -0.95)[2]		(-1.90, -1.44)[2]
% with HbA1c < 8% at end	55.9 %	18.8 %	86.0 %
% with HbA1c < 7% at end	16.7 %	1.0 %	32.0 %

Adapted from Exubera® Inhaler Product Dossier, June 2006.
[1]OAs = Treatment with 2 oral agents (an insulin secretagogue in addition to metformin or a thiazolidinedione)
[2]$P<0.001$

Results of Two 24-Week, Active-Control, Open-Label Trials in Patients With Type 2 Diabetes Previously On Oral Agent Therapy

	Study E				Study F			
	EXU + SU[5]	MET[6] + SU	EXU + SU	MET + SU	EXU + MET	GLI[7] + MET	EXU + MET	GLI + MET
	High Stratum		Low Stratum		High Stratum		Low Stratum	
Sample Size	113	103	101	93	109	103	125	119
HbA1c								
Baseline Mean	10.5	10.6	8.8	8.8	10.4	10.6	8.6	8.7
Adj. Mean Change	-2.2	-1.8	-1.9	-1.9	-2.2	-1.9	-1.8	-1.9
EXU-OAs	-0.38[8]		-0.07		-0.37[9]		0.04	
95% CI	(-0.63, -0.14)		(-0.33, -0.19)		(-0.62, -0.12)		(-0.19, 0.27)	
% with HbA1c < 8% at end	48.7%	44.7 %	81.2%	73.1%	72.5%	56.3%	80.8%	86.6%
% with HbA1c < 7% at end	20.4%	14.6 %	30.7%	32.3%	33.9%	17.5%	40.0%	42.9%

AdaptAdapted from Exubera® Inhaler Product Dossier, June 2006.
[5]SU = Sulfonylurea [6]Met = Metformin [7]GLI = Glibenclamide
[8]p=0.002 [9]p=0.004

Results of a 24-Week, Active-Control, Open-Label Trial in Patients With Type 2 Diabetes Previously Treated With Subcutaneous Insulin (Study G)

	EXU (TID) + UL (QD)	SC R + NPH
Sample Size	146	149
HbA1c		
Baseline Mean	8.1	8.2
Adj. Mean Change	-0.7	-0.6
EXU-SC R	-0.07	
95% CI	(-0.31, 0.17)	
% with HbA1c < 8% at end	76.0 %	69.1 %
% with HbA1c < 7% at end	45.2 %	32.2 %

Adapted from Exubera® Inhaler Product Dossier, June 2006.

REFERENCES

1. Exubera® Inhaler Product Dossier. Pfizer Inc. June 2006.
2. Insulin Human Inhaled. In: Klasco RK (Ed): DRUGDEX® System. Thomson Micromedex, Greenwood Village, Colorado (Vol. 129 expires [9/2006]).

APPENDIX I

30 Day Notice to Prior Authorize Glumetza™ (metformin hydrochloride) Extended Release Tablets

Oklahoma Health Care Authority
September 2006

Manufacturer Depomed, Inc.
Classification FDA classification: Oral Antihyperglycemic
Status: prescription only

Summary

Glumetza™ is an extended release metformin hydrochloride tablet indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes (monotherapy). It may also be used concomitantly with a sulfonylurea or insulin to improve glycemic control in adults. It utilizes the AcuForm™ Deliver Technology which lengthens the time of the drug in the stomach. It currently has an FDA Therapeutic Equivalence Code of BX and is presumed be to therapeutically inequivalent to other extended release metformin currently available.

Cost Comparison

	EAC / unit	SMAC / unit	Average Daily Dose[2]	$ / Month (30 day supply)
Glumetza™ (tablet) 500 mg	$ 1.10		1000 mg QD	$ 66.00
Metformin ER (tablet) 500 mg	N/A	$ 0.23	1000 mg QD	$ 13.80
Metformin (tablet) 1000 mg	N/A	$ 0.12	1000 mg BID	$ 7.20

Recommendations

The College of Pharmacy recommends prior authorization of Glumetza™. Approval based on clinical documention of inability to take other forms of generic metformin ER.

