



Agenda

State and Public School Life and Health Insurance Board

Drug Utilization and Evaluation Committee

EBD Board Room – 501 Building, Suite 500

11/04/2013

1:00 p.m.

Call to Order	Kat Neill, Chair
Approval of August 05th Minutes	Kat Neill, Chair

Statin Reference Price Review	David Keisner, UAMS
Niaspan 2nd Review	Jill Johnson, UAMS
Acthar Gel 2nd Review	Jill Johnson, UAMS
Bisphosphonate Review	Jill Johnson, UAMS
Fibric Acid Review	Jill Johnson, UAMS
Anticoagulant Review	Jill Johnson, UAMS

Chemotherapy Sub-Committee Consideration	David Keisner, UAMS
Principles for Drug Placement	Jill Johnson, UAMS
Specialty Tier Drug Placement	David Keisner, UAMS
New Drugs	Jill Johnson, UAMS
MS Coverage Review	Jill Johnson, UAMS



Agenda

Director's Report

Bob Alexander, EBD Executive Director

Upcoming Meetings

February 7, 2014

**State and Public School Life and Health Insurance
Board Clinical and Fiscal Drug Utilization and
Evaluation Committee
Minutes
August 5, 2013**

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, August 5, 2013 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Suite 500, Little Rock, AR.

Members present:

Matthew Hadley
Kat Neill
Dr. William Golden
Larry Dickerson
Scott Pace
Dr. Hank Simmons
Connie Bennett
John Kirtley
Dr. Joe Stallings – Teleconference

Members absent:

Mark McGrew

Doug Shackelford, Interim Executive Director, Employee Benefits Division

OTHERS PRESENT

Jill Johnson, Dwight Davis, David Keisner, UAMS College of Pharmacy/EBRx; Connie Bennett, Informed Rx; John Kirtley, State Board of Pharmacy; Doug Shackelford; Michelle Hazelett, Stella Greene, Tracy Butler-Oberste, Leslie Smith, Lori Eden, Janna Keathley, EBD

CALL TO ORDER

Meeting was called to order by Dr. Kat Neill, Chair.

APPROVAL OF MINUTES

The motion was made by Dr. Neill to approve the April 8, 2013 minutes. Dr. Simmons made the motion to approve. Dr. Hadley seconded. All were in favor. Minutes were approved.

CONTRACEPTIVES, MEDICAL FOODS, SECOND REVIEW, & NEW DRUGS by
Jill Johnson, UAMS

Johnson reported and the Committee reviewed Zytiga, Contraceptives, Medical Foods, Second Review, & New Drugs. The following are the recommendations:

REVIEW OF DRUGS:

1. **Tecfidera** – Treatment of patients with multiple sclerosis.

Recommendation: T3 with a PA

Dr. Hadley motioned to approve with PA. Simmons seconded. All were in favor.

2. **Zytiga** – Treatment of patients with metastatic castrate resistant prostate cancer.

Recommendation: T3 with a PA

Dr. Hadley motioned to approve with a PA. Dickerson seconded. All were in favor.

CONTRACEPTIVES:

1. **LoLoestrin, Loestrin, & Ortho Tri Cyclen Lo** – Oral Contraceptives

Recommendation: Move to Tier & the remaining generics will be \$0.00 co-pay for 55 years of age or less.

Pace has concerns that if we are encouraging members to switch oral contraceptives that we have additional communication to take appropriate caution to avoid accruing extra beneficiaries on major medical. The additional information will be included in the EBD Buzz.

Dr. Hadley motioned to approve. Pace seconded. All were in favor.

MEDICAL FOOD:

1. **Deplin** – Medical Food -

Recommendation: Exclude due to lack of regulated data

2. **Foltx** – Medical Food - .

Recommendation: Exclude due to lack of regulated data

3. **Metanx** – Medical Food -

Recommendation: Exclude due to lack of regulated data

Dr. Neill inquired is there a requirement to cover medical foods.

Keisner reported they are tier 2 and they are not reported as essential. These are new formulations and can be considered as new drugs. These are reported as the three most utilized medical foods. But we cover many other medical foods.

Kirtley reported there should be a medical food discussion at the Board level.

Pace suggested we communicate with the members OTC vitamins that are available.

Dr. Neill motioned to exclude these medical foods and make a recommendation to the Board for the remaining medical foods. Dr. Hadley seconded. All were in favor.

REFERENCE PRICING:

1. **Amphetamines** – Treatment of ADHD

Recommendation: Continue to cover due to the change did not occur May 20, 2013. Reference price long acting for over the age of 26; effective January 1, 2014.

2. **Antidepressants** – Treatment of Depression

Recommendation: Move Venafaxin capsule into Tier 1 price structure and reference price SSRI's & SNRI's effective January 1, 2014.

Dr. Neill motioned to approve. Dr. Hadley seconded. All were in favor.

3. **ARB's** – Treatment of patients with High Blood Pressure

Recommendation: Reference price and reevaluate the reference price frequently.

Dr. Simmons motioned to approve. Dr. Neill seconded. All were in favor.

SECOND REVIEW OF MEDICATIONS:

1. **Lyrica** – Treatment of patients with Neuropathic Pain

Recommendation: Option 1; Exclude; Option 2 Reference price to Gabapentin.

Keinser reported there are 820 members taking Lyrica.

Pace motioned to approve option 2. Dr. Neill seconded. All were in favor.

NEW MEDICATIONS:

1. **Signifor** – Treatment of patients with Cushing's disease.

Recommendation: Exclude

Dickerson motioned to exclude. Dr. Hadley seconded. All were in favor.

2. **Suclear** – Treatment of patients with bowel syndrome

Recommendation: Exclude Suclear & Prepopik

Dickerson motioned to exclude. Dr. Hadley seconded. All were in favor.

3. **Invokana** – Treatment of patients with type 2 Diabetes.

Recommendation: Exclude

Dr. Hadley motioned to exclude. Dickerson seconded. All were in favor.

4. **TOBI Podhalr** – Treatment of patients with cystic fibrosis
Recommendation: Exclude
Dr. Golden motioned to exclude. Dr. Neill seconded. All were in favor.

5. **Cystaran** – Treatment of patients with cystinosis
Recommendation: Cover Tier 3 with PA
Dr. Hadley motioned to approve. Dickerson seconded. All were in favor.

6. **Cerefolin**– Medical Food
Recommendation: Exclude
Dr. Hadley motioned to exclude. Pace seconded. All were in favor.

7. **Osphena** – Treatment of patients with moderate to severe dyspareunia
Recommendation: Exclude
Dr. Neill motioned to exclude. Dickerson seconded. All were in favor.

8. **Simbrinza** – Treatment of patients with Glaucoma & Ocular Hypertension
Recommendation: Cover Tier 2
Dr. Hadley motioned to approve. Pace seconded. All were in favor.

9. **Sirturo** – Treatment of patients with Tuberculosis
Recommendation: Cover on Tier 3 with PA
Dr. Neill motioned to exclude. Dr. Hadley seconded. All were in favor.

10. **Diclegis** – Treatment of patients with pregnancy Nausea
Recommendation: Exclude
Dr. Golden motioned to exclude. Dr. Hadley seconded. All were in favor.

11. **Liptruzet**- Treatment of patients with hypercholesterolemia/hyperlipoproteinemia

Recommendation: Exclude Liptruzet & Zetia with Communication to the members a 90 day notice. There are 120 members.

Dr. Hadley motioned to exclude. Dickerson seconded. All were in favor.

12. **Procybi** – Treatment of patients with cystinosis

Recommendation: Exclude

Dr. Neill motioned to exclude. Dr. Hadley seconded. All were in favor.

13. **Minastrin** – Oral Contraceptive

Recommendation: Exclude

Dr. Neill motioned to exclude. Dr. Hadley Seconded. All were in favor.

14. **Quartette** – Oral Contraceptive

Recommendation: Exclude

Dr. Neill motioned to exclude. Dickerson Seconded. All were in favor.

15. **Mekinist** – Treatment of patients with unresectable or metastatic melanoma

Recommendation: Approved with specialty Tier PA with criteria

Dr. Hadley motioned to approve with criteria. Pace seconded. All were in favor.

16. **Tafinlar** – Treatment of patients with unresectable or metastatic melanoma

Recommendation: Exclude & review in six (6) months.

Dr. Hadley motioned to exclude. Dickerson seconded. All were in favor

17. **Belviq** – Treatment of Anti-obesity

Recommendation: Exclude

Pace motioned to approve. Dr. Simmons seconded. All were in favor.

18. **Breo Ellipta** – Treatment of patients with bronchitis, COPC, emphysema

Recommendation: Exclude

Dr. Neill motioned to exclude. Dr. Hadley seconded. All were in favor.

19. **LidoRx** – Topical Anesthesia

Recommendation: Exclude

Dr. Hadley motioned to exclude. Dickerson seconded. All were in favor.

20. **Prolensa/Bromfenac** – Treatment of patients with ocular pain/inflammation

Recommendation: Exclude

Dr. Neill motioned to exclude. Dr. Hadley seconded. All were in favor.

21. **Prezista** – Treatment of Patients with HIV

Recommendation: Cover Tier 2 with PA & age limit seven (7)

Dr. Hadley motioned to approve. Pace seconded. All were in favor.

22. **Namenda** – Treatment of Patients with Alzheimer's

Recommendation: Cover with T3 with a PA criteria for new users

Dr. Stallings motioned to approve with Criteria. Dr. Hadley seconded. All were in favor.

23. **Afinitor** – Treatment of children with rare brain tumors

Recommendation: Table due to additional research on brain tumors

24. **Suprax** – Treatment of patients with STD

Recommendation: Cover with Tier 2 Qty limit 1 pill

Dr. Hadley motioned to approve with Criteria. Pace Seconded. All were in favor.

