Appendix F

Fiscal Year 2010 Annual Review of NDSAIDs and 30 Day Notice to Prior Authorize Vimovo™ (esomeprazole/naproxen)

Oklahoma HealthCare Authority

October 2010

Current Prior Authorization Criteria

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)		
Tier 1	**Tier 2**	**Special PA**
diclofenac ER (Voltaren® XR) diclofenac potassium (Cataflam®) diclofenac sodium (Voltaren®) etodolac (Lodine®) etodolac ER (Lodine® XL) fenoprofen (Nalfon®) flurbiprofen (Ansaid®) ibuprofen (Motrin®) ketoprofen (Orudis®) ketoprofen ER (Oruvail®) meclofenamate (Meclomen®) meloxicam (Mobic®) nabumetone (Relafen®) naproxen (Naprosyn®) naproxen sodium (Anaprox®) naproxen EC (Naprosyn® EC) oxaprozin (Daypro®) sulindac (Clinoril®) tolmetin (Tolectin®)	celecoxib (Celebrex®) diclofenac sodium/misoprostol (Arthrotec®)	diclofenac epolamine (Flector®) diclofenac potassium (Zipsor®) diclofenac sodium (Voltaren Gel®) diclofenac potassium (Cambia® pwdr pk) diclofenac sodium (Pennsaid® top drops) indomethacin (Indocin®) mefanamic acid (Ponstel®) naproxen sodium (Naprelan®) piroxicam (Feldene®) naproxen/lansoprasole (Prevacid NapraPac®)

Approval Criteria:

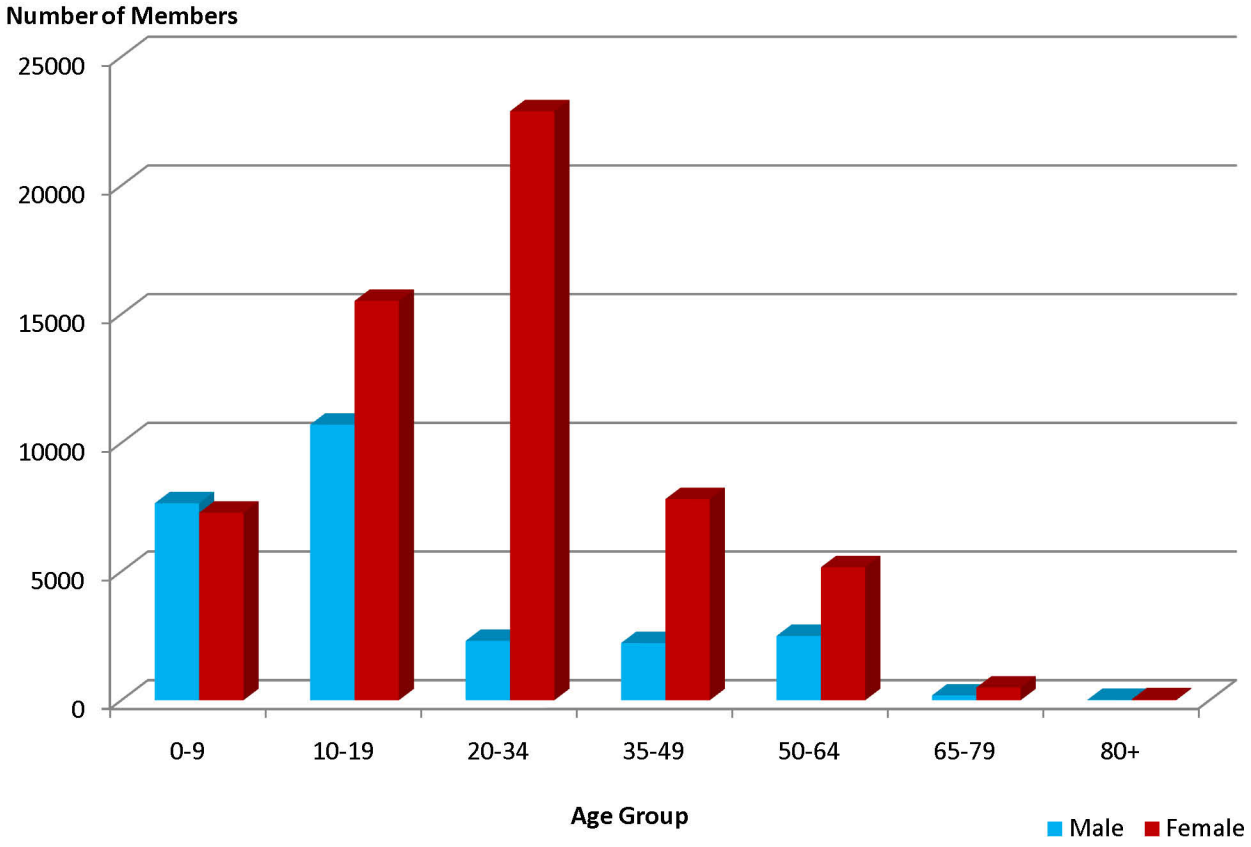
1. Criteria for the non-steroidal, anti-inflammatory drugs in Tier 2 are demonstrated by the following conditions:
    a. Previous use of at least two Tier 1 NSAIDs (from different product lines) plus a PPI
    b. For those with prior GI bleed who must have an NSAID, then a Tier 2 product may be approved (Celebrex should also be taken with a PPI).
2. Criteria for the NSAIDs in the Special PA Category are:
    a. Special indications, such as the diagnosis of gout for indomethacin, OR
    b. Previous use of at least two Tier 1 NSAIDs (from different product lines) AND
    c. Reason why a special formulation is needed over a Tier 1 product

Utilization of NSAIDs

Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2009	73,071	133,173	$1,743,433.37	$13.09	$0.65	8,029,892	2,692,910
2010	84,784	151,546	$1,795,648.43	$11.85	$0.58	8,771,064	3,103,266
Percent Change	**16.0%**	**13.8%**	**3.0%**	**(9.5%)**	**(10.8%)**	**9.2%**	**15.2%**
Change	**11,713**	**18,373**	**$52,215.06**	**($1.24)**	**($0.07)**	**741,172**	**410,356**

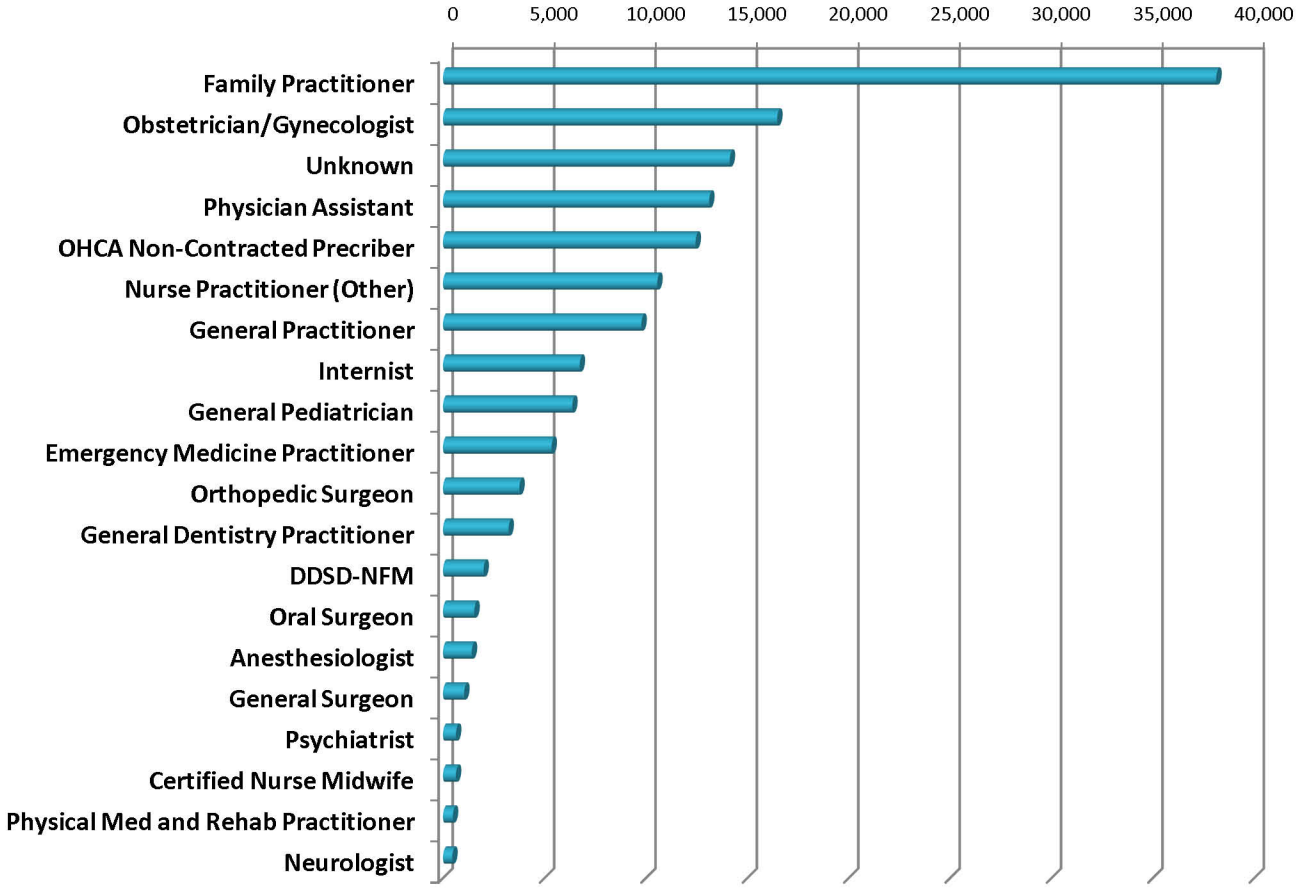
Demographics of Members Utilizing NSAIDs: FY 2010