REFERENCE

Glumetza™ Product Information. Depomed Inc. 2006.

APPENDIX J

30 Day Notice to Prior Authorize Zanaflex Capsules™ (tizanidine hydrochloride)

Oklahoma Health Care Authority
September 2006

Zanaflex Capsules™ (tizanidine hydrochloride) marketed by Acorda is a short-acting medication for the management of spasticity. Use of Zanaflex Capsules™ should be reserved for activities and times when relief of spasticity is most important due to its short duration of effect. Spasticity is thought to be reduced with this medication by blocking nerve impulses through pre-synaptic inhibition of motor neurons, resulting in decreased spasticity without losing muscle strength.

Zanaflex Capsules™ and Zanaflex® (tizanidine hydrochloride) tablets both contain tizanidine hydrochloride. However, Zanaflex Capsules™ are not the same as generic tizanidine tablets or Zanaflex® tablets. A person's response to taking Zanaflex Capsules™ may change depending on whether the medication is taken with food or not, including possible changes in efficacy and side effects. Patients should follow their doctor's instructions on how to take this medication. Zanaflex Capsules™ are available in 2mg, 4mg and 6mg strengths. Tablets are available in scored 2mg and 4mg strengths.

Zanaflex Capsules™ may be easier to take than tablets, and for patients who have an impaired ability to swallow, the capsules can be opened and sprinkled on soft foods such as applesauce. The 6mg dose, not available in the tablet form, may allow the patients to take fewer pills per day.

Cost comparison

	Average Wholesaler Price (AWP)/150	Daily Dose*	Monthly Dose (30 day supply) #90	SMAC
Zanaflex Tab 2mg	$224.03	TID	$134.42	$11.58
Zanaflex Tab 4mg	$295.49	TID	$177.29	$14.76
Zanaflex Cap 2mg	$272.25	TID	$163.35	N/A
Zanaflex Cap 4mg	$324.44	TID	$194.66	N/A
Zanaflex Cap 6mg	$542.24	TID	$325.34	N/A

May increase by 2-4mg as needed every 6-8hours to a maximum of three doses in 24 hours. Maximum dose is 36/day.

RECOMMENDATIONS:

The College of Pharmacy recommends prior authorization of Zanaflex Capsules™. Tizanidine tablets must be tried prior to consideration of the capsules. The capsules may be considered for authorization if there is supporting information as to why the member cannot take the tablets.

Important Information for Zanaflex Capsules™

- Use of fluvoxamine or ciprofloxacin is contraindicated due to significant increases in tizanidine plasma levels.

- There is limited data for chronic use of single doses above 8mg and multiple doses above 24mg per day.

- Tizanidine is an α2-adrenergic agonist and may cause hypotension. In a single-dose study where doses were not titrated, two-thirds of patients given 8mg of Zanaflex® (tizanidine hydrochloride) experienced hypotension. The hypotensive effect is dose related and has been measured following single doses of $\geq$ 2mg.

- Liver injury can be caused by Tizanidine, most often of the hepatocellular type. In controlled clinical studies, approximately 5% of patients treated with tizanidine had elevated liver enzyme tests (ALT, AST). During the first 6 months of treatment, monitoring of these levels is recommended (baseline, 1, 3 and 6 months) and periodically thereafter. Most cases resolve rapidly with drug withdrawal and no reported residual problems.

- Due to the potential for toxic hepatic effect of tizanidine, the medication should be used with extreme caution in patients with impaired hepatic function.

- Sedation may interfere with daily activities. These effects seem to be dose related.

- In two North American clinical trials, visual hallucinations or delusions occurred in 3% (5/170) of study patients.

- Use with caution in patients with renal impairment.

- Use with oral contraceptives decreased tizanidine clearance by 50%.

- To discontinue therapy, taper the dose in patients receiving high doses over long time periods to reduce the risk of hypertension, tachycardia and hypertonia.

- *In vitro* studies indicate that the metabolism of other drugs metabolized by cytochrome P450 isoenzymes are not likely affected by tizanidine and its major metabolites.