25. **Suprax Suspension** – Third generation antibiotic

Recommendation: Exclude

Dickerson motioned to exclude. Dr. Neill seconded. All were in favor.

26. **Zenzedi 2.5 mg/7.5 mg** – Treatment of patients with ADHD

Recommendation: Exclude

Dr. Neill motioned to exclude. Dr. Simmons seconded. All were in favor.

27. **Flumist** – Flu Vaccine

Recommendation: Cover free to be administered not for take home

Pace motioned to approve. Dr. Neill seconded. All were in favor.

28. **Fluzone** – Flu Vaccine

Recommendation: Cover free to be administered not for take home

Pace motioned to approve. Dr. Neill seconded. All were in favor.

29. **Flu Shot Kit/Flu shot Kit PF** – For treatment of Influenza

Recommendation: Exclude

Dr. Simmons motioned to exclude. Dr. Hadley seconded. All were in favor.

30. Topicort Spray – Generic Cream

Recommendation: Exclude

Pace motioned to exclude. Dr. Hadley seconded. All were in favor.

31. Nymalize Solution – Treatment of post stroke

Recommendation: Exclude

Dr. Hadley motioned to exclude. Dr. Simmons seconded. All were in favor.

PLAN PERFORMANCE SUMMARY 2004 – July, 2013 *by Dwight Davis, UAMS*

Davis reports on the prescription Drug Program Trend Analysis for CY 2004 – July, 2013. Davis reports the three (3) primary components of per member per month is; average claim cost, average co-payment, & utilization rate. There has been an increase in the trend. Generic's has increased from 46% in 2004 up to 84% in 2013. Generic drugs are 84% of prescriptions filled.

Specialty drugs have almost doubled in cost since 2004. The total percent the plan paid in 2004 was 8.6%; in 2013 17.4%.

Kirtley reports looking at brand generics to ensure they should be only \$10.00 co-pay.

DIRECTOR'S REPORT *by Doug Shackelford, Interim Executive Director*

Shackelford reports the Committee is in the process of selecting a new Executive Director. A decision should be made before the next DUEC Meeting November 4, 2013.

Meeting adjourned

STATIN CONVERSION CHART

% LDL Reduction	Simvastatin (Zocor)	Atorvastatin (Lipitor)	Rosuvastatin (Crestor)	Fluvastatin (Lescol)	Lovastatin (Mevacor)	Pravastatin (Pravachol)	Ezetimibe/Simvastatin (Vytorin)
<24%	5 mg	-	-	20 mg	10 mg	10 mg	-
25-32%	10 mg	-	-	40 mg	20 mg	20 mg	-
31-39%	20 mg	10 mg	-	80 mg	40 mg	40 mg	-
37-45%	40 mg	20 mg	5 mg	-	80 mg	80 mg	10/10
48-52%	80 mg	40 mg	10 mg	-	-	-	10/20
55-60%	-	80 mg	20 mg	-	-	-	10/40
60-63%	-	-	40 mg	-	-	-	10/80

proposed coverage of statins

	Tier 1	Tier 2		
Antihyperlipidemic-HMG (Statins)	atorvastatin, lovastatin, pravastatin, simvastatin	Crestor 40mg*(PA)		
	<p>*(RP) Reference Priced Antihyperlipidemic-HMG (Statins): Plan pays \$0.30 per unit. Member is responsible for remaining cost.</p> <p>Crestor 5mg, Crestor 10mg, Crestor 20mg</p>			

Current Coverage of Statins

	Tier 1	Tier 2	Tier 3	
Antihyperlipidemic-HMG (Statins)	atorvastatin 40mg*(PA), atorvastatin 80mg*(PA), lovastatin, pravastatin, simvastatin	Crestor 10mg*(PA), Crestor 20mg*(PA), Crestor 40mg*(PA)	Lipitor 40mg*(PA), Lipitor 80mg*(PA)	
	*(RP) Reference Priced Antihyperlipidemic-HMG (Statins): Plan pays \$0.30 per unit. Member is responsible for remaining cost.		Altoprev, atorvastatin 10mg, atorvastatin 20mg, Crestor 5mg, Lescol, Lescol XL, Lipitor 10mg, Lipitor 20mg, Mevacor, Pravachol, Zocor	

Niacin: A Review of the Evidence--DUEC

November 4, 2013

Jordan Brazeal, Pharm.D./Jill Johnson, Pharm.D.

Drug Name	Members	# Claims	Avg Net Plan Cost/Rx	Net Plan Cost
Niacin IR (50, 100, 500mg)	14	23	\$0.30	\$7
Niaspan (500, 750, 1000 mg)	429	890	\$179.37	\$159,636
Simcor (500-20, 500-40 mg)	1	3	\$31.77	\$95
Niacin ER (500 mg)	13	22	\$1.74	\$38
<i>Totals/quarter</i>	<i>457</i>	<i>938</i>		<i>\$159,776</i> <i>\$639,104 annualized</i>

Niacin ER is not interchangeable or AB-rated to Niaspan. A new authorized generic Niaspan hit the market 9/20/13 with exclusivity and therefore similar cost to brand for at least 6 months.

The above data are from the 3Q13 report.

- Extended-release (ER) niacin (Niaspan) and combination preparations (Advicor, Simcor) are only available by prescription. Immediate-release (IR) niacin preparations are available over-the-counter at much lower prices. Niacin, especially IR formulations, is well-known for causing hot flushes and GI upset. Generally, patients are advised to drink a glass of cold water and take an aspirin or ibuprofen prior to taking niacin. Niaspan and other ER formulations are touted to cause less flushing and stomach upset.
- Niacin is FDA-approved for use as monotherapy or in combination with other lipid-lowering agents to treat hyperlipidemia. Its exact mechanism of action is unknown; however, it lowers VLDL-C, LDL-C, and triglycerides, while simultaneously raising HDL-C. Previous studies with niacin monotherapy demonstrated significant reductions in clinical events and stabilization of atherosclerosis.^{2,6} These studies occurred, however, before the advent of the statins. Subsequent studies have evaluated the efficacy of niacin plus statin therapy;^{3,4} there are no head-to-head trials comparing niacin to a statin.
- Several studies have shown immediate-release niacin's efficacy as monotherapy in meeting surrogate endpoints, such as lowering triglycerides and raising HDL-C^{2,5-6}. However, recent large-scale trials demonstrate ER niacin's lack of efficacy, when combined with a statin, in achieving clinical outcomes¹. Moreover, as yet unpublished data from the HPS2-THRIVE study, a large trial involving over 25,000 patients, indicate an alarming adverse effect profile of niacin, including new-onset diabetes (NNH=56), diabetic complications (NNH=28), infections (NNH=72), and excessive bleeding (NNH=167). Additionally, niacin use, both IR and ER, has a high dropout rate due to untoward side effects like flushing and gastrointestinal problems.⁷

CONCLUSION: Niacin's place in antihyperlipidemic therapy is questionable.

RECOMMENDATION:

Option 1. Exclude niacin from coverage. Immediate release niacin is available OTC along with aspirin or ibuprofen to help with the flushing. Send letters to physicians and members who are currently on the excluded product.

REFERENCES.

1. Boden, W et al. Niacin in Patients with Low HDL Cholesterol Levels Receiving Intensive Statin Therapy. NEJM. 2011; 365;24:2255-67.
2. Canner PL, Berge KG, Wenger, NK et al. Fifteen year mortality in Coronary Drug Project patients: long-term benefit with niacin. J Am Coll Cardiol 1986;8:1245-55
3. Lavigne, P and R Karas, The Current State of Niacin in Cardiovascular Disease Prevention, A Systematic Review and Meta-Regression. J Am Coll Cardiol 61;4:440-6
4. Michos, ED et al. Niacin and Statin Combination Therapy for Atherosclerosis Regression and Prevention of Cardiovascular Disease. J Am Coll Cardiol 59;23:2058-64
5. Taylor, A et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. N Engl J Med 2009 361;22:2113-22
6. The Coronary Drug Project Research Group. Clofibrate and niacin in coronary heart disease. JAMA 1975;231:360-81
7. <http://www.cardiosource.org/News-Media/Media-Center/News-Releases/2013/03/HPS2-THRIVE.aspx>

Adrenocorticotrophic Hormone, ACTH (Acthar HP)
Pharmacologic Category: Systemic Corticosteroid
DUEC Discussion, Jill Johnson, Pharm.D., BCPS
November 4, 2013

Background: H.P. Acthar Gel Repository Injection is a 39 amino acid peptide natural form of adrenocorticotrophic hormone (ACTH) that works by stimulating the adrenal cortex to secrete cortisol, corticosterone, and aldosterone. Corticotropin-releasing hormone (CRH) in the hypothalamus stimulates the release of ACTH from the anterior pituitary. High levels of cortisol inhibit release of ACTH. The FDA labeled H.P. Acthar Gel to be used for diagnostic testing of adrenal function and the package insert lists other diseases it may be used in but stresses that patients should preferably be treated with corticosteroids. Cosyntropin (Cortrosyn®) is a synthetic form of ACTH using the first 24 amino acids from the 39 amino acid peptide. A dose of cosyntropin 0.25mg is similar to a dose of 25 units of ACTH peptide and stimulates the adrenals. Cortrosyn brand can be given IM or IV; cosyntropin solution should be given only IV. H.P. Acthar Gel must be given IM or SQ. On August 27, 2007, the AWP of H. P. Acthar Gel Repository Injection increased from \$2062.79 per vial to \$23,000 per vial “in order to fund projects that could contribute to the manufacturer’s growth”.