Age Category	0-9	10-19	20-34	35-49	50-64	65-79	80+	Total
Male	7,653	10,708	2,304	2,221	2,497	183	14	25,580
Female	7,286	15,517	22,888	7,817	5,166	491	34	59,199
Total	14,939	26,225	25,192	10,038	7,663	674	48	84,779*

*5 Members did not have an age or sex identified.

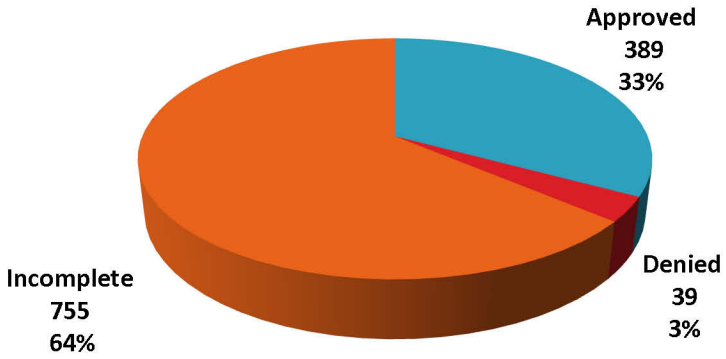
Top 20 Prescribers of NSAIDs by Number of Claims: FY 2010



Prior Authorization of NSAIDs

There were a total of 1,183 petitions submitted for the NSAIDs during fiscal year 2010. The following chart shows the status of the submitted petitions. At the point of sale, approval of a Tier 2 NSAID would be granted if previous use of at least two Tier 1 NSAIDs (from different product lines) plus a PPI was in the member's claims history.

Status of Petitions for NSAIDs: FY 2010



Market News and Update

Vimovo™ (Esomeprazole magnesium/Naproxen) was approved by the FDA in April 2010 for the treatment of (1) ankylosing spondylitis, (2) osteoarthritis, (3) rheumatoid arthritis, and to reduce the risk of occurrence of gastric ulcers in patients at risk of developing NSAID-associated gastric ulcer. Vimovo™ is available in the following strengths: 20 MG-375 MG, 20 MG-500 MG. The dosage regimen is twice daily for all indications.

Cost Comparison

Product	AWP	EAC	SMAC	Estimated Monthly Cost
Vimovo™ (both strengths)	**$1.77**	**$1.56**	**-**	**$93.60**
Naproxen 375mg	-	-	$0.11	$6.60
Naproxen 500mg	-	-	$0.11	$6.60
Nexium® (Esomeprazole) 20mg	$6.50	$5.72	-	$343.20
Omeprazole 20mg	-	-	$0.32	$19.20
Omeprazole 40mg	-	-	$0.38	$22.80
Naproxen + Omeprazole 20mg				**$25.80**
Naproxen + Omeprazole 40mg				**$29.40**

AWP = Average Wholesale Price
EAC= Estimated Acquisition Cost
SMAC=State Maximum Allowable Cost

Conclusion and Recommendations

The College of Pharmacy recommends continuing the current criteria for the NSAIDs with the following addition:

- Place Vimovo™ (Esomeprazole Mg - Naproxen) in the special PA category of the NSAIDs with the same criteria for the NSAIDs in the Special PA Category:
    a. Special indications, such as the diagnosis of gout for indomethacin, OR
    b. Previous use of at least two Tier 1 NSAIDs (from different product lines) AND
    c. Reason why a special formulation is needed over a Tier 1 product

Utilization Details of NSAIDs: Fiscal Year 2010

MEDICATION	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	PERCENT COST
IBUPROFEN TAB 800MG	41,516	2,140,747	716,156	28,139	$274,290.72	2.99	1.48	$0.38	15.28%
NAPROXEN TAB 500MG	16,921	810,663	407,216	10,624	$119,326.99	1.99	1.59	$0.29	6.65%
MELOXICAM TAB 15MG	13,873	492,760	484,349	6,563	$88,420.76	1.02	2.11	$0.18	4.92%
CHLD IBUPROF SUS 100/5ML	12,764	1,526,933	169,093	9,626	$108,531.73	9.03	1.33	$0.64	6.04%
IBUPROFEN TAB 600MG	12,146	535,969	162,317	9,413	$63,939.20	3.3	1.29	$0.39	3.56%
MELOXICAM TAB 7.5MG	7,512	307,645	231,358	3,899	$51,654.21	1.33	1.93	$0.22	2.88%
IBUPROFEN SUS 100/5ML	5,834	777,440	60,173	4,473	$49,663.79	12.92	1.30	$0.83	2.77%
IBUPROFEN TAB 400MG	5,467	254,313	75,757	3,882	$29,361.32	3.36	1.41	$0.39	1.64%
DICLOFENAC TAB 75MG DR	3,873	219,995	110,895	2,160	$85,499.63	1.98	1.79	$0.77	4.76%
NAPROXEN SOD TAB 550MG	2,723	90,111	43,917	2,057	$26,825.30	2.05	1.32	$0.61	1.49%
IBUPROF CHLD SUS 100/5ML	2,569	306,714	37,288	2,050	$18,577.49	8.23	1.25	$0.50	1.03%
NAPROXEN TAB 375MG	2,337	107,532	54,963	1,515	$16,159.98	1.96	1.54	$0.29	0.90%
ETODOLAC TAB 400MG	2,205	117,550	55,820	1,280	$31,236.71	2.11	1.72	$0.56	1.74%
CELEBREX CAP 200MG	2,197	105,281	80,572	492	$401,630.11	1.31	4.47	$4.98	22.37%
NABUMETONE TAB 750MG	1,817	108,694	54,656	761	$44,741.13	1.99	2.39	$0.82	2.49%
KETOPROFEN CAP 75MG	1,800	58,036	22,357	1,465	$15,775.74	2.6	1.23	$0.71	0.88%
KETOROLAC TAB 10MG	1,791	28,541	13,079	1,527	$12,526.22	2.18	1.17	$0.96	0.70%
NABUMETONE TAB 500MG	1,426	83,367	40,890	678	$27,171.35	2.04	2.10	$0.66	1.51%
NAPROXEN TAB 250MG	1,107	52,898	22,990	794	$9,347.33	2.3	1.39	$0.41	0.52%
SM IBUPROFEN SUS INFANTS	867	19,815	11,938	789	$7,647.02	1.66	1.10	$0.64	0.43%
NAPROXEN DR TAB 500MG	826	43,536	21,754	503	$12,004.95	2	1.64	$0.55	0.67%
ETODOLAC TAB 500MG	762	41,307	21,035	378	$14,863.10	1.96	2.02	$0.71	0.83%
CHLD IBU DRO 40MG/ML	749	11,725	9,163	658	$6,337.24	1.28	1.14	$0.69	0.35%
DICLOFEN POT TAB 50MG	675	35,769	13,737	485	$8,963.67	2.6	1.39	$0.65	0.50%
IBU TAB 800MG	640	37,161	12,866	459	$4,650.50	2.89	1.39	$0.36	0.26%
KETOPROFEN CAP 50MG	590	28,582	8,008	476	$6,801.86	3.57	1.24	$0.85	0.38%
DICLOFENAC TAB 50MG EC	472	27,417	12,157	314	$13,335.45	2.26	1.50	$1.10	0.74%
ETODOLAC CAP 300MG	467	29,598	12,547	252	$8,406.32	2.36	1.85	$0.67	0.47%
DICLOFENAC TAB 50MG DR	400	21,952	9,676	281	$10,737.70	2.27	1.42	$1.11	0.60%
NAPROXEN SUS 125/5ML	395	109,516	7,294	232	$9,665.71	15.01	1.70	$1.33	0.54%
IBUPROFEN SUS INFANTS	350	6,225	4,556	308	$2,674.90	1.37	1.14	$0.59	0.15%
SULINDAC TAB 200MG	344	21,432	10,836	160	$6,862.78	1.98	2.15	$0.63	0.38%
OXAPROZIN TAB 600MG	320	17,295	9,284	173	$4,185.18	1.86	1.85	$0.45	0.23%
IBU-DROPS DRO 40MG/ML	302	4,665	2,776	272	$2,787.61	1.68	1.11	$1.00	0.16%
ETODOLAC ER TAB 400MG	245	13,327	7,987	95	$10,621.07	1.67	2.58	$1.33	0.59%
KETOPROFEN CAP 200MG ER	245	11,698	9,182	100	$21,099.57	1.27	2.45	$2.30	1.18%
DICLOFENAC TAB 100MG ER	209	9,005	7,060	88	$4,815.36	1.28	2.38	$0.68	0.27%
CHILD ADVIL SUS 100/5ML	190	22,798	2,349	162	$1,570.14	9.71	1.17	$0.67	0.09%
CELEBREX CAP 100MG	187	10,636	6,339	56	$25,014.49	1.68	3.34	$3.95	1.39%
DICLOFENAC TAB 75MG EC	173	9,726	4,898	79	$4,932.46	1.99	2.19	$1.01	0.27%