- Adverse events most common are dry mouth (49%), somnolence (48%), asthenia [weakness, fatigue and/or tiredness] (41%), dizziness (16%) and increased ALT (5%). UTI, infection and constipation.

- Food has complex effects on the pharmacokinetics of tizanidine, which different with the different formulations. The pharmacokinetic differences can be clinically significant when switching formulations, or changing administration from a fed or fasted state. The changes may result in either increased adverse events or a delayed/more rapid onset of activity, depending on the nature of the change.

Zanaflex Capsules™ Prescribing Information. Acorda Pharmaceuticals. April 2005. Available at: http://www.zanaflexcapsules.com/Zanaflex_Insert.pdf.

APPENDIX K

New Product Summaries

Oklahoma Health Care Authority
September 2006

Drug	Manufacturer	Indications	Dosage	Adverse Effects	Contraindications	New Molecular Entity	AWP/ unit
Symbicort® (budesonide and formoterol fumerate dihydrate) Inhalation Aerosol	AstraZeneca	Long-term maintenance treatment of asthma in patients 12 years of age and older. NOT indicated for the relief of acute bronchospasm.	Available in 80/4.5 and 160/4.5 strengths. Med to high: 160/4.5, 2 inhalations BID, Low to med: 80/4.5, 2 inhalations BID. Steroid naïve: 2 inhalations BID either strength.	Long-acting beta$_2$-adrenergic agonists may increase the risk of asthma-related death. Nasopharyngitis, headache, URI, pharyngolaryngeal pain, sinusitis.	Contraindicated in the primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required. Hypersensitivity to any of the ingredients.	No	N/A
Vivitrol™ (naltrexone for extended-release injectable suspension)	Alkermes, Inc.	Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL.	Available in single use cartons, each containing one 380 mg vial of VIVITROL microspheres, one vial containing 4 ml diluent for the suspension of VIVITROL, one 5 ml prepackaged syringe, one 20-gauge ½-inch needle, and two 20-gauge 1 ½ -inch needles with safety device. Dose is 380 mg delivered IM every 4 weeks, or once a month.	Gastrointestinal disorders, upper respiratory tract infection, insomnia, injection site tenderness, injection site pain/induration, asthenic conditions, arthralgia/joint pain, headache, anxiety	Contraindicated in patients receiving opioid analgesics, patients with current physiologic opioid dependence, patients in acute opiate withdrawal, any individual who has failed the naloxone challenge test or has a positive urine screen for opioids, patients with hypersensitivity to any of the components.	No	$868.75 / kit

Drug	Manufacturer	Indications	Dosage	Adverse Effects	Contraindications	New Molecular Entity	AWP / unit
Seasonique™ (levonorgestrel /ethinyl estradiol) 0.15/ 0.03 mg and (ethinyl estradiol) 0.01 mg tablets	Duramed Pharmaceuticals (subsidiary of Barr Pharmaceuticals)	Prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.	Available in Extended-Cycle Tablet Dispensers, each containing a 13-week supply of tablets: 84 light blue-green tablets, each containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol, and 7 yellow tablets each containing 0.01 mg of ethinyl estradiol.	Common: Nausea, vomiting, GI symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema/fluid retention, breast changes, mood changes (including depression), weight/appetite fluctuations, change in cervical ectropion and secretion, cholestatic jaundice, migraine headache. Severe: thrombophlebitis, arterial thromboembolism, pulmonary embolism, myocardial infarction, hypertension, cerebral thrombosis/hemorrhage	Contraindicated in women who currently have the following conditions: Thrombophlebitis or thromboembolic disorders, cerebrovascular or coronary artery disease (current or history), valvular heart disease with thrombogenic complications, uncontrolled HTN, diabetes with vascular involvement, headaches with focal neurological symptoms, major surgery with prolonged immobilization, known or suspected carcinoma of the breast or hx of breast cancer, carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia, undiagnosed abnormal genital bleeding, cholestatic jaundice of pregnancy or jaundice with prior pill use, hepatic adenomas or carcinomas, or active liver disease, known or suspected pregnancy, hypersensitivity to any component of this product.	No	$1.86

APPENDIX L

FDA News

FOR IMMEDIATE RELEASE
P06-100
July 19, 2006

Media Inquiries:
Laura Alvey, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves First Generic Meloxicam

The Food and Drug Administration today approved several first generic versions of Boehringer Ingelheim's Mobic Tablets, an important step in the agency's effort to increase the availability of lower-cost generic medications. Meloxicam (mel-OX-i-kam) is indicated for the treatment of osteoarthritis.