Current utilization (April 1, 2013 through Aug 31, 2013):

	Utilizing members	#Rxs	Ing cost	Net Plan Cost	Avg Net Plan Cost/Rx	Cost/unit	Cost/day
Acthar HP inj 80 unit	1	4	\$181082	\$180972	\$45,242.86	\$6032.38	1615.82

Indications w/ doses:

- Acute exacerbation of multiple sclerosis (MS): I.M., SUBQ: 80-120 units/day for 2-3 weeks.
- Infantile spasms: children <2 years: IM: 75 units/m²/dose twice daily for 2 weeks; followed by a gradual taper over a 2-week period.
- All other indications: IM, SubQ: 40-80 units every 24-72 hours:
 - Adjunctive therapy for exacerbations/acute episodes of rheumatic disorders (psoriatic arthritis, RA, JIA, AS);
 - Exacerbations or maintenance therapy for collagen diseases (SLE, systemic dermatomyositis);
 - Severe erythema multiforme;
 - Stevens-Johnson syndrome;
 - Serum sickness;
 - Severe acute/chronic allergic and inflammatory ophthalmic disease (keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation);
 - Symptomatic sarcoidosis;
 - To induce diuresis for remission of proteinuria in nephrotic syndrome w/o idiopathic uremia or due to SLE.

Currently we cover ACTH for:

1. Acute exacerbation of MS after we ascertain they have IV access and IV corticosteroids can be administered. We cover up to **120 units/day for up to 21 days. Each 5ml vial of Acthar Gel contains 400 units. This is 7 vials per 21 day treatment**
2. Infantile spasms. We cover up to 40 units/day, or 150 units/m²/day* for up to 12 weeks. Each 5ml vial of Acthar Gel contains 400 units. Approve 3 vials per 28 days to provide 40 units per day OR Approve MAX of 9 vials per 28 days. *(9 vials per 28 days supply based on estimate of 0.82m² body surface area for a 20 kg 6 y.o.)

We deny coverage for:

1. Diagnostic purposes and recommend cosyntropin (Cortrosyn®) use instead.

Issue: The drug's price (AWP) now (9/13/13) is \$36144.00 for 80 units/mL (5mL vial). The drug works by increasing cortisol from the adrenal glands, providing the same effect as administering exogenous corticosteroids.

Current state of the literature:

1. Thompson AJ, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology*. 1989;39:969-971.

N=61 MS pts (51 w/ RRMS, 10 w/ progressive), mean age=35, mean duration of MS relapse 15 d, mean disability on entry of 4.6 on Kurtzke disability status scale. Randomly assigned to IV methylprednisolone 1g qd X 3d or IM ACTH over 14 days: 80 units X 7d, 40 units X 4d, and 20 units X3d. Matched dummies. Disability was measured at days 3, 7, 14, 28, and 3m. Both groups had a clear improvement with no significant difference between the 2 groups in either rate of recovery or final outcome at 3m. Conclusion: giving a 3d course of IV treatment rather than 14 days of IM injections is more appealing logistically and fiscally.

2. Filippini G, Brusaferrri F, Sibley WA, Citterio A, Ciucci G, Midgard R, Candelise L. Corticosteroids or ACTH for acute exacerbations in MS. *Cochrane Database of Systematic Reviews* 2000, Issue 4, Issue 4. Art. No.: CD001331. DOI: 10.1002/1461858.CD001331.

From this Systematic Review: ACTH or IV methylprednisolone appears better than placebo for treating acute exacerbation symptoms. Data are insufficient for either preventing new exacerbations or for reducing long term disability. The best available evidence suggests a short term high dose IV methylprednisolone may provide benefit w/o relevant adverse effects. There is insufficient evidence to establish the net benefit of repeated courses for recurrent exacerbations. Oral methylprednisolone may be associated with frequent adverse effects (GI and psychic disorders) and is not recommended.

3. BURTON JM, O'CONNOR PW, HOHOL M, BEYENE J. Oral versus intravenous steroids for treatment of relapses in multiple sclerosis. *Cochrane Database of Systematic Reviews* 2012, Issue 12. Art. No.: CD006921. DOI: 10.1002/14651858.CD006921.pub3.

With this current update, a total of five eligible studies (215 patients) were identified. Only one outcome, the proportion of patients with Expanded Disability Status Scale (EDSS) improvement at four weeks, was common to three trials, while two trials examined magnetic resonance imaging (MRI) outcomes. The results of this review shows there is no significant difference in relapse recovery at week four (MD -0.22, 95% confidence interval (95% CI), 0.71 to 0.26, P = 0.20) nor differences in magnetic resonance imaging (MRI) gadolinium enhancement activity based on oral versus intravenous steroid treatment. However, only two of the five studies employed more current and rigorous methodological techniques, so these results

must be taken with some caution. The Oral Megadose Corticosteroid Therapy of Acute Exacerbations of Multiple Sclerosis (OMEGA) trial and the “Efficacy and Safety of Methylprednisolone Per os Versus IV for the Treatment of Multiple Sclerosis (MS) Relapses” (COPOUSEP) trial, designed to address such limitations, are currently underway.

Authors’ conclusions: The analysis of the five included trials comparing intravenous versus oral steroid therapy for MS relapses do not demonstrate any significant differences in clinical (benefits and adverse events), radiological or pharmacological outcomes. Based on the evidence, oral steroid therapy may be a practical and effective alternative to intravenous steroid therapy in the treatment of MS relapses.

4. Filippini G, Del Giovane C, Vacchi L, D’Amico R, Di Peietrantonj C, Beecher D, Salanti G. Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD008933. DOI: 10.1002/14651858.CD008933.pub2.

From this Systematic Review: Natalizumab and IFNB-1a (Rebif) are superior to all other treatments for preventing clinical relapses and disability progression in the short-term (24 months) in RRMS pts. High quality evidence shows natalizumab can induce progressive multifocal leukoencephalopathy, especially with more than 2 y of treatment. Moderate quality evidence supports IFNB-1b (Betaseron), glatiramer (Copaxone), and mitoxantrone for preventing relapse and disability progression in RRMS in the short term but the benefit-risk may be unfavorable.

There is a lack of convincing efficacy data from both direct and indirect comparisons that shows that IFNB-1a (Avonex), IV immunoglobulins, cyclophosphamide, and long-term corticosteroids have an unfavorable benefit-risk balance in RRMS.

For progressive MS, IFNB-1a (Avonex or Rebif), glatiramer, mitoxantrone, methotrexate, cyclophosphamide, IV immunoglobulins, and long-term corticosteroids are not effective in decreasing disability progression in progressive MS pts.

It is important to consider the clinical effects of all these treatments beyond 2y are uncertain which a relevant consideration for a disease of 30-40 y duration.

5. Gettig J, Cummings JP, Matuszewski K. H.Pp. Acthar Gel and Cosyntropin Review: clinical and financial implications. P&T Journal. 2009;34(5):250-257.

Infantile spasms

The use of ACTH in infantile spasms is not easily dismissed. Practice guidelines, reviews, and a metaanalysis support its use, and many of these sources cite ACTH as the first-line treatment choice.

These sources generally agree that:

1. ACTH appears to be as effective as, if not more effective than, other therapies for the short-term cessation of infantile spasms.
2. ACTH appears to be as effective as, if not more effective than, other therapies for the short-term termination of hypsarrhythmia (characteristic pattern on EEG in pts w/ IS).
3. The effect of ACTH on long-term developmental outcomes in patients with infantile spasms warrants further research.
4. The preferred dose and duration of treatment of infantile spasms with ACTH cannot be determined from the available evidence.

Other considerations:

1. Some of the less-well-designed and more poorly reported studies do not explicitly

distinguish between ACTH and cosyntropin; it cannot be determined whether the study patients received natural or synthetic ACTH.

2. Because some countries (e.g., Japan) do not have ready access to ACTH, cosyntropin is used interchangeably with ACTH.

3. Some countries (e.g., United Kingdom) advocate the use of vigabatrin (we cover this w/ T3PA) as a first-line therapy for infantile syndrome.

6. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD001770. DOI:10.1002/14651858.CD001770. pub3.

The strongest evidence suggests that hormonal treatment (prednisolone or tetracosactide depot (the) leads to resolution of spasms faster and in more infants than does vigabatrin. Responses without subsequent relapse may be no different, but one study suggested that hormonal treatment prednisolone or tetracosactide) might improve longterm neurodevelopmental outcomes in infants and young children for whom no underlying cause for their infantile spasms has been identified. This makes hormonal treatment more attractive, at least for this group of infants. More information and further research are needed to compare currently available therapies.

**ACTH - at the time this Cochrane review was undertaken, two ACTH preparations were in widespread use: ACTH (adrenocorticotrophin hormone) and tetracosactide. ACTH is naturally occurring, and the therapeutic product is derived from a bovine or porcine source and is administered as an intramuscular injection. However in the UK, with existing concerns surrounding bovine spongiform encephalopathy (BSE), ACTH has been withdrawn from the market. Tetracosactide is a synthetic alternative to ACTH and consists of the first 24 amino acids occurring in ACTH. It displays the same physiological properties as ACTH. It can be provided in depot and non-depot preparations. The Depot preparation is usually given on alternate days.