MEDICATION	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	PERCENT COST
NAPROXEN DR TAB 375MG	148	7,513	3,799	97	$2,183.72	1.98	1.53	$0.57	0.12%
ETODOLAC ER TAB 500MG	147	7,514	3,911	63	$5,999.51	1.92	2.33	$1.53	0.33%
INDOMETHACIN CAP 50MG	140	8,549	3,259	66	$2,578.91	2.62	2.12	$0.79	0.14%
ETODOLAC CAP 200MG	137	6,859	2,695	90	$2,099.61	2.55	1.52	$0.78	0.12%
ARTHROTEC 75 TAB	132	8,360	4,075	40	$20,888.18	2.05	3.30	$5.13	1.16%
PONSTEL CAP 250MG	121	3,955	1,040	101	$31,881.68	3.8	1.20	$30.66	1.78%
NAPROXEN SOD TAB 275MG	117	4,644	1,958	86	$1,265.75	2.37	1.36	$0.65	0.07%
ETODOLAC ER TAB 600MG	107	4,589	3,749	64	$6,630.24	1.22	1.67	$1.77	0.37%
NAPRELAN TAB 500MG CR	107	4,704	2,959	57	$18,169.39	1.59	1.88	$6.14	1.01%
INDOMETHACIN CAP 25MG	106	6,854	2,451	41	$1,700.90	2.8	2.59	$0.69	0.09%
SULINDAC TAB 150MG	94	4,763	2,511	48	$1,279.79	1.9	1.96	$0.51	0.07%
IBUPROFEN DRO INFANTS	80	2,416	1,183	72	$860.88	2.04	1.11	$0.73	0.05%
FLURBIPROFEN TAB 100MG	76	3,877	2,013	43	$998.31	1.93	1.77	$0.50	0.06%
DICLOFENAC TAB 100MG XR	74	3,670	3,005	27	$1,613.66	1.22	2.74	$0.54	0.09%
PIROXICAM CAP 20MG	64	2,481	2,471	34	$479.36	1	1.88	$0.19	0.03%
INDOMETH CAP 75MG ER	63	2,570	1,930	18	$5,539.68	1.33	3.50	$2.87	0.31%
KETOPROFEN POW	59	4,408	1,243	36	$1,969.29	3.55	1.64	$1.58	0.11%
KETOROLAC INJ 30MG/ML	58	232	339	44	$440.36	0.68	1.32	$1.30	0.02%
IBU-DROPS DRO INFANTS	50	1,485	805	44	$581.69	1.84	1.14	$0.72	0.03%
IBU TAB 600MG	44	2,051	613	39	$255.58	3.35	1.13	$0.42	0.01%
ARTHROTEC 50 TAB	43	3,000	1,270	14	$5,781.31	2.36	3.07	$4.55	0.32%
MEDI-PROFEN SUS 100/5ML	40	4,794	310	33	$366.62	15.46	1.21	$1.18	0.02%
NAPRELAN TAB 375MG CR	40	2,203	1,187	15	$7,394.50	1.86	2.67	$6.23	0.41%
IBU TAB 400MG	29	1,344	309	23	$163.49	4.35	1.26	$0.53	0.01%
KETOROLAC INJ 30MG/ML	23	252	405	11	$382.62	0.62	2.09	$0.94	0.02%
MELOXICAM SUS 7.5/5ML	23	1,845	759	12	$1,188.62	2.43	1.92	$1.57	0.07%
MECLOFEN SOD CAP 50MG	21	1,220	481	5	$742.35	2.54	4.20	$1.54	0.04%
DICLOFENAC TAB 25MG EC	21	1,545	716	15	$1,814.57	2.16	1.40	$2.53	0.10%
KETOROLAC INJ 60MG/2ML	17	65	351	8	$212.34	0.19	2.13	$0.60	0.01%
TOLMETIN SOD CAP 400MG	14	1,260	420	2	$960.16	3	7.00	$2.29	0.05%
DICLOFENAC TAB 50MG EC	13	750	375	4	$362.64	2	3.25	$0.97	0.02%
ZIPSOR CAP 25MG	8	622	157	6	$1,427.68	3.96	1.33	$9.09	0.08%
IBUPROFEN POW	8	649	99	6	$47.24	6.56	1.33	$0.48	0.00%
NAPRELAN TAB 750MG CR	7	272	242	5	$1,892.69	1.12	1.40	$7.82	0.11%
CELEBREX CAP 400MG	4	360	360	1	$2,083.77	1	4.00	$5.79	0.12%
MECLOFEN SOD CAP 100MG	4	150	60	3	$161.02	2.5	1.33	$2.68	0.01%
FLURBIPROFEN TAB 50MG	3	212	68	3	$40.62	3.12	1.00	$0.60	0.00%
CHILD ADVIL DRO 40MG/ML	3	75	30	3	$32.95	2.5	1.00	$1.10	0.00%
PIROXICAM CAP 10MG	3	220	110	3	$20.02	2	1.00	$0.18	0.00%
CHILD ADVIL DRO 50/1.25	3	45	50	3	$18.07	0.9	1.00	$0.36	0.00%
KETOROLAC INJ 60MG/2ML	2	4	10	1	$11.42	0.4	2.00	$1.14	0.00%
TOLMETIN SOD TAB 200MG	2	120	60	1	$87.37	2	2.00	$1.46	0.00%
INDOCIN SUS 25MG/5ML	2	40	43	1	$41.03	0.93	2.00	$0.95	0.00%

MEDICATION	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	PERCENT COST
MEFENAM ACID CAP 250MG	1	30	7	1	$198.78	4.29	1.00	$28.40	0.01%
TOLMETIN SOD TAB 600MG	1	60	30	1	$76.23	2	1.00	$2.54	0.00%
MOBIC SUS 7.5/5ML	1	60	60	1	$67.04	1	1.00	$1.12	0.00%
TOTALS	**151,546**	**8,771,065**	**3,103,266**	**84,784***	**$1,795,648.43**	**2.83**	**1.79**	**$0.58**	**100.00%**

***Total number of unduplicated members**

Vimovo™ (Esomeprazole magnesium - Naproxen) Product Information

Manufacturer	AstraZeneca LP.
Classification	NSAID/PPI
Status	Prescription Only

Indication
Vimovo™ is indicated for the treatment of (1) ankylosing spondylitis, (2) osteoarthritis, (3) rheumatoid arthritis, and to reduce the risk of occurrence of gastric ulcers in patients at risk of developing NSAID-associated gastric ulcer.

Dosage Forms
Oral Tablet, Delayed Release (Esomeprazole Mg - Naproxen): 20 MG-375 MG, 20 MG-500 MG

Black Box Warning
Cardiovascular Risk: Vimovo™ may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke.
Gastrointestinal Risk: Vimovo™ (NSAID component) may cause a risk of serious gastrointestinal bleeding ulceration, and perforation of stomach or intestines.

Contraindications
- **CABG-** treatment of preoperative pain in CABG surgery
- **Hypersensitivity**- patients with known hypersensitivity to the drug or its ingredients or Aspirin.