"This is another example of our agency's endeavor to counter rising health care costs by approving safe and effective generic alternatives to brand name drugs," said Gary Buehler, Director, Office of Generic Drugs. "Meloxicam is a widely-used nonsteroidal anti-inflammatory drug (NSAID) and its generic versions can bring significant savings to the millions of Americans with osteoarthritis."

The approval of meloxicam was the result of a "cluster" review approach, one of the process improvements FDA has instituted to facilitate the review of generic drug applications. FDA's Office of Generic Drugs (OGD) has begun to review groups of applications submitted at the end of 5 year new chemical entity (NCE) exclusivity in "clusters" to increase efficiency and decrease review time. At the expiration of 5 year exclusivity, FDA often receives multiple applications from different sponsors, submitted on the same day.

In the case of meloxicam, OGD received over 20 abbreviated new drug applications (ANDAs) and FDA's review team effort resulted in the approval of 13 generic applications for this product in a little over 9 months of review time, resulting in the first time any generic version of this product is available.

Because all of the patents have expired for Mobic, approval of meloxicam is likely to represent immediate savings to the American public. In 2005, according to the online magazine, Drug Topics, Mobic was ranked 38th in dollar sales of brand-name drugs in the United States, with sales totaling $916,397,000.

Generic drug products are used to fill over 50 percent of all prescriptions and because they can cost a fraction of the price of brand name drugs, the economic impact of FDA's generic drug program is significant. With this in mind, the Office of Generic Drugs (OGD) continues working expeditiously to review and take action on generic drug applications as quickly as possible. For more information on other first generic versions, please see http://www.fda.gov/cder/ogd/approvals/1stgen0506.htm.

For additional information related to FDA's Office of Generic Drugs, please go to: http://www.fda.gov/cder/consumerinfo/generic_equivalence.htm.

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FDA Public Health Advisory

Combined Use of 5-Hydroxytryptamine Receptor Agonists (Triptans), Selective Serotonin Reuptake Inhibitors (SSRIs) or Selective Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs) May Result in Life-threatening Serotonin Syndrome

List of Drug Names

The FDA has important new safety information about taking triptans (drugs used to treat migraine headaches) together with certain types of antidepressant medicines. The antidepressant medicines of concern are selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs). Names of the triptans, SSRIs and SNRIs are provided below.

A life-threatening condition called serotonin syndrome may occur when triptans are used together with a SSRI or a SNRI

Serotonin syndrome occurs when the body has too much serotonin, a chemical found in the nervous system. Serotonin syndrome symptoms may include restlessness, hallucinations, loss of coordination, fast heart beat, rapid changes in blood pressure, increased body temperature, overactive reflexes, nausea, vomiting, and diarrhea. Serotonin syndrome may be more likely to occur when starting or increasing the dose of a triptan, SSRI or SNRI.

The FDA has determined that serotonin syndrome occurs with combined use of triptans and a SSRI or SNRI through reports describing serotonin syndrome in people taking these medications together. Each of these types of medicine increases serotonin levels on its own, as well.

Patients who are taking a triptan along with an SSRI or SNRI should talk to their doctor before stopping their medications.

Physicians prescribing a triptan, SSRI or SNRI should:

- keep in mind that triptans are often used intermittently and that either the triptan, SSRI or SNRI may be prescribed by a different physician
- weigh the potential risk of serotonin syndrome with the expected benefit of using a triptan with an SSRI or SNRI
- discuss the possibility of serotonin syndrome with patients if a triptan and an SSRI or SNRI will be used together
- follow patients closely if a triptan and an SSRI or SNRI are used together, particularly during treatment initiation, with dose increases, or with the addition of another serotonergic medication
- instruct patients who take a triptan and an SSRI or SNRI together to seek medical attention

immediately if they experience the symptoms of serotonin syndrome (described above).