Jill's Conclusion/recommendations:

- 1. For treating acute exacerbations of RRMS, IV methylprednisolone should be used in place of ACTH. IV methylprednisolone is preferred and works effectively the same. Oral steroid therapy may be a practical and effective alternative to IV steroid for the treatment of MS relapses although they have an unfavorable risk-benefit balance for people with RRMS.**
- 2. There is no role for ACTH (natural or synthetic) for progressive forms of MS.**
- 3. The Cochrane Collaboration Systematic Review showed either natural ACTH or synthetic ACTH (Cosyntropin) may be effective for infantile spasms.**
- 4. Make Acthar a non-covered product. Use synthetic ACTH instead.**
- 5. Send letter to the current user with 3 months notice advising to use synthetic instead.**

Anti-osteoporotic Agents and Fracture Risk Reduction

Jordan Brazeal, Pharm.D.

Anti-osteoporotic Agents				
Generic	Trade	Route	Dosages	Price/month*
Alendronate	Fosamax, Binosto	Oral	Prophylaxis: 5 mg/day or 35 mg/week Treatment: 10 mg/day or 70 mg/week	\$81.95
Ibandronate	Boniva	Oral, IV	PO: 150 mg/month IV: 3 mg every 3 months	\$138.73
Risedronate	Actonel, Atelvia	Oral	5 mg/day 35 mg/week 150 mg/month	\$187.92
Zoledronic Acid	Reclast	IV	Prophylaxis: 5 mg every 2 years Treatment: 5 mg/year	\$83.70
Denosumab	Prolia	SubQ	60 mg every 6 months	\$168.14
Teriparatide	Forteo	SubQ	20 mcg/day	\$1560.36
Raloxifene	Evista	Oral	60 mg/day	\$201.80
Calcitonin salmon	Fortical, Miacalcin	Nasal Spray	200 units (1 spray) in one nostril/day	\$102.89

*Price based on AWP, not actual acquisition costs, of lowest-priced available formulation for *treatment*

CLINICAL TRIALS OF ANTI-OSTEOPOROTIC AGENTS:

(Note, for the following, All *italicized* entries denote statistically significant differences. Where applicable, interventional groups' statistics are listed before those of the control group.)

BISPHOSPHONATES AS TREATMENT OF OSTEOPOROSIS:

In a network meta-analysis by Jansen, et al (12), the bisphosphonates were compared regarding their ability to reduce the risk of vertebral, hip, and non-vertebral-non-hip fractures. The figures below depict this ability relative to one another and placebo. The relative risk was calculated based on a conglomeration of randomized, controlled trials. Please note that *none* of these agents have been compared in a head-to-head trial.

	Vertebral Fractures			
	RR ^a	95% Credibility Interval	Probability (>10% Risk Reduction than Comparator)	Probability (>20% Risk Reduction than Comparator)
Zoledronic acid vs				
Placebo	0.30	0.23 to 0.37	>99%	>99%
Alendronate	0.55	0.41 to 0.76	99%	99%
Risedronate	0.50	0.36 to 0.70	99%	>99%
Ibandronate	0.58	0.37 to 0.92	97%	92%
Etidronate	0.63	0.30 to 1.76	72%	63%
Alendronate vs				
Placebo	0.53	0.44 to 0.65	>99%	>99%
Risedronate	0.90	0.66 to 1.24	50%	23%
Ibandronate	1.05	0.68 to 1.63	25%	12%
Etidronate	1.24	0.54 to 3.11	23%	15%
Risedronate vs				
Placebo	0.59	0.47 to 0.75	99%	99%
Ibandronate	1.16	0.74 to 1.84	14%	5%
Etidronate	1.37	0.60 to 3.47	23%	15%
Ibandronate vs				
Placebo	0.51	0.34 to 0.74	>99%	99%
Etidronate	1.07	0.48 to 3.15	27%	20%
Etidronate vs placebo	0.43	0.18 to 0.96	97%	93%

^aRelative risk < 1.0 shows an advantage of treatment over the reference.

All therapies compared for fracture risk reduction from a meta-analysis by Freemantle, et al (13):

Comparator vs placebo	New vertebral, RR (95% CI)	Hip, RR (95% CI)
Alendronate	0.56 (0.46 to 0.69)	0.65 (0.41 to 1.03)*
Etidronate	0.46 (0.17 to 1.31)	2.97 (0.12 to 72.11)
Ibandronate (2.5 mg/day)	0.51 (0.34 to 0.74)	Not done
Risedronate	0.62 (0.50 to 0.77)	0.74 (0.59 to 0.94)
Zoledronic acid	0.30 (0.24 to 0.38)	0.59 (0.42 to 0.83)
Denosumab	0.33 (0.26 to 0.41)	0.61 (0.37 to 0.98)
Raloxifene	0.65 (0.54 to 0.78)	Not done
Teriparatide	0.35 (0.22 to 0.55)	0.25 (0.03 to 2.24)

*In the trials with postmenopausal osteoporosis (1-6), alendronate never fails to achieve statistical significance in reducing risk of hip fracture. The data from this table also include trials other than postmenopausal osteoporosis.

Note that in both studies above, the authors were heavily conflicted with the funding source of the trials. Moreover, Jansen, et al, was funded by the manufacturers of Reclast, and Freemantle, et al, was funded by the manufacturers of Prolia.

Calcitonin has been associated with significant reduction in vertebral fractures (0.33), but not hip fractures. (7)

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Fibrate Therapy
Jill T. Johnson, Pharm.D., BCPS
Nov 4, 2013

EBD Data	Utilizers	#Rxs	Ing Cost	Net Plan Cost	Avg Net Plan Cost	Cost/unit	Cost/ day
Gemfibrozil	586	1151	31797	21920	19.04	0.28	0.53
Fenofibrate	1361	3084	287329	252835			
Generic						2.46	2.48
Antara						5.21	5.21
Tricor						3.34	3.34
Lipofen						2.57	2.57
Fenoglide						6.78	6.78

6/1/2013-8/31/2013

Summary of the evidence:

FIELD Investigators. Effects of long term fenofibrate therapy on CV events in 9795 people with type 2 DM (the FIELD study): RCT. Lancet 2005;366:1849-61. Authors' conclusion: "Fenofibrate did not significantly reduce the risk of the primary outcome of coronary events in T2DM not initially on statins. It did reduce total CV events, mainly due to fewer non-fatal MIs and revascularisations. The higher rate of starting statin therapy (17%placebo vs 8%fenofibrate) in pts allocated placebo might have masked a moderately larger treatment benefit. What benefit it affords to high risk (T2DM) patients stable on statin therapy was to be addressed in the ACCORD trial."

	Plasma concentrations at baseline (mean [SD])		Absolute (mmol/L) and relative (%) differences between treatment groups in plasma lipid concentrations after randomisation*				Plasma concentrations at study close (mean [SD])	
	Placebo	Fenofibrate	4 months	1 year	2 years	Study close	Placebo	Fenofibrate
Full cohort (fenofibrate n=4895, placebo n=4900)								
Total cholesterol	5.03 (0.71)	5.04 (0.69)	-0.58 (-11.4%)	-0.58 (-11.6%)	-0.56 (-11.1%)	-0.33 (-6.9%)	4.56 (0.90)	4.23 (0.78)
LDL cholesterol	3.07 (0.66)	3.07 (0.64)	-0.39 (-12.0%)	-0.38 (-11.9%)	-0.36 (-11.7%)	-0.17 (-5.8%)	2.60 (0.78)	2.43 (0.65)
HDL cholesterol	1.10 (0.26)	1.10 (0.26)	0.05 (5.1%)	0.05 (4.5%)	0.04 (3.5%)	0.01 (1.2%)	1.12 (0.29)	1.13 (0.30)
Triglycerides	1.93 (0.88)	1.95 (0.87)	-0.56 (-28.6%)	-0.58 (-30.2%)	-0.52 (-27.4%)	-0.41 (-21.9%)	1.87 (0.96)	1.47 (0.78)
Started other lipid-lowering therapy (fenofibrate n=944, placebo n=1776)								
Total cholesterol	5.2 (0.67)	5.25 (0.69)	-0.42 (-8.0%)	-0.39 (-7.6%)	-0.33 (-6.5%)	-0.08 (-1.6%)	4.12 (0.88)	3.98 (0.85)
LDL cholesterol	3.31 (0.63)	3.23 (0.64)	-0.24 (-6.6%)	-0.19 (-5.5%)	-0.15 (-4.6%)	0.02 (0.7%)	2.18 (0.74)	2.13 (0.66)
HDL cholesterol	1.08 (0.25)	1.03 (0.24)	0.05 (4.6%)	0.03 (2.8%)	0.01 (1.7%)	-0.01 (-0.5%)	1.12 (0.28)	1.05 (0.29)
Triglycerides	2.08 (0.99)	2.22 (0.99)	-0.54 (-24.6%)	-0.55 (-24.8%)	-0.45 (-21.0%)	-0.24 (-10.9%)	1.84 (0.97)	1.74 (0.96)
Did not start other lipid-lowering therapy (fenofibrate n=3951, placebo n=3124)								
Total cholesterol	4.87 (0.68)	4.99 (0.69)	-0.63 (-12.5%)	-0.66 (-13.1%)	-0.68 (-13.4%)	-0.66 (-13.1%)	4.82 (0.80)	4.29 (0.74)
LDL cholesterol	2.93 (0.64)	3.03 (0.64)	-0.44 (-13.6%)	-0.45 (-14.3%)	-0.48 (-15.3%)	-0.46 (-14.7%)	2.84 (0.70)	2.50 (0.63)
HDL cholesterol	1.11 (0.27)	1.11 (0.26)	0.05 (5.1%)	0.05 (4.8%)	0.04 (4.0%)	0.02 (2.1%)	1.13 (0.29)	1.15 (0.30)
Triglycerides	1.85 (0.81)	1.89 (0.83)	-0.57 (-29.6%)	-0.60 (-31.6%)	-0.55 (-29.1%)	-0.51 (-27.3%)	1.88 (0.95)	1.41 (0.72)

*Fenofibrate minus placebo. p<0.05 for all differences between groups at every timepoint shown, except in patients who started other lipid-lowering therapy, for HDL cholesterol and LDL cholesterol at study close.