Pregnancy Risk Factor C during the 1st and 2nd trimester
Pregnancy Risk Factor D during the 3rd trimester

Precautions
- **Cardiovascular disease-** may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke.
- **Gastrointestinal ulceration-** may cause a risk of serious gastrointestinal bleeding ulceration, and perforation of stomach or intestines.
- **Bleeding risk**- Active bleeding may occur.
- **Renal impairment**- not recommend due to increased risk of renal toxicity and injury, monitoring is recommended if required. Concurrent use of ACE Inhibitor may worsen renal function.
- **Atrophic gastritis**- has been reported with long-term omeprazole use.
- **Bone fracture, osteoporosis**-related, may occur with proton pump inhibitor use. Increased risk with higher dose and/or longer duration of use.
- **Elderly-** increased risk of potentially fatal gastrointestinal injury, or renal toxicity and injury.

- **Hepatic abnormalities**- including elevated transaminases and rare cases of severe hepatic reactions (i.e., jaundice and fatal fulminant hepatitis, liver necrosis, and hepatic failure) have been reported.
- **Edema/CHF-** may exacerbate fluid retention, edema, and peripheral edema, and subsequently renal toxicity and injury.
- **Skin reactions-** may occur with NSAID use and can occur without warning. Discontinue if signs of skin rash or hypersensitivity.

Common Adverse Effect

- Gastritis Erosive
- Dyspepsia
- Diarrhea
- Gastic Ulcer
- Upper Abdominal Pain
- Nausea
- Hypertension

Less Common Adverse effects

- Nervous system disorders
- Respiratory, Thoracic Disorders
- Mediastinal Disorders
- Infection/ Infestations
- Peripheral Edema

Drug interactions

- Ace-inhibitors
- Aspirin
- Cholestyramine
- Diuretics
- Lithium
- Methotrexate
- Anticoagulants
- SSRIs
- Anti-retrovirals
- Oral contraceptives
- P450 (2C19, 3A4)- warfarin, clarithromycin
- Albumin bound drugs- sulphonylureas, hydantoins

Patient Information

- It is best to take this medicine on an empty stomach or 30 minutes before a meal.
- Swallow the delayed-release tablet whole with water. Do not break, crush, chew, or dissolve it.
- Do not use any other NSAID medicine unless monitored by health professional.
- Antacids may be used while take Vimovo™.

REFERENCE

[1] Vimovo(TM) (Naproxen/Esomeprazole) Product Information. AstraZeneca LP. September 17, 2010.

Appendix G

FISCAL YEAR 2010 ANNUAL REVIEW OF OCULAR ALLERGY PRODUCTS AND 30 DAY NOTICE TO PRIOR AUTHORIZE BEPREVE™ (BEPOTASTINE BESILATE) AND LASTACAFT™ (ALCAFTADINE)

OKLAHOMA HEALTH CARE AUTHORITY

OCTOBER 2010

CURRENT PRIOR AUTHORIZATION OF OCULAR ALLERGY MEDICATIONS

- Tier-1 products are covered with no authorization necessary
- Tier-2 authorization requires:
  - FDA approved diagnosis
  - A trial of at least one Tier 1 product of a similar type for a minimum of two weeks in the last 30 days
  - Documentation of clinical need for Tier 2 product over a Tier 1 should be noted on the petition
  - Clinical exceptions granted for products with allergic reaction or contraindication

Tier-1	Tier-2
cromolyn sodium (Crolom®)	nedocromil sodium (Alocril®)
ketotifen fumarate (Alaway®,Zaditor OTC®)	pemirolast potassium (Alamast®)
olopatadine (Patanol®)	emedastine difumarate (Emadine®)
	loteprednol etabonate (Alrex®)
	olopatadine (Pataday®)
	lodoxamide tromethamine (Alomide®)
	epinastine (Elestat®)
	azelastine (Optivar®)

Current Tiers based on Supplemental Rebates

TRENDS IN UTILIZATION

Comparison of Fiscal Years 2009 & 2010

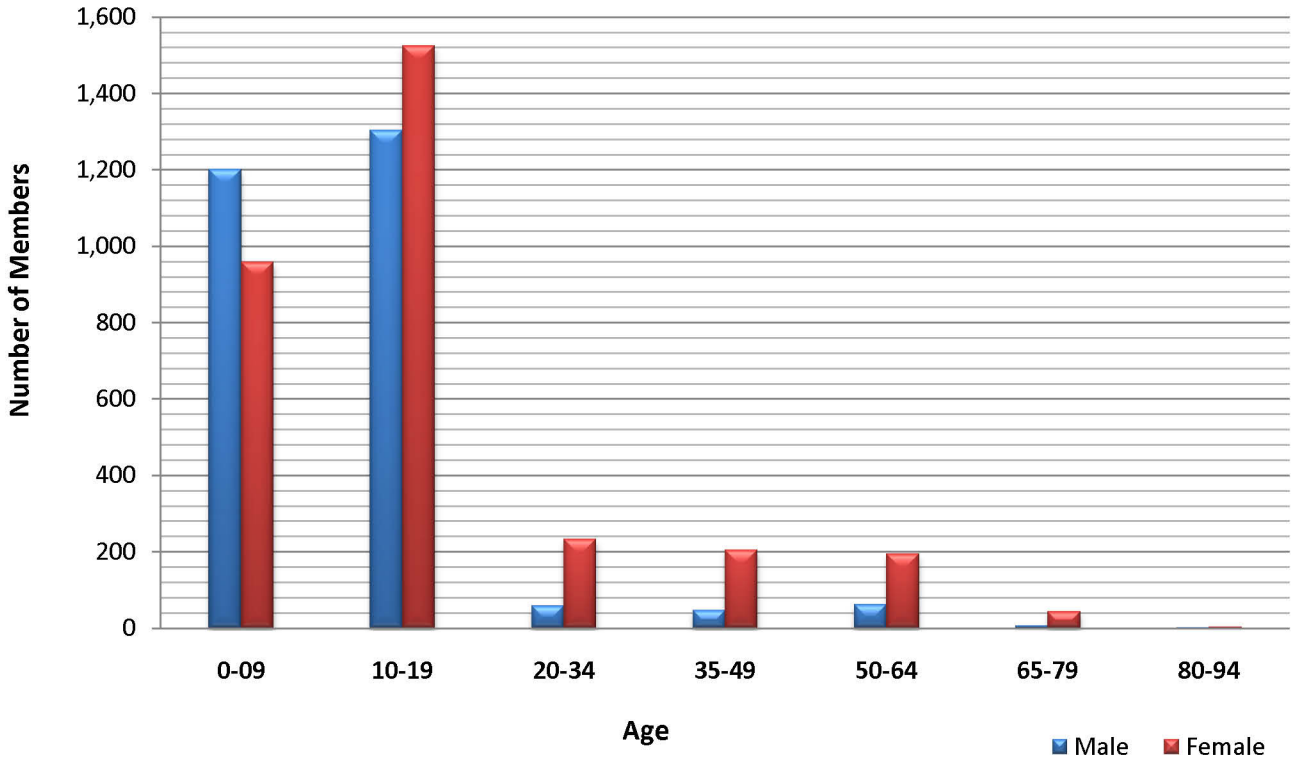
Fiscal Year	Members	Claims	Paid	Paid/Claim	Per-Diem	Units	Days
2009	5,313	7,728	$669,173.07	$86.59	$3.17	35,721	211,208
2010	5,936	8,382	$760,578.28	$90.74	$2.98	43,121	255,110
% change	**+11.7%**	**+8.5%**	**+13.6%**	**+4.8%**	**-6.0%**	**+20.7%**	**+20.8%**
change	**+623**	**+654**	**+$91,405.21**	**+$4.15**	**-$0.19**	**+7,400**	**+43,902**