Patients should know which medicines they take and tell all of their healthcare providers (physicians, nurses, and pharmacists) what these medicines are.

Triptans are drugs used to treat migraine headaches, and SSRIs and SNRIs are drugs used to treat depression and other mood disorders.

The FDA has requested that all manufacturers of triptans, SSRIs and SNRIs update their prescribing information to warn of the possibility of serotonin syndrome when triptans and SSRIs or SNRIs are taken together.

Drug Names

SSRIs and a Combination Drug Containing an SSRI	SNRIs	Triptans
• Celexa (citalopram) • Fluvoxamine • Lexapro (escitalopram) • Paxil (paroxetine) • Prozac (fluoxetine) • Symbyax (olanzapine/fluoxetine) • Zoloft (sertraline)	• Cymbalta (duloxetine) • Effexor (venlafaxine)	• Amerge (naratriptan) • Axert (almotriptan) • Frova (frovatriptan) • Imitrex (sumatriptan) • Maxalt and Maxalt-MLT (rizatriptan) • Relpax (eletriptan • Zomig and Zomig ZMT (zolmitriptan)

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Date created: July 19, 2006

FDA News

FOR IMMEDIATE RELEASE
P06-110
August 8, 2006

Media Inquiries:
Kimberly Rawlings, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves First Generic Venlafaxine

The Food and Drug Administration today approved the first generic version of Effexor (venlafaxine), an important step in the agency's effort to increase the availability of lower-cost generic medications. Venlafaxine is indicated for the treatment of major depressive disorder (MDD).

"This approval is another example of our agency's efforts to increase access to safe and effective generic alternatives as soon as the law permits," said Gary J. Buehler, Director, Office of Generic Drugs. "Venlafaxine is a widely used antidepressant, and its generic version can bring significant savings to the millions of Americans diagnosed with MDD."

The economic benefits of FDA's generic drug approval program are significant because generic drug products are used to fill over 50 percent of all prescriptions and can cost a fraction of the price of the brand name drugs. Competition from generic drugs that are safe and effective alternatives may quickly lead to reductions in spending. The savings would likely increase as more competitors enter the market. (See http://www.fda.gov/cder/ogd/generic_competition.htm).

Venlafaxine Tablets 25 mg, 37.5 mg, 50 mg, 75 mg and 100 mg are manufactured by TEVA Pharmaceuticals USA (TEVA) in North Wales, PA. This product will carry the same labeling including the black box warning as the originator drug. TEVA is eligible for 180 days of generic drug exclusivity. The FDA may approve other applications after the exclusivity period has expired.

The Office of Generic Drugs continues working expeditiously to review and take action on generic drug applications as quickly as possible. For more information on other first generic versions, please see http://www.fda.gov/cder/ogd/approvals/1stgen0506.htm

For additional information related to FDA's Office of Generic Drugs, please go to:
http://www.fda.gov/cder/consumerinfo/generic_equivalence.htm

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RSS Feed for FDA News Releases [what's this?]

FDA News

FOR IMMEDIATE RELEASE
P06-118
August 24, 2006

Media Inquiries:
Julie Zawisza, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves Over-the-Counter Access for Plan B for Women 18 and Older
Prescription Remains Required for Those 17 and Under

The U.S. Food and Drug Administration (FDA) today announced approval of Plan B, a contraceptive drug, as an over-the-counter (OTC) option for women aged 18 and older. Plan B is often referred to as emergency contraception or the "morning after pill." It contains an ingredient used in prescription birth control pills--only in the case of Plan B, each pill contains a higher dose and the product has a different dosing regimen. Like other birth control pills, Plan B has been available to all women as a prescription drug. When used as directed, Plan B effectively and safely prevents pregnancy. Plan B will remain available as a prescription-only product for women age 17 and under.