Table 2: Plasma concentration of lipids at baseline and study close, with treatment group differences during follow-up

ACCORD Study Group. Effects of combination lipid therapy in T2DM. N Engl J Med.

2010;362:1563-74. Author's conclusion: "Combination fenofibrate and simvastatin did not reduce the rate of fatal CV events, NFMI, or NF stroke, as compared with simvastatin alone. These results do not support the routine use of combination therapy with fenofibrate and simvastatin to reduce CV risk in the majority of high risk patients with T2DM."

Table 2. Prespecified Primary and Secondary Outcomes.

Outcome	Fenofibrate (N=2765)		Placebo (N=2753)		Hazard Ratio (95% CI)	P Value
	no. of events	rate/yr	no. of events	rate/yr		
Primary outcome (major fatal or nonfatal cardiovascular event)	291	2.24	310	2.41	0.92 (0.79–1.08)	0.32*
Secondary outcomes						
Primary outcome plus revascularization or hospitalization for congestive heart failure	641	5.35	667	5.64	0.94 (0.85–1.05)	0.30
Major coronary disease event†	332	2.58	353	2.79	0.92 (0.79–1.07)	0.26
Nonfatal myocardial infarction	173	1.32	186	1.44	0.91 (0.74–1.12)	0.39
Stroke						
Any	51	0.38	48	0.36	1.05 (0.71–1.56)	0.80
Nonfatal	47	0.35	40	0.30	1.17 (0.76–1.78)	0.48
Death						
From any cause	203	1.47	221	1.61	0.91 (0.75–1.10)	0.33*
From cardiovascular cause	99	0.72	114	0.83	0.86 (0.66–1.12)	0.26
Fatal or nonfatal congestive heart failure	120	0.90	143	1.09	0.82 (0.65–1.05)	0.10

Jun M, Foote C, Lv J, Neal B, et al. Effects of fibrates on CV outcomes: a systematic review and meta-analysis. Lancet 2010;375:1875-84.

Conclusion: Overall fibrates can reduce the risk of major cardiovascular events predominantly by prevention of coronary events, and might have a role in individuals at high risk of CV events and in those with combined dyslipidaemia.

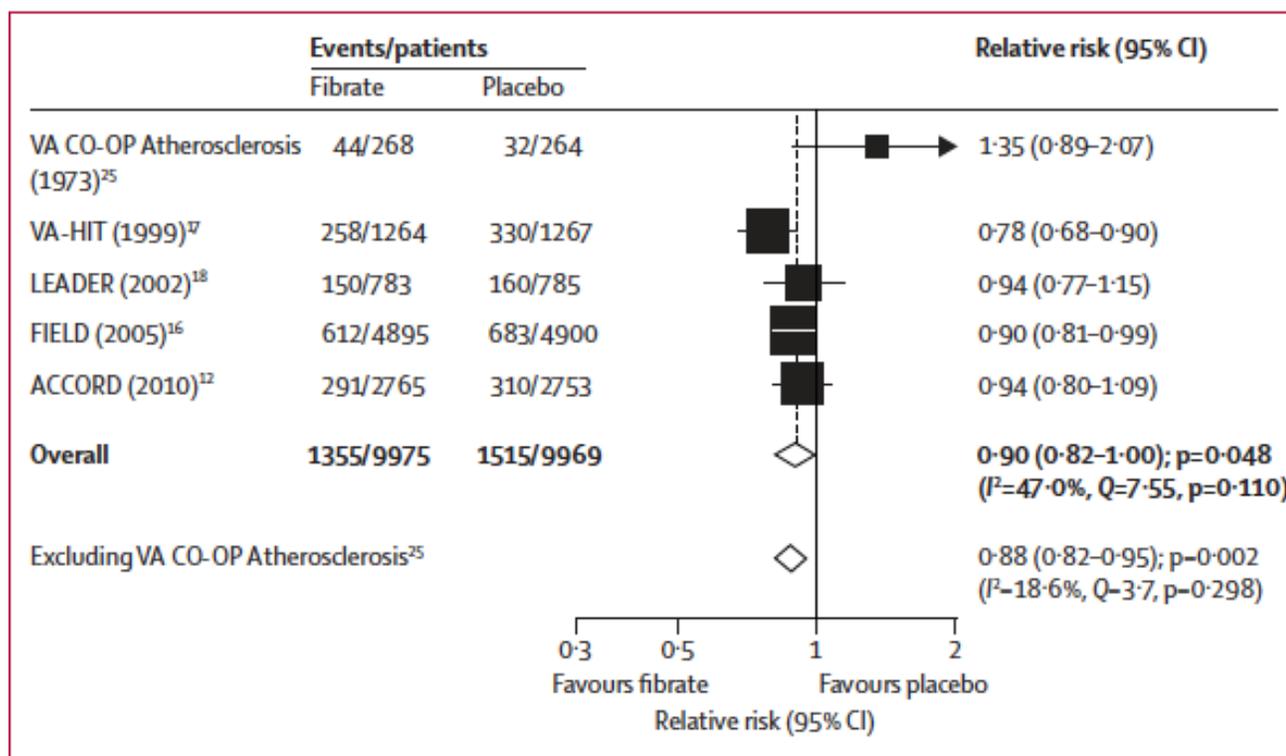
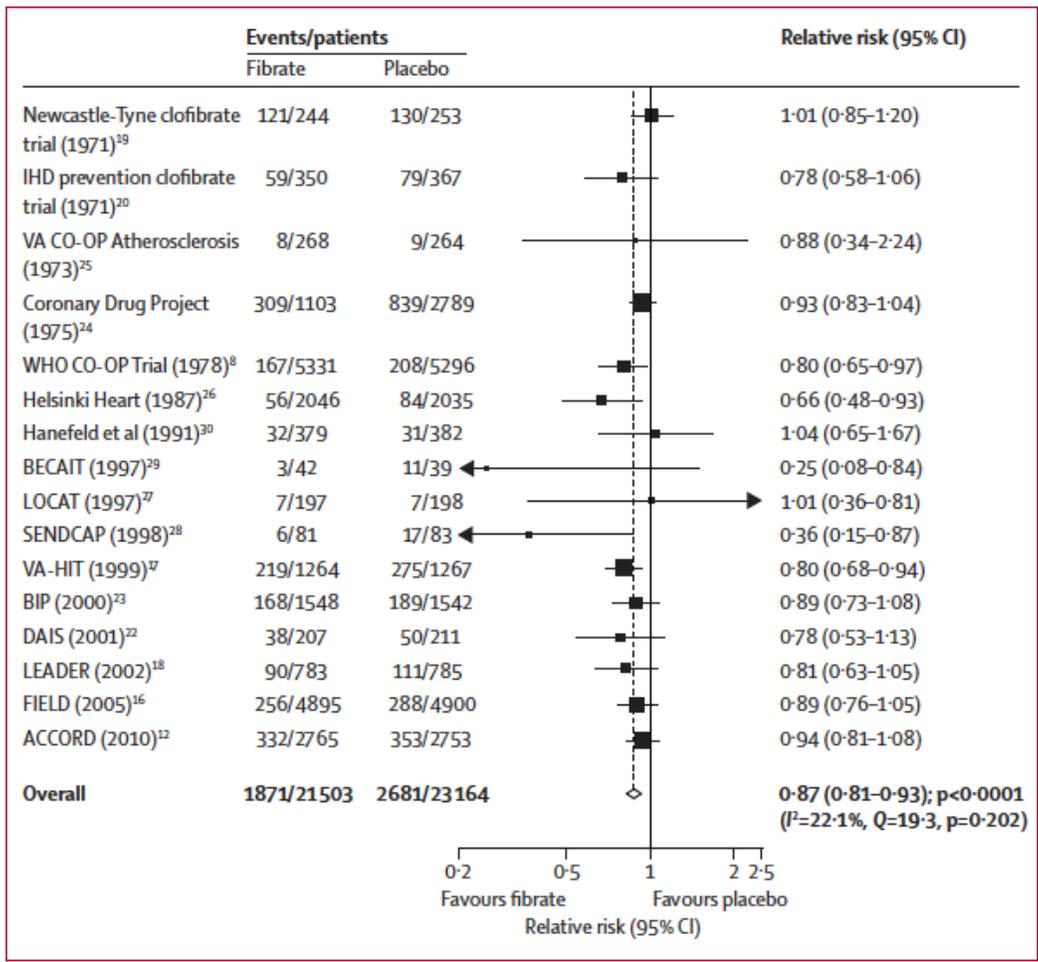


Figure 2: Effect of fibrates on risk of major cardiovascular outcomes



- Newcastle (clofibrate)
- IHD (clofibrate)
- VA CO-OP (clofibrate)
- Coronary Drug Project (clofibrate)
- WHO Co-OP Trial (clofibrate)
- Helsinki Heart (gemfibrozil)**
- Hanefeld (clofibrate)
- BECAIT (Bezafibrate-N/A in US)
- LOCAT (gemfibrozil)
- SENDCAP (bezafibrate-N/A in US)
- VA-HIT (gemfibrozil)**
- BIP (bezafibrate-N/A in US)
- DAIS (fenofibrate)
- LEADER (bezafibrate-N/A in US)
- FIELD (fenofibrate)
- ACCORD (fenofibrate)

Figure 3: Effect of fibrates on the risk of coronary events

Pancreatitis risk

Preiss D, Tikkanen MJ, Welsh P, Ford I, et al. Lipid-modifying therapies and risk of pancreatitis: a Meta-analysis. JAMA. 2012;308(8):804-811. In a pooled analysis of randomized trial data, use of statin therapy was associated with a lower risk of pancreatitis in patients with normal or mildly elevated triglyceride levels. This was not systematically measured in all trials

Hypertriglyceridemia has been reported to be the third most common cause of pancreatitis which led to major guidelines for lipid-modifying therapies, including advice to commence triglyceride-lowering therapy, usually fibrates, in persons with moderate and severe hypertriglyceridemia (above 400 to 500 mg/dL). However, high quality evidence for this approach is lacking, and only observational data exist. There is concern that fibrates might increase the risk of pancreatitis in individuals with triglyceride levels lower than those mentioned in guidelines. Fibrates increase the cholesterol concentration in bile and may increase the risk of gallstones. However, few large randomized placebo-controlled trials of fibrate therapy have published data on pancreatitis.