Utilization Details for Fiscal Year 2010

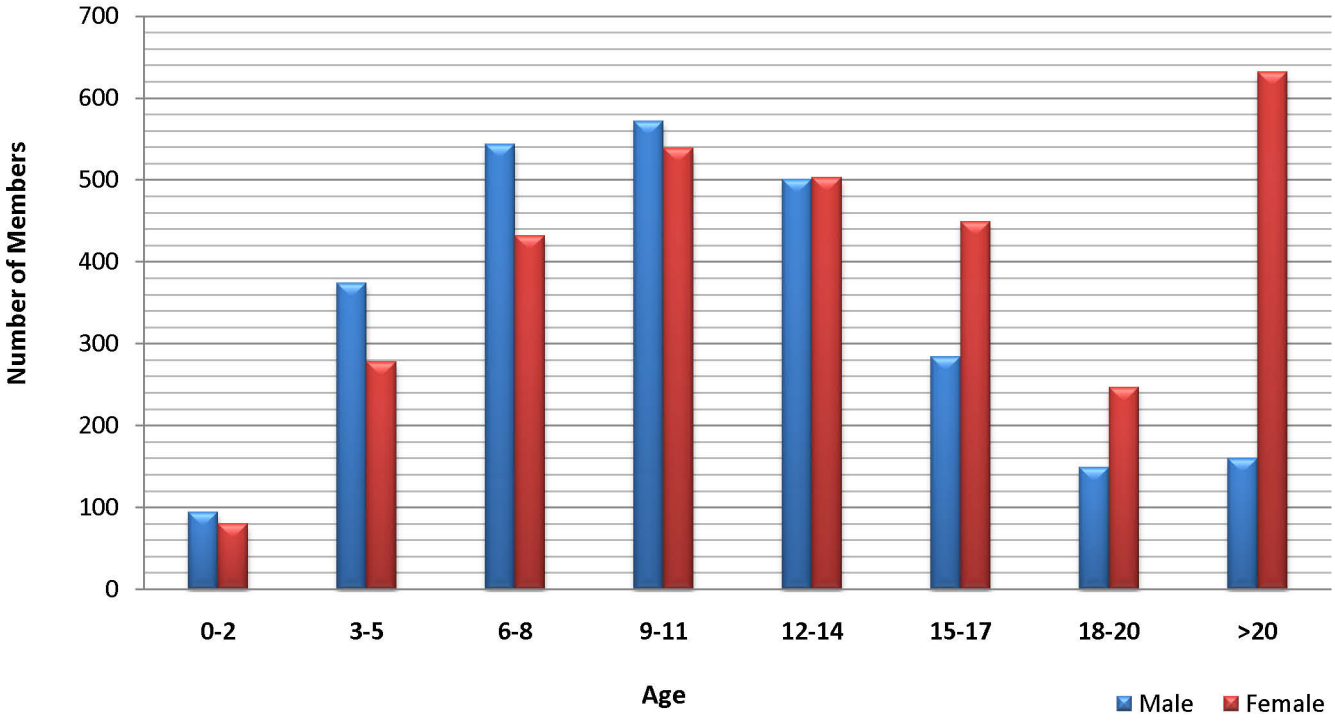
Generic	Brand	Claims	Members	Paid	Claims/ Member	Paid/ Day	% Paid
Olopatadine HCl 0.1%	PATANOL	7,228	5,148	$675,525.12	1.4	$3.08	83.37%
Epinastine HCl 0.05%	ELESTAT	349	223	$33,706.03	1.57	$3.08	4.16%
Azelastine HCl 0.05%	OPTIVAR	257	193	$26,203.14	1.33	$3.19	3.23%
Cromolyn Sodium 4%	CROMOLYN	162	120	$2,805.73	1.35	$0.55	0.35%
Azelastine HCl 0.05%	AZELASTINE	93	74	$8,098.50	1.26	$2.81	1.00%
Olopatadine HCl 0.2%	PATADAY	69	20	$6,403.40	3.45	$3.09	0.79%
Ketotifen Fumarate 0.025%	KETOTIFEN	66	51	$950.50	1.29	$0.48	0.12%
Loteprednol Etabonate 0.2%	ALREX	58	21	$4,967.85	2.76	$3.01	0.61%
Ketotifen Fumarate 0.025%	ZADITOR	47	40	$672.29	1.18	$0.47	0.08%
Ketotifen Fumarate 0.025%	ALAWAY	40	35	$458.88	1.14	$0.37	0.06%
Bepotastine Besilate 1.5%	BEPREVE	7	5	$708.01	1.4	$2.62	0.09%
Ketotifen Fumarate 0.025%	EYE ITCH REL	5	5	$64.58	1	$0.43	0.01%
Ketotifen Fumarate 0.025%	REFRESH EYE	1	1	$14.25	1	$0.48	0.00%
Totals		**8,382**	**5,936***	**$760,578.28**	**1.44**	**$2.98**	**100%**

*Total number of unduplicated members

Member Demographics of Members Utilizing Ocular Allergy Products in FY2010



Member Demographics for Selected Ages, 0-20

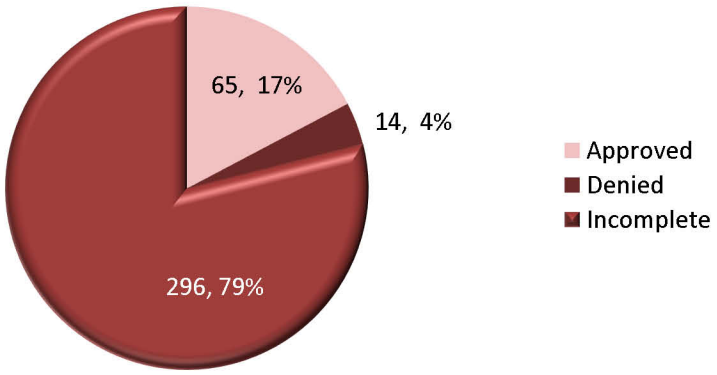


Prescribers of Ocular Allergy Products in FY2010

Specialty	Number of Claims	Total Cost
Optometrist	3,493	$322,610.01
General Pediatrician	1,171	$105,682.46
Family Practitioner	925	$81,101.34
Ophthalmologist	731	$67,847.71
Nurse Practitioner (Other)	588	$52,175.50
Physician Assistant	392	$35,096.68
DDSD-NFM	257	$24,017.51
General Practitioner	211	$18,636.65
Prescriber Only	207	$16,515.29
Allergist	107	$9,827.51
Internist	75	$6,398.72
Otologist, Laryngologist, Rhinologist	63	$5,711.30
Emergency Medicine Practitioner	51	$4,894.61
Others combined*	111	$10,062.99

*includes hand surgeon, anesthesiologist, OB/GYN, psychiatrist, pulmonary disease specialist, gastroenterologist, general dentistry prescriber, personal care (individual), certified registered nurse anesthetist, family nurse practitioner, orthopedic surgeon, pediatric nurse practitioner, general surgeon, urologist, proctologist, podiatrist, radiologist, geriatric practitioner, neurologist, & general internist

Prior Authorizations of Ocular Allergy Products in FY2010



MARKET UPDATE

Bepreve™ (bepotastine besilate, 1.5% - approved September 2009) is a topically-active histamine H_1 receptor antagonist that also inhibits the release of histamine from mast cells. It is available as a 1.5% solution in 5mL (AWP - $105.00) and 10ml (AWP - $182.40) bottles. Bepreve™ is indicated for the treatment of ocular itching associated with allergic conjunctivitis and is to be used as one drop in affected eye(s) twice daily. Package insert states that Bepreve™ was more effective than placebo in relieving ocular itching when evaluated in a Conjunctival Antigen Challenge (CAC) study involving 237 patients. The safety of Bepreve™ has been evaluated in 861 patients over 6 weeks in a randomized controlled trial. No studies have been found comparing the efficacy of Bepreve™ against current therapies.

Lastacaft™ (alcaftadine, 0.25% - approved July 2010) is a topically active histamine H_1 receptor antagonist that also inhibits the release of histamine from mast cells. It is available as a 0.25% solution in a 3mL volume (dispensed in a 5mL sized dropper bottle). Lastacaft™ is indicated for the prevention of ocular itching in patients with allergic conjunctivitis and is to be used one drop in each eye once daily. Package insert states that Lastacaft™ was more effective than placebo at preventing ocular itching in patients with allergic conjunctivitis who were in a CAC study. The safety of Lastacaft™ has been evaluated in a randomized controlled trial with 909 patients over 6 weeks. No studies have been found comparing the efficacy of Lastacaft™ against current therapies. Lastacaft is currently not available on the market yet.

RECOMMENDATIONS

The College of Pharmacy recommends the addition of Bepreve™ 1.5% and Lastacaft™ to Tier 2 of the Ocular Allergy PBPA Category. Existing prior authorization criteria for this category will apply.

PRODUCT DETAILS OF BEPREVE™ (BEPOTASTINE BESILATE) OPHTHALMIC SOLUTION

FDA-APPROVED IN U.S. SEPTEMBER 8, 2009

INDICATIONS : Bepreve™ is indicated for the treatment of ocular itching associated with allergic conjunctivitis. It is a topically-active histamine H_1 receptor antagonist and also inhibits the release of histamine from mast cells.

DOSAGE FORMS : Bepreve™ is a 1.5% (15 mg/mL) topical ophthalmic solution that comes in dropper bottles of 2.5mL, 5mL, and 10mL.

ADMINISTRATION: Instill one drop of Bepreve™ into affected eye(s) twice a day for the relief of symptoms associated with allergic conjunctivitis.

CONTRAINDICATIONS: None known

SPECIAL POPULATIONS:

- Pregnancy category C – no adequate, well-controlled studies have been done in pregnant women. Bepreve™ should only be used during pregnancy if the potential benefit outweighs any potential risk. It is not known if Bepreve™ is excreted in human milk.
- Safety in pediatric patients under age 2 has not been established.
- No differences in safety or effectiveness have been observed in elderly patients.