Duramed, a subsidiary of Barr Pharmaceuticals, will make Plan B available with a rigorous labeling, packaging, education, distribution and monitoring program. In the CARE (Convenient Access, Responsible Education) program Duramed commits to:

- Provide consumers and healthcare professionals with labeling and education about the appropriate use of prescription and OTC Plan B, including an informational toll-free number for questions about Plan B;
- Ensure that distribution of Plan B will only be through licensed drug wholesalers, retail operations with pharmacy services, and clinics with licensed healthcare practitioners, and not through convenience stores or other retail outlets where it could be made available to younger women without a prescription;
- Packaging designed to hold both OTC and prescription Plan B. Plan B will be stocked by pharmacies behind the counter because it cannot be dispensed without a prescription or proof of age; and
- Monitor the effectiveness of the age restriction and the safe distribution of OTC Plan B to consumers 18 and above and prescription Plan B to women under 18.

Today's action concludes an extensive process that included obtaining expert advice from a joint meeting of two FDA advisory committees and providing an opportunity for public comment on issues regarding the scientific and policy questions associated with the application to switch Plan B to OTC use. Duramed's application raised novel issues regarding simultaneously marketing both prescription and non-prescription Plan B for emergency contraception, but for different populations, in a single package.

The agency remains committed to a careful and rigorous scientific process for resolving novel issues in order to fulfill its responsibility to protect the health of all Americans.

For more information on Plan B and today's action, please see: http://www.fda.gov/cder/drug/infopage/planB/default.htm.

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IMPORTANT PRESCRIBING INFORMATION

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709

www.gsk.com

8/4/2006

Dear Healthcare Professional:

GlaxoSmithKline would like to inform you of important revisions to the prescribing information for DEXEDRINE® (dextroamphetamine sulfate) Spansule® sustained-release capsules and Tablets. DEXEDRINE is approved for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD) and narcolepsy. These revisions are in response to a Food and Drug Administration (FDA) request sent to the manufacturers of all CNS stimulant products approved for the treatment of ADHD. The FDA issued this request for additional, standardized language in prescribing information based on the recommendations made by members of two different advisory committees that convened earlier this year. Please read the following full text that has been added to the prescribing information for DEXEDRINE (a copy of the revised prescribing information is enclosed):

The boxed **WARNING** at the beginning of the DEXEDRINE prescribing information has been updated to include the following additional text:

> MISUSE OF AMPHETAMINES MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

In addition, the following language has been added to the **WARNINGS** section of the DEXEDRINE prescribing information:

WARNINGS

Serious Cardiovascular Events

Sudden Death in Patients with Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems

Children and Adolescents

Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.

(Continued on back)

Adults

Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs (see CONTRAINDICATIONS).

Hypertension and Other Cardiovascular Conditions

Stimulant medications cause a modest increase in average blood pressure (about 2-4 mmHg) and average heart rate (about 3-6 bpm), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia (see CONTRAINDICATIONS).

Assessing Cardiovascular Status in Patients Being Treated with Stimulant Medications

Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

Psychiatric Adverse Events

Pre-Existing Psychosis

Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness

Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Emergence of New Psychotic or Manic Symptoms

Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3,482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression

Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for the appearance of, or worsening of, aggressive behavior or hostility.

(Continued on next page)

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well. Therefore, growth should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Disturbance

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

Additional Change to Prescribing Information

Lastly, the following statement has been deleted from the **PRECAUTIONS** section of the DEXEDRINE prescribing information as it is explained in the new **WARNINGS** section:

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.

The medical community can further our understanding of DEXEDRINE by reporting adverse events to GlaxoSmithKline at 1-888-825-5249 or to FDA's MedWatch Adverse Event Reporting program online (at www.fda.gov/MedWatch/report.htm), by phone (1-800-FDA-1088), or by returning the postage-paid FDA form 3500 (which may be downloaded from www.fda.gov/MedWatch/getforms.htm) by mail (to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787) or fax (1-800-FDA-0178).

GlaxoSmithKline encourages you to familiarize yourself with these revisions to labeling. If you have any questions about the new information, please contact our Customer Response Center at 1-888-825-5249.

Sincerely,

Joseph P. Horrigan MD

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