Table 2. Baseline Data From Trials Comparing Fibrate Therapy With Placebo

Source	No.		Treatment, Active/Control	Follow-up, y	Trial Population (Triglyceride Inclusion Criteria)	Age, y	Triglycerides	
	Fibrate	Control					Baseline, Mean (SD), mg/dL	Difference at 1 y, %
Coronary Drug Project, ^{37,38} 1975 ^b	1103	2789	Clofibrate/placebo	6.2	Male, previous MI (NR)		184	25
WHO-COOP, ³⁹ 1978 ^{b,d}	5331	5296	Clofibrate/placebo	5.3	Male, upper third of cholesterol range (NR)	46	NA	NA
HHS, ^{40,44} 1987 ^c	2362	2347	Gemfibrozil/placebo	5.0	Male, no CHD or possible symptoms of CHD (NR)	47	177 (119)	35
VA-HIT, ⁴¹ 1999 ^b	1264	1267	Gemfibrozil/placebo	5.1 ^a	Male, CHD (triglycerides ≤300 mg/dL)	64	161 (68)	31
BIP, ⁴² 2000	1548	1542	Bezafibrate/placebo	6.2	Previous MI or stable angina (triglycerides ≤300 mg/dL)	60	145 (51)	21 ^e
FIELD, ¹² 2005	4895	4900	Fenofibrate/placebo	5.0 ^a	Diabetes mellitus, not taking statin (triglycerides 89-445 mg/dL)	62	174 (78)	30
ACCORD Lipid, ⁴³ 2010	2765	2753	Simvastatin + fenofibrate/simvastatin + placebo	4.7	Diabetes mellitus, CVD or risk factors (triglycerides <750 mg/dL with no lipid-lowering therapy; <400 mg/dL with therapy)	62	162 (113-229) ^a	20
Total	19268	20894		5.3 (0.5)				

Abbreviations: ACCORD, Action to Control Cardiovascular Risk in Diabetes; BIP, Bezafibrate Infarction Prevention; CHD, coronary heart disease; CVD, cardiovascular disease; FIELD, Fenofibrate Intervention and Event Lowering in Diabetes; HHS, Helsinki Heart Study; MI, myocardial infarction; NA, not available; NR, not reported (no triglycerides inclusion or exclusion criteria specified); VA-HIT, Veterans Affairs Cooperative Studies Program High-Density Lipoprotein Cholesterol Intervention Trial; WHO-COOP, World Health Organization Co-operative Trial.

SI conversion factor: To convert triglyceride values to mmol/L, multiply by 0.0113.

^aMedian or median (interquartile range).

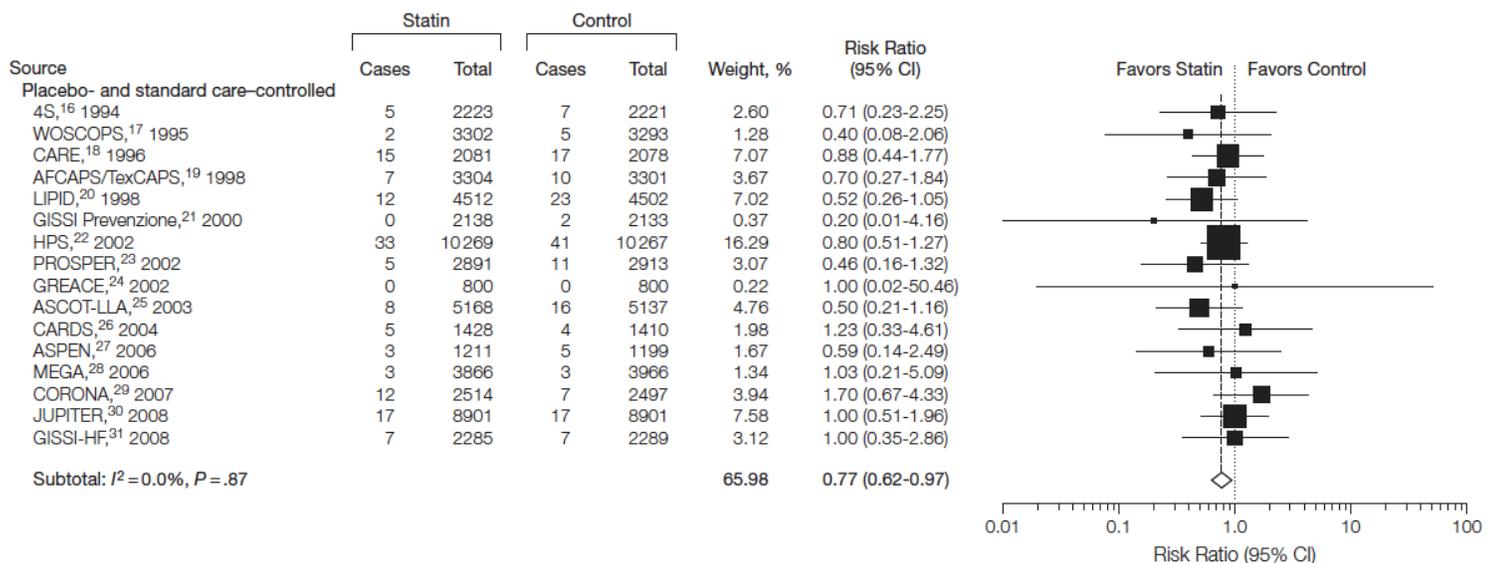
^bOnly fatal cases of pancreatitis available.

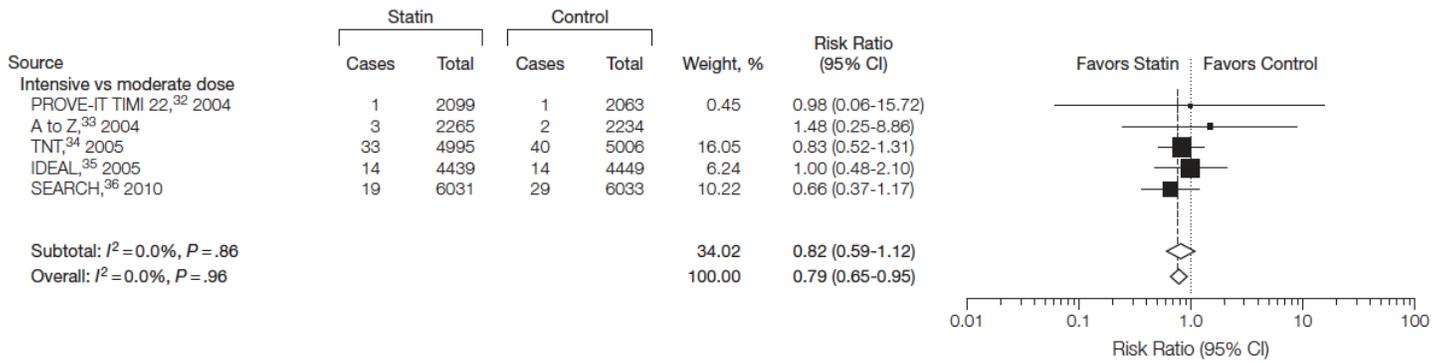
^cIncludes cases from both the HHS and its ancillary study (age, baseline triglyceride levels, and % difference in triglyceride levels are weighted means).

^dIncludes cases during the trial and during first year after the trial.

^eAverage difference during trial.

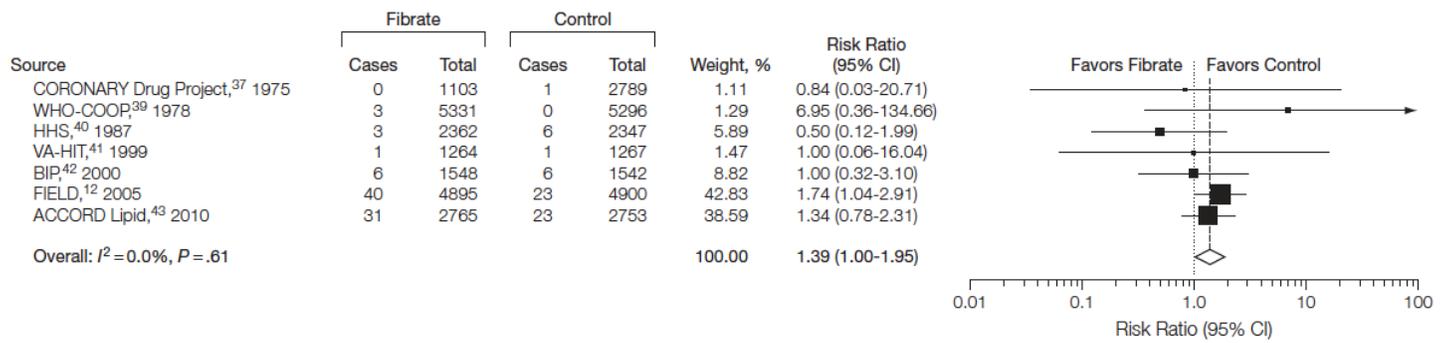
Figure 2. Meta-analysis of Incident Pancreatitis in 21 Large Statin Trials





For abbreviations, see Table 1. Size of data markers indicates relative weight of the study (from random-effects analysis).