WARNINGS & PRECAUTIONS:

- Care should be taken not to touch the eyelids or surrounding areas with the dropper tip.
- Bepreve™ should not be used to treat contact lens-related irritation. Contact lenses should be removed prior to instillation of Bepreve™ and may be reinserted after 10 minutes. The preservative in Bepreve™, benzalkonium chloride, may be absorbed by soft contact lenses.

ADVERSE REACTIONS:
Common (occurring in approximately 25% of patients): mild taste following instillation.
Less common (occurring in approximately 2-5% of patients): irritation, headache, and nasopharyngitis.

DRUG INTERACTIONS: None known

PATIENT INFORMATION: Patients should be advised that Bepreve™ is for topical ophthalmic use only. The dropper tip should not be touched to any surface as this may cause contamination. Contact lenses should be removed prior to instillation of Bepreve™ and can be reinserted after 10 minutes. Store at 15^{o} to 25^{o} C (59^{o} to 77^{o} F).

PRODUCT DETAILS OF LASTACAFT™ (ALCAFTADINE) OPHTHALMIC SOLUTION

FDA-APPROVED IN U.S. JULY 28, 2010

INDICATIONS : Lastacaft™ is indicated for the prevention of ocular itching associated with allergic conjunctivitis. It is a topically-active histamine H_1 receptor antagonist that also inhibits the release of histamine from mast cells.

DOSAGE FORMS : Lastacaft™ is a 0.25% (2.5 mg/mL) topical ophthalmic solution that comes as 3mL in a 5mL dropper bottle.

ADMINISTRATION : Instill one drop of Lastacaft™ in each eye once daily for the prevention of itching associated with allergic conjunctivitis.

CONTRAINDICATIONS: None known.

SPECIAL POPULATIONS:

- Pregnancy category B – no adequate, well-controlled studies have been done in pregnant women. Lastacaft™ should only be used during pregnancy if it is clearly needed. It is not known whether Lastacaft™ is excreted in human milk.
- Safety and efficacy in pediatric patients under age 2 has not been established.
- No differences in safety or efficacy have been observed in elderly patients.

WARNINGS & PRECAUTIONS:

- Care should be taken not to touch the eyelids or surrounding areas with the dropper tip.
- Lastacaft™ should not be used to treat contact lens-related irritation. Contact lenses should be removed prior to instillation of Lastacaft™ and may be reinserted after 10 minutes. The preservative in Lastacaft™ (benzalkonium chloride) may be absorbed by soft contact lenses.

ADVERSE REACTIONS:

- Most common ocular reactions (occurring in <4% of patients): eye irritation, burning and/or stinging upon instillation, eye redness, and eye pruritus.
- Most common non-ocular reactions (occurring in <3% of patients): nasopharyngitis, headache, and influenza.

DRUG INTERACTIONS: None known.

PATIENT INFORMATION: Patients should be advised that Lastacaft™ is for topical ophthalmic use only. The dropper tip should not be touched to any surface as this may cause contamination. Contact lenses should be removed prior to instillation of Lastacaft™ and can be reinserted after 10 minutes. Store at 15° to 25° C (59° to 77° F).

REFERENCES

Bepreve™ [Full Prescribing Information]. Irvine, CA: ISTA Pharmaceuticals, Inc., 2009

Lastacaft™ [Full Prescribing Information]. Jacksonville, FL: Vistakon Pharmaceuticals, LLC, 2010.

Appendix H

MERCK

URGENT: DRUG RECALL

PegIntron® (Peginterferon alfa-2b) Powder for Injection REDIPEN® Single-dose Delivery System
50 mcg per 0.5 mL, 80 mcg per 0.5 mL, 120 mcg per 0.5 mL and 150 mcg per 0.5 mL

September 29, 2010

Dear Health Care Provider:

This is to inform you that Schering Corporation, a subsidiary of Merck & Co., Inc., is conducting a voluntary recall, to the pharmacy/ retailer level, of all strengths of PegIntron® (Peginterferon alfa-2b) Powder for Injection REDIPEN® Single-dose Delivery System. Please see attached list of lot numbers involved in this recall.

This voluntary recall has been initiated as a precautionary measure due to the potential for a low frequency defect in the glass cartridge component of the REDIPEN product delivery system.

Defective REDIPEN glass cartridges have a potential risk of contamination since container seal integrity may, in certain circumstances, be compromised. As a result, in a very limited number of REDIPEN units, sterility cannot be assured. The overall potential for serious adverse events is considered to be remote, based on the low frequency of occurrence of the defect and the method of injection. This defect has not resulted in any known instances of sterility failure. However, as a result of this potential risk of contamination, as a precautionary measure, a voluntary recall to the pharmacy/retailer level is being implemented.

Distribution of these PegIntron REDIPENs has been suspended. Patients may continue to use REDIPENs currently in their possession. Although we have already begun resupplying certain strengths of PegIntron RediPens, there may be occasions over the next few weeks where a patient is not able to obtain a REDIPEN when they return to the pharmacy for a refill of their prescription. In these cases, we recommend that patients be switched to single-use vials of PegIntron, which are unaffected by this recall and available for use in current and new patients.

We have implemented a 100% visual examination of the glass cartridge components and are working expeditiously to resupply the REDIPENs. We expect ongoing resupply to continue through October. We expect all strengths, with the exception of 50mcg, to be available by the end of October. 50mcg resupply is targeted for the end of November.

If you have any questions concerning this issue, please contact the Merck National Service Center at 1-800-444-2080. You may also contact your Merck representative for resources regarding use of PegIntron in the vial presentation.

Merck is committed to patient safety and we are working as quickly as possible to resolve this issue and to ensure that a steady supply of PegIntron REDIPENs is available in the market.

Sincerely,

Elaine Perry, MD, MS
Office of the Chief Medical Officer

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Ongoing Safety Review of Actos (pioglitazone) and Potential Increased Risk of Bladder Cancer After Two Years Exposure

Safety Announcement

[09-17-2010] The U.S. Food and Drug Administration (FDA) is reviewing data from an ongoing, ten-year epidemiological study designed to evaluate whether Actos (pioglitazone), is associated with an increased risk of bladder cancer. Findings from studies in animals and humans suggest this is a potential safety risk that needs further study.

Actos is used along with diet and exercise to control blood sugar or improve control of blood sugar in adults with type 2 diabetes mellitus.

Bladder cancer is estimated to occur in 20 per 100,000 persons per year in the United States and is thought to be higher in diabetics.[1]

The drug manufacturer, Takeda, has conducted a planned analysis of the study data at the five-year mark, and submitted their results to FDA. Overall there was no statistically significant association between Actos exposure and bladder cancer risk. However, further analyses were also performed looking at how long patients were on Actos and the total amount of the drug they received during that time. An increased risk of bladder cancer was observed among patients with the longest exposure to Actos, as well as in those exposed to the highest cumulative dose of Actos.

At this time, FDA has not concluded that Actos increases the risk of bladder cancer. Its review is ongoing, and the Agency will update the public when it has additional information.

- Healthcare professionals should continue to follow the recommendations in the drug label when prescribing Actos.
- Patients should continue taking Actos unless told otherwise by their healthcare professional.
- Patients who are concerned about the possible risks associated with using Actos should talk to their healthcare professional.

This communication is in keeping with FDA's commitment to inform the public about its ongoing safety review of drugs.

Additional Information for Patients

- Do not stop taking your Actos unless told to do so by your healthcare professional.
- FDA has not concluded that Actos increases the risk of bladder cancer. The Agency is reviewing this safety concern and will update the public when additional information is available.
- Talk to your healthcare professional if you have concerns about Actos.
- Report any side effects from the use of Actos to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of th page.

Additional Information for Healthcare Professionals

- FDA has not concluded that Actos increases the risk of bladder cancer. The Agency is reviewing information related to the safety concern and will update the public when additional information is available.
- Follow the recommendations in the drug label when prescribing Actos.
- Report adverse events involving Actos to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of this page.

Data Summary

Actos was approved July 15, 1999 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Across the approved doses Actos reduced HbA1c compared to placebo by an average of 1.5%.

In preclinical carcinogenicity studies of pioglitazone, bladder tumors were observed in male rats receiving doses of pioglitazone that produced blood drug levels equivalent to those resulting from a clinical dose. Additionally, results from two, three-year controlled clinical studies of Actos (the PROactive study[2] and a liver safety study) demonstrated a higher percentage of bladder cancer cases in patients receiving Actos versus comparators. These findings are currently included in the *Precautions--Carcinogenesis, Mutagenesis, Impairment of Fertility* section of the Actos drug label.