Figure 3. Meta-analysis of Incident Pancreatitis in 7 Large Fibrate Trials



For abbreviations, see Table 2. Size of data markers indicates relative weight of the study (from random-effects analysis).

Rivaroxaban, Apixaban, Dabigatran
Review of Trial Results
Jill Johnson, Pharm.D., BCPS

Dabigatran—Efficacy either worse or not different; Bleeding either not worse than or more bleeding

Indications: AF 150mg BID. Avoid if CrCl<15			Cost (AWP): 150mg=\$318.47/60, 75mg=318.47/60
Knee		Any VTE & all-cause Mortality	Major bleeding & clinically relevant NM bleeding
RE-MOBILIZE	D150or220 vs E30bid	E30bid superior to D	No difference
REMODEL	D150or220 vs E40qd	Not different	NO difference
Hip			
RENOVATE	D150or220 vs E40qd	Not different	Trend towards more bleeding w D
RENOVATEII	D220 vs E40qd	Not different	Trend towards more bleeding w D
OVERALL ORTHO		Not different	Not different but trend towards more bleeding w/ D
AF		Stroke/Systemic embolism	Major bleeding
RE-LY	D150BID vs warf	D Superior; D1.11%, W1.69% ; NNT=173	No difference

Apixaban—Less efficacy than E30 bid but less bleeding. More efficacy than E40 QD with no difference in bleeding.

Indications: AF 5mg BID. Avoid if CrCl<15 Knee Replacement: 2.5mg BID 12-24h post op X 10-14d Hip Replacement: 2.5mg BID 12-24h post op X 32-38d Avoid if on dialysis.			Cost (AWP): 2.5mg = \$300.44/60, 5mg=\$300.44/60	
Knee		Any VTE & all-cause Mortality	Major bleeding & clinically relevant NM bleeding	
ADVANCE1	A2.5bid vs E30bid	A not noninferior to E30bid; A9%, E8.8%; NNT=719 for E	A superior to E30bid; A2.9%, E4.34%; NNT=69	
ADVANCE2	A2.5bid vs E40qd	A superior to E40qd; A=15.1%, E24.4%; NNT=11 for A	Not different (trend towards A benefit) A3.5%, E4.8%; NNT=81	
Hip				
ADVANCE3	A2.5bid vs E40qd	A superior to E40qd; A1.39%,3.86%; NNT=41	Not different; A4.8%, E5%	
OVERALL ORTHO		A trend toward superior to E; A6.8%, E10.3%; NNT=29	A trend toward superior to E; A3.9%, E4.78%; NNT=114	
AF		Ischemic or hemorrhagic stroke or systemic embolism	All cause death	Major bleeding
ARISTOTLE	A5bid vs warf (2-3)	A superior to W; A1.27%/y vs W1.6%/y; NNT=303	A superior to W; A3.52% vs W 3.94%;NNT=238	A superior to W; A2.13%/y, W3.09%/y; NNT=105
VTE Treatment		Recurrent symptomatic VTE or VTE related death	Major bleeding plus clinically relevant NM bleeding	Major bleeding
AMPLIFY	A 10 BID X 7d, then 5mg BID X 6m or E/W	A2.3% and W2.7%; met noninferiority; W-TTR was 61%	A4.3%, W9.7%, p<0.001	A0.6%, W1.8%, HR with A=0.31 (0.17-0.55)

Rivaroxaban 10mg, 15mg, 20mg—Ortho: more efficacy, more bleeding. AF: noninferior to poorly controlled W. VTE: noninferior to a relatively poorly controlled E/W group.

Indications: VTE Treatment: 15 BID X3w, then 20QD. Avoid if CrCl<30. AF 20 QD. Avoid if CrCl<15. Knee or Hip Replacement: 10 QD. Avoid if CrCl<30 Avoid if on HD.		Cost: (AWP) 10mg=\$300.42/#30 15mg=\$901.26/90 20mg=\$901.26/90	
Knee		Any VTE & all-cause Mortality	Major bleeding & clinically relevant NM bleeding
RECORD1	Riv 10qd vs E40qd	R superior to E40; NNT=39	R worse than E40; NNH=143ns
RECORD3	Riv 10qd vs E30bid	R superior to E30bid; NNT=11	Not different
Hip			
RECORD4	Riv 10qd vs E40qd	R superior to E40; NNT=32	Not different
OVERALL		R superior to E; NNT=22	E superior to R; NNH 138
AF		Stroke or Systemic Embolism	Major bleeding & clinically relevant NM bleeding
ROCKET	Riv 20qd vs	R noninferior to poorly controlled W (55%TTR)	R14.9%/y vs @14.5%/y, ns. R fewer intracranial hemorrhage R 0.5%, W 0.7%, NNT=500 R fewer fatal bleeding R 0.2%, W 0.5%, NNT=334
VTE Tx		Recurrent VTE	Major bleeding & clinically relevant NM bleeding
EINSTEIN	Riv 15mg qd X3w, then 20qd vs enox to W for 3, 6, or 12m in acute, symptomatic DVT; Parallel design—Riv 20 vs placebo beyond 6 or 12m	R 2.1% vs W 3%, achieved NI by ITT analysis. PPA was not shown although text stated the results were similar. (TTR=58%) NNT=112	Major bleeding (6 or 12 m extension) R 0.7% vs P 0%, ns. 1 st major OR clinically relevant NM bleeding: R 6%, P 1.2%, P<0.001. Clinically relevant NM bleeding: R 5.4%. P 1.2%,

Current Coverage:

UAS:

Dabigatran(Pradaxa) T2PA: 1. Dx of NVAF
Apixaban (Eliquis) T2PA: 1. Dx NVAF, 2. Dx of THA (2.5mg BID X35d), 3. TKA (2.5mg BID X 14d)
Rivaroxaban (Xarelto) 1. T3. QL of 35/year.

PSE/ASE:

Dabigatran (Pradaxa) PA: 1. Dx of NVAF
Apixaban (Eliquis) PA: NVAF 2.5 or 5mg BID, THA (2.5mg BID up to 76 tabs in 6m), or TKA 2.5mg BID up to 28 tabs in 6m)
Rivaroxaban (Xarelto) PA 1. Hip or knee replacement surgery during the current year that consumed 35 days of rivaroxaban and now needs VTE prevention due to replacement of another joint (hip or knee). QL is 35tab/35 days, once per year.

Product	Cost (AWP)
Enoxaparin 30mg (each)	19.8
E 40	26.4
E 60	39.60
E 80	65.03
E100	81.28
E 120	97.57
E150	121.97
Warfarin /#100	\$49-97 depending on mg

VTE Scenario: A 120kg man with 1st VTE, good kidney function.

- E/W requires 120mg q12h X 5 days (\$975 x 5 days enox.), plus warfarin and q3d INR X 1 w, qW INR X 2 w, q2w INR X twice, then q m INR. (probably 5 times the first month). **>\$1000 for 3 months.**
- Apixaban 10mg BID X 7d, then 5mg BID. Comes in 2.5 and 5mg. \$300.44/60 regardless of dose. \$5/tablet. \$20/d X 7d = \$140 for week 1, then \$210 for the other 3 weeks. \$350 for first month, \$300/m for subsequent months. **3 months tx is \$950.**
- Rivaroxaban 15mg qd X 3w, then 20mg qd. \$10.01/d regardless of dose. \$300/m. **3 months tx is \$900.**

Jill's Recommendation:

Dabigatran:

1. Remove PA from dabigatran.
2. Place at T2 since it showed superiority to warfarin for AF without difference in major bleeding.
3. Place a QL of 2 doses/1 day.

Note: more GI bleeding, less intracranial bleeding with dabigatran.

Apixaban:

1. Remove PAs on apixaban.
2. Place at T2.
3. Place a QL of 2/1 for the 2.5mg; QL of 4/1 for the 5mg so that initiation with the regimen of 10mg BID can be achieved with the 5mg form. This allows access to AF pts and showed superiority to W for ischemic stroke/systemic embolism, death, and less major bleed/clinically relevant NM bleeding. It also allows access to VTE tx patients providing noninferiority to W (TTR 61%) but with less bleeding. It also allows access for ortho patients with noninferiority or superior efficacy and with either superior or noninferior bleeding risk. Note the exception is in knee where it missed noninferiority compared to E30BID.

Rivaroxaban:

1. Remove PA from rivaroxaban. Place at T2. Place a QL of 1/1d for all strengths except 15mg. 15mg should have 2/1 to allow for initiation of the drug in the setting of VTE tx with corresponding noninferiority with no difference in bleeding.

Principles for Drug Placement and Strategy for DUEC
2013

The focus for the Arkansas Drug Utilization and Evaluation Committee when placing drugs new to market on the tiered formulary is to provide for the coverage of medically necessary drugs by considering efficacy and safety first as evidenced by peer-reviewed and published medical literature when available. Within the literature is an information hierarchy with meta-analyses and systematic reviews representing the highest quality evidence, then large randomized controlled trials (RCTs), followed by small RCTs, cohort studies, case-controlled studies, case series, and case reports. Consideration of drugs with published data measuring meaningful clinical endpoints provides for more certain drug coverage decisions than does data with only surrogate endpoint data. Using evidence-based medicine provides for an ongoing necessity to assess the current best literature and when a higher quality of evidence is published, the probability exists that it will trump the lower quality evidence.