To further address the long-term risk of bladder cancer associated with Actos use the drug manufacturer, Takeda, is conducting a ten-year, observational cohort study as well as a nested case-control study in patients with diabetes who are members of Kaiser Permanente Northern California (KPNC) health plan.[3] Patients selected in this study had diabetes mellitus and were $\geq$40 years of age at study entry. Patients with bladder cancer prior to study entry or within six months of joining KPNC were excluded from this study. The cohort included 193,099 patients with diabetes.

The primary outcome of the cohort study is an incident (new) diagnosis of bladder cancer identified from the KPNC cancer registry. The primary exposure of interest is treatment with Actos. Data on drug dose, duration of exposure and potential confounding factors are also obtained in the study

A planned five-year interim analysis was performed with data collected from January 1, 1997 through April 30, 2008. The median duration of therapy among Actos-treated patients was 2 years (range 0.2-8.5 years). The study investigators did not observe a statistically significant association between any Actos exposure and increased bladder cancer risk in the study (Hazard ratio = 1.2, 95% Confidence Interval: 0.9-1.5). However, the risk of bladder cancer increased with increasing dose and duration of Actos use, reaching statistical significance after 24 months of exposure.

FDA is reviewing the data from this observational cohort study and a case control study that is nested within it, and will update the public in several months when the review is complete or earlier should additional data become available.

References

1. Seer Stat Fact Sheets: Urinary Bladder. National Cancer Institute Web site. Bethesda, MD. http://seer.cancer.gov/statfacts/html/urinb.html[1]. Accessed September 16, 2010.
2. Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, et al. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlle trial. *Lancet*. 2005;366:1279-89.
3. Lewis JD, Ferrara A, Strom BL, Selby JV, Bilker W, Peng T, et al. The risk of bladder cancer among diabetic patients treated with pioglitazone: analysis through April 30, 2008. University of Pennsylvania and Kaiser Permanente Northern California Division of Research. Submitted to FDA, unpublished results.

Related Information

- FDA Drug Safety Podcast for Healthcare Professionals: Ongoing Safety Review of Actos (pioglitazone) and Potential Increased Risk of Bladder Cancer After Two Years Exposure[2]
- Actos (pioglitazone): Ongoing Safety Review - Potential Increased Risk of Bladder Cancer[3]
  MedWatch - 9/17/2010
- FDA reviewing preliminary safety information on Actos (pioglitazone)[4]
  FDA Note to Correspondents - 9/17/2010
- SEER Stat Fact Sheets: Urinary Bladder[5]
- Pioglitazone HCl (marketed as Actos, Actoplus Met, and Duetact) Information[6]

Contact Us

- **Report a Serious Problem**
- 1-800-332-1088
- 1-800-FDA-0178 Fax

MedWatch Online[7]

Regular Mail: Use postage-paid FDA Form 3500[8]

Mail to: MedWatch 5600 Fishers Lane

Rockville, MD 20857

Links on this page:

1. http://seer.cancer.gov/statfacts/html/urinb.html
2. http://www.fda.gov/Drugs/DrugSafety/DrugSafetyPodcasts/ucm226749.htm
3. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm226257.htm
4. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm226244.htm
5. http://seer.cancer.gov/statfacts/html/urinb.html
6. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109136.htm
7. http://www.fda.govhttps://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
8. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

News & Events

FDA NOTE TO CORRESPONDENTS

For Immediate Release: Sept. 24, 2010
Contact: Elaine Gansz Bobo, 301-796-7567, elaine.bobo@fda.hhs.gov

FDA approves combination contraceptive containing a folate

The U.S. Food and Drug Administration today approved Beyaz tablets, an estrogen/progestin combined oral contraceptive that also contains a folate (levomefolate calcium 0.451 mg).

Levomefolate calcium is a metabolite of folic acid, a water-soluble B-vitamin that helps produce and maintain new cells in the body. A known association of low folate levels and neural tube defects (e.g., spina bifida) has resulted in recommendations that women of childbearing age supplement their diet with folate.

Beyaz is based on the approved product YAZ, which contains the same doses of estrogen and progestin, and is approved for:

- Prevention of pregnancy
- Treatment of symptoms of premenstrual dysphoric disorder (PMDD) in women who choose to use an oral contraceptive for contraception and
- Treatment of moderate acne vulgaris in women at least 14 years of age, only if the patient desires an oral contraceptive for birth control.

In addition to the approved YAZ indications, Beyaz also is approved for the secondary indication in women who choose to use an oral contraceptive as their method of contraception, to raise folate levels for the purpose of reducing the risk of a neural tube defect in a pregnancy conceived while taking the product or shortly after discontinuing the product.

The primary efficacy study for Beyaz was a multicenter, double-blind, randomized, controlled U.S. trial in 379 healthy women age 18 to 40 who were treated with Beyaz or YAZ alone for up to 24 weeks. Beyaz was found to increase folate levels in women. In a German study of Beyaz, folate levels remained elevated for several weeks following discontinuation of Beyaz. Safety and efficacy data for contraception, PMDD, and acne indications were obtained from previous YAZ clinical trials.

The most common side effects reported by users of combined oral contraceptives are irregular uterine bleeding, nausea, breast tenderness, and headaches. Other serious side effects include vascular events (blood clots) and liver disease. Women over age 35 who smoke should not use this product as cigarette smoking increases further the risk of serious cardiovascular events. The common adverse events for Beyaz are expected to be th same as those for YAZ. There were no findings from the clinical trials with Beyaz to suggest a change in the overall safety profile compared to that of YAZ.

Beyaz is manufactured by Bayer HealthCare Pharmaceuticals Inc., the U.S.-based business arm of Bayer HealthCare LLC, a subsidiary of Bayer AG.

Approved Drugs: Questions and Answers[1]

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Links on this page:

1. http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm054420.htm

U.S. Food and Drug Administration

Safety

Avandia (rosiglitazone): REMS - Risk of Cardiovascular Events

[Posted 09/23/2010]

AUDIENCE: Endocrinology, Cardiology

ISSUE: FDA notified healthcare professionals and patients that it will significantly restrict the use of the diabetes drug Avandia (rosiglitazone) to patients with Type 2 diabetes who cannot control their diabetes on other medications. These new restrictions are in response to data that suggest an elevated risk of cardiovascular events, such as heart attack and stroke, in patients treated with Avandia.

BACKGROUND: Avandia is in a class of drugs known as thiazolidinediones, or TZDs. It is intended to be used in conjunction with diet and exercise to improve glucose (blood sugar) control in patients with Type 2 diabetes mellitus. Rosiglitazone also is available in combination with other diabetes medications, metformin under the brand name Avandamet or glimepiride under the brand name Avandaryl.

RECOMMENDATION: FDA will require that GSK develop a restricted access program for Avandia under a risk evaluation and mitigation strategy, or REMS. Under the REMS, Avandia will be available to new patients only if they are unable to achieve glucose control on other medications and are unable to take Actos (pioglitazone), the only other drug in this class. Current users of Avandia who are benefiting from the drug will be able to continu using the medication if they choose to do so.

Doctors will have to attest to and document their patients' eligibility; patients will have to review statements describing the cardiovascular safety concerns associated with this drug and acknowledge they understand the risks. The agency anticipates that the REMS will limit use of Avandia significantly.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm[1]
- Download form[2] or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[09/23/2010 - News Release[3] - FDA]
[09/23/2010 - Q&As[4] - FDA]
[09/23/2010 - Avandia Related Information[5] - FDA]

Links on this page:

1. http://www.fda.gov/MedWatch/report.htm
2. http://www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm
3. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm226975.htm
4. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm226976.htm
5. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm226956.htm

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: Sept. 14, 2010
Media Inquiries: Karen Riley, 301-796-4674, karen.riley@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new drug for gout

The U.S. Food and Drug Administration today approved Krystexxa (pegloticase) to treat the painful condition known as gout in adults who do not respond to or who cannot tolerate conventional therapy.

Gout occurs due to an excess of the bodily waste uric acid, which is eventually deposited as needle-like crystals in the joints or in soft tissue. These crystals can cause intermittent swelling, redness, heat, pain and stiffness in the joints.

Gout is strongly associated with obesity, high blood pressure, high cholesterol and diabetes, and occurs more often in men, in women after menopause, and in people with kidney disease.

"About 3 percent of the three million adults who suffer from gout are not helped by conventional therapy. This new drug offers an important new option for them," said Badrul Chowdhury, M.D., director of the Division of Pulmonary, Allergy, and Rheumatology Products in the FDA's Center for Drug Evaluation and Research.

For patients with gout, the conventional therapy is to receive drugs that lower the amount of uric acid in the blood, as, for example, the xanthine oxidase inhibitors Zyloprim (allopurinol) and Uloric (febuxostat). Krystexxa is an enzyme that lowers uric acid levels by metabolizing it into a harmless chemical that is excreted in the urine. The drug is administered to patients every two weeks as an intravenous infusion.

Two six-month clinical trials of 212 total patients demonstrated that the drug lowered uric acid levels and reduced deposits of uric acid crystals in joint and soft tissue.

Since one out of every four patients in the clinical trials experienced a severe allergic reaction when receiving an infusion of Krystexxa, health care providers should dispense a corticosteroid and an antihistamine to their patients beforehand to minimize the risk of such a reaction. Other reactions during the clinical trials included gout flare, nausea, injection site bruising, irritation of the nasal passages, constipation, chest pain and vomiting.

Physicians are also being warned to be cautious about administering Krystexxa to patients with congestive heart failure because the drug was not studied in this patient population.

Krystexxa is being approved with a Risk Evaluation and Mitigation Strategy that includes a medication guide for patients and materials for healthcare providers to communicate the risk of severe infusion and allergic reactions.

Krystexxa is manufactured by Savient Pharmaceuticals Inc. of East Brunswick, N.J.

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RSS Feed for FDA News Releases[1] [what is RSS?[2]]

Links on this page:

1. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml
2. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: New dosing recommendations to prevent potential Valcyte (valganciclovir) overdose in pediatric transplant patients

Safety Announcement

[09-15-2010] The U.S. Food and Drug Administration (FDA) is notifying healthcare professionals of new pediatric dosing recommendations for Valcyt (valganciclovir hydrochloride) oral tablets and oral solution. This change is being made to prevent potential valganciclovir overdosing in children with low body weight, low body surface area, and below normal serum creatinine.

The revised dosing recommendations are being updated to include an upper limit on the calculated creatinine clearance using the modified Schwartz formula, which is used to calculate the pediatric dose of Valcyte.

Valganciclovir is an antiviral medication that can be effective for the prevention of cytomegalovirus (CMV) disease in children 4 months to 16 years of age who have undergone a kidney or heart transplant. Cytomegalovirus is a member of a group of herpes-type viruses that can cause disease in different parts of the body.[1] Patients with weakened immune systems, such as organ transplant patients, are particularly susceptible to CMV infection and must take medications such as Valcyte to prevent the disease.

See the Data Summary for the new dosing recommendations for Valcyte.

Additional Information for Patients

- Talk to your healthcare professional about any concerns with your Valcyte dose.
- The side effects from Valcyte overdosing include abdominal pain, vomiting, diarrhea, tremor or seizure.
- Report any side effects you experience to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page

Additional Information for Healthcare Professionals

- The dosing recommendations for Valcyte in children have changed. The dosing calculation can be found in the Data Summary and in the drug label[1].
- Be aware of possible valganciclovir overdose in pediatric patients with low body weight, low body surface area, or below normal serum creatinine.
- When calculating the pediatric dose of Valcyte with the modified Schwartz formula, a maximum value of 150 mL/min/1.73 m^2 should be used in the formula.
- When the calculated pediatric dose of Valcyte exceeds 900 mg, a dose of 900 mg should be administered to the child.
- Advise patients to contact a healthcare professional immediately if they experience signs and symptoms of valganciclovir overdose while taking Valcyte.
- Report adverse events involving Valcyte to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page

Data Summary

Healthcare professionals should follow the updated pediatric dosing algorithm in the Valcyte label[2].[2] The pediatric dose of Valcyte is based on body surface area (BSA) and creatinine clearance (CrCl) derived from a modified Schwartz formula. Under the previous dosing recommendations, pediatric patients with low body weight, low body surface area, and below normal serum creatinine could have a high calculated Schwartz creatinine clearance, resulting in a pediatric dose that approached the adult dose of 900 mg. This type of patient was not routinely observed in the clinical trials used to derive and confirm the pediatric dose, and may have been overdosed according to the previous dosing algorithm. As a result, FDA has updated the dosing algorithm so that when calculating the pediatric dose, a maximum value of 150 mL/min/1.73 m^2 should be used in the formula, even if the calculated Schwartz creatinine clearance exceeds 150 mL/min/1.73 m^2. Furthermore, if the calculated Valcyte dose exceeds 900 mg, a dose of 900 mg should be given to the child.

The revised language in Section 2.3 of the label, *Pediatric Patients*, is as follows (new language underlined)[2]:

Prevention of CMV Disease: For pediatric patients 4 months to 16 years of age who have received a kidney or heart transplant, the recommended once daily dose of Valcyte starting within 10 days of transplantation until 100 days post-transplantation is based on body surface area (BSA) and creatinine clearance (CrCl) derived from a modified Schwartz formula, and is calculated using the equation below:

Pediatric Dose (mg) = 7 x BSA x CrCl (calculated using a modified Schwartz formula). If the calculated Schwartz creatinine clearance exceeds 150 mL/min/1.73 m^2, then a maximum value of 150 mL/min/1.73m^2 should be used in the equation.

$$\text{Mosteller BSA } (m^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

$$\text{Schwartz Creatinine Clearance } (\text{mL/min/1.73 } m^2) = \frac{k \times \text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}}$$

Where k =

0.45 for patients aged 4 months to < 1 year,

0.45 for patients aged 1 to < 2 years (note k value is 0.45 instead of the typical value of 0.55),

0.55 for boys aged 2 to < 13 years and girls aged 2 to 16 years, and

0.7 for boys aged 13 to 16 years.

In summary, the FDA has determined that adding an upper limit of 150 mL/min/1.73 m^2 to the creatinine clearance calculated using the Schwartz formula for the determination of pediatric doses can help prevent the potential for Valcyte overdosing. If the calculated pediatric dose of Valcyte exceeds 900 mg, a dose of 900 mg should be given to the child.

References

1. MedLinePlus health topics page. U.S. National Library of Medicine Web site. http://www.nlm.nih.gov/medlineplus/ency/article/000663.htm[3]. Accessed August 25, 2010.
2. Updated Valcyte label[4]

Related Information

- Valcyte Label - 8/05/2010 [5]
- FDA issues new dosing guide for children using Valcyte[6]
  9/15/2010 - FDA Note To Correspondents
- Valganciclovir (marketed as Valcyte) Information[7]

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9. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Drugs

FDA Statement on ASBMR report: Possible Increased Risk of Certain Types of Thigh Bone Fractures with Long-Term Bisphosphonates Use

[9/14/2010] FDA appreciates the report from the American Society of Bone and Mineral Research's (ASBMR's) expert Task Force, released today, providing important perspectives on the potential association between long term treatment with the class of osteoporosis drugs known as bisphosphonates and a rare but serious type of fracture of the thigh bone (femur). The report includes a case definition that describes the atypical features of these unusual femur fractures. FDA believes this case definition will help greatly in identifying cases and reporting on them, and should facilitate future studies comparing the frequency of these unusual fractures both in patients treated with bisphosphonates and those who have not received bisphosphonates.

Bisphosphonates have long been effective in reducing common bone fractures in individuals with osteoporosis. Although it is not clear if bisphosphonates are the cause, these unusual femur fractures have been identified in patients taking these drugs. FDA recommends that healthcare professionals be aware of the possible risk of unusual femur fractures in patients taking bisphosphonates. Patients should talk to their healthcare professional if they develop new thigh or groin pain so that they may be evaluated to rule out a femur fracture. Patients should not stop taking their medication unless told to do so by their healthcare professional. Patients and healthcare professionals should report any side effects with the use of bisphosphonates to FDA's MedWatch program.

The optimal duration of bisphosphonate treatment for osteoporosis is unknown. Clinical trial data for bisphosphonates approved for the prevention and/or treatment of osteoporosis support effectiveness for the reduction of common bone fractures for three to five years.

Since the initial report of unusual fractures with bisphosphonates was published, FDA has been diligently monitoring this issue. We have been reviewing all the scientific data available regarding their safety and effectiveness when used for more than three to five years for the treatment and prevention of osteoporosis. We have talked with patient groups and have requested clinical trial data from the manufacturers of bisphosphonate products as part of this ongoing safety review.

The ASBMR Task Force's recommendations include recommended changes to product labels alerting healthcare professionals and patients to the possibility of unusual femur fractures with long-term use of bisphosphonates. FDA has assembled and is thoroughly reviewing all long term data available on the products, as well as all safety reports, and is considering label revisions. FDA will keep the public informed of additional findings and actions on this issue.

Related Information

- Bisphosphonates (marketed as Actonel, Actonel+Ca, Aredia, Boniva, Didronel, Fosamax, Fosamax+D, Reclast, Skelid, and Zometa) Information[1]

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