Consideration of ingredient cost, cost/month, and cost/day of treatment are considered after efficacy and safety trials show no difference or non-inferiority with other drugs in the class, or with other drugs used to treat the same condition. Although cost is not a primary factor, it is a consideration in the environment of multiple drugs in a drug class. New brand-only drugs to a drug class with several generic options will be required to show superior efficacy and/or less toxicity than existing drugs in the class.

The DUEC may exclude drugs from coverage for a variety of reasons coded below:

1	Lacks meaningful clinical endpoint data; has shown efficacy for surrogate endpoints only.
2	Drug's best support is from single arm trial data
3	No information in PubMed or Drug Facts & Comparisons or Lexicomp
4	Convenience kit Policy
5	Medical food
6	Cough & Cold Policy
7	Multivitamin Policy
8	Drug has limited medical benefit &/or lack of overall survival data or has overall survival data showing minimal benefit
9	Not medically necessary
10	Peer-reviewed, published cost effectiveness studies support the drug lacks value to the plan.
11	Oral Contraceptives Policy
12	Other

Convenience Kit Policy:

As new drugs are released to the market through Medispan, those drugs described as “kits” will not be considered for inclusion in the plan and will therefore be excluded products unless the product is available solely as a kit.

Medical Food Policy:

Medical foods will be excluded from the plan unless two sources of peer-reviewed, published medical literature supports the use in reducing a medically necessary clinical endpoint.

A medical food is defined below:

A medical food, as defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is “a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”

FDA considers the statutory definition of medical foods to narrowly constrain the types of products that fit within this category of food. Medical foods are distinguished from the broader category of foods for special dietary use and from foods that make health claims by the requirement that medical foods be intended to meet distinctive nutritional requirements of a disease or condition, used under medical supervision, and intended for the specific dietary management of a disease or condition. Medical foods are not those simply recommended by a physician as part of an overall diet to manage the symptoms or reduce the risk of a disease or condition, and all foods fed to sick patients are not medical foods. Instead, medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in a natural state) for a patient who is seriously ill or who requires use of the product as a major component of a disease or condition’s specific dietary management.

Cough & Cold Policy:

As new cough and cold products enter the market, they are often simply re-formulations or new combinations of existing products already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new cough and cold products are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new cough and cold products to “excluded” unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.

Multivitamin Policy:

As new vitamin products enter the market, they are often simply re-formulations or new combinations of vitamins/multivitamins in similar amounts already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new vitamins are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new vitamin/multivitamin products to “excluded” unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.

Oral Contraceptives (OC) Policy:

OCs which are new to the market may be covered by the plan with a zero dollar, tier 1, 2, or 3 copay, or may be excluded. If a new-to-market OC provides an alternative product not similarly achieved by other OCs currently covered by the plan, the DUEC will consider it as a new drug. IF the drug does not offer a novel alternative or offers only the advantage of convenience, it may not be considered for inclusion in the plan.

DUEC Jul 22-Sept 30 2013							
DRUG NAME	Generic	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	Jill's Notes	DUEC Vote Nov 4, 2013	IB Vote
Enteragam Powder 5GM		\$60/5gm	Prescription medical food product for management of diarrhea - predominant irritable bowel syndrome.		Exclude. SERUM-DERIVED BOVINE IMMUNOGLOB/PROTEIN ISOLATE 5 GM PACKET. For enteropathy. Only clinical trial was open-label with 8 pts on the manufacturer's website.		
Podiarn Capsules	L-methylfolate-B-12-B-6-Alpha lipoic AC Capsules	\$34/bottle of 60	Dietary management product (medical food)		Exclude. No data		
Astagraf XL capsules 0.5, 1, or 5mg capsules (SPECIALTY DRUG)	Tacrolimus XR	\$71 - \$713/30 days	Extended-release form (given once daily) of tacrolimus for transplant rejection prophylaxis	Tacrolimus 5mg immediate release twice daily = \$1380/30 days	Exclude. No benefit over immediate-release, which is generically available.		
Tivicay 50mg tabs (SPECIALTY)	Dolutegravir 50mg tablet	50mg daily = \$1,410. Max dose = 100mg/day	Tx of HIV infection	Raltegravir	T3PA. Efficacy in INSTI-resistant cases of HIV.T3PA; Must be taken in combination with HAART therapy.		
Tarceva	erlotinib		NSCLC		See handout.		
Gilotrif (20,30, & 40mg tabs)	AFATINIB DIMALEATE TAB 20 MG, 30, 40mg (BASE EQUIVALENT)	\$6,660/30 days. All strengths are \$222/cap. If coverage is elected, QL of 30/30 days would be recommended	Approved for first-line tx of metastatic non-small cell lung cancer whose tumors have epidermal growth factor exon 19 deletions or exon21 substitution mutations as detected by an FDA-approved test.		Exclude. No OS data benefit. PFS about 3m > than placebo. QoL improvements vs. placebo, but not beneficial (cough, dyspnea, pain).		
Lo Minastrin Pak FE	10mcg EE, 1mgNorethindrone. 24 active, 4 Fe(without therapeutic use).	\$99/28 days	Oral contraceptive		OC policy. Could exclude. 10mcg EE, 1mgNorethindrone. 24 active, 4 Fe(without therapeutic use).		
Mirvaso gel	brimonidine 0.33%	\$296/30gm	For topical treatment of the facial erythema(redness) of rosacea in adults 18 years or older	Metronidazole 0.75% cm = \$181/45gm	T3. QL: 1 tube/month. Available strength 0.33% of brim free base. For topical non transient facial erythema of rosacea in adults 18 and older. Apply pea-so\ize amount QD to each of 5 areas of the face avoid eyes and lips.		
LINE EXTENSIONS							
Fioricet cap w/Cod	butalbital/APAP/Caffeine/Codeine 50/300/40/30mg	\$5.70/capsule	Treatment of headache	Multiple generic versions of butalbital/APAP/Caffeine/Cod (50/325/40/30). Cost - \$1.49/cap	Exclude. Reformulated for APAP. Generic available.		
Brisdelle 7.5mg	Paroxetine	\$161/30 days	7.5mg po at bedtime for moderate to severe hot flashes associated w/menopause	AWP generic paroxetine 10mg = 2.53/10mg	Exclude. Generics available.		
Naftin Gel 2% (new strength)	NAFTIFINE HCL GEL 2%	\$340/45gm	Antifungal	Clotrimazole 1% 45gm - \$48. Ketoconazole cream 60gm - \$43. Tolnaftate 1% cream 30gm - \$10	Exclude. Cheaper alternatives exist. Naftifine comes in 1 & 2% gel and cream as Naftin brand. Alternatives are not naftin.		
Vytone 1-1.9% cream	hydrocortisone 10mg/Iodoquinol 10mg/g of cream	\$200/box of 30	Topical antifungal		Exclude.only possibly effective. Unusual prescribing info: "INDICATIONS AND USAGE Based on a review of a related drug by the National Research Council and subsequent FDA classification for that drug, the indications are as follows: "Possibly" Effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis, bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis, intertrigo. Final classification of the less-than-effective indications requires further investigation."		
Epaned Solution	enalapril 1mg/ml enalapril for oral solution	\$342/150ml bottle	Tx of heart failure or hypertension	Enalapril tabs: 2.5mg/\$0.80 5mg/\$1.02 10mg/\$1.07	Exclude. Tablets able to be crushed.		
Trokendi XR	topiramate oral extended release caps 25,50,100, or 200mg -	Dose of extended release is 200-400mg/day = \$684-\$1,367/30 days	Oral antiepileptic	generic immediate release topiramate 200mg = \$477	Cheaper alternatives exist. Exclude.		
Selrx Shampoo	2.3% (selenium sulfide-pyrithione zine urea shampoo)	\$360/180ml bottle	Tx of dandruff, seborrheic dermatitis, tinea versicolor	Generic strengths of 2.25% available	Exclude. Cheaper alternative exists. Selenium sulfide generic shampoo 1% is OTC. AlsoDandrex. This is 2.3% and is Rx only.		
Utopic Cream	urea cream 41%	\$420/227 gm bottle. Plan currently has urea cream 39,43, and 45% set to reject	Treatment of Xerosis plus pruritus, irritation, or inflammation, keratolytic and dry skin.	Generic strengths of 10-50% available.	Exclude. Cheaper alternative exists.		
Tretin-X cream	tretinoin cream 0.075% - new strength	\$284/35gm tube	Tx of acne		Exclude		
Fabior Aer 0.1%	TAZAROTENE (ACNE) FOAM 0.1%	\$340/50gm can; \$6.816/gram, 100g & 50g can	Tazarotene (acne) foam	Tazorac Cream 0.05% 60gm tube = \$558 Tazorac Gel 0.05% 30gm tube = \$279	Exclude. Cheaper alternatives exist.		
Riax 5.5 or 9.5%	(benzoyl peroxide foam	\$330/can. Benzoyl peroxide foam 5.3% and 9.8% currently set to reject.	Treatment of acne	Benzoyl peroxide 5% gel = \$13/60 gm. 10% = \$21/60gm	Exclude OTC.		

EBD Summary of MS Drug Coverage
 Jill Johnson, Pharm.D., BCPS
 11/4/13

Multiple Sclerosis Utilization 2013 Q2

Product	Util Member	#rxs	Quantity	Days supply	AWP cost	Ingr cost	Disp fee	Net plan cost	avg net plan cost	% total plan cost	market share	daCon	Cost/unit	cost/day	copay
Copaxone Kit 20mg/mL glatiramer, 20mg SC daily	62	136	151	4,526	\$834,334.00	\$733,413.00	\$174.00	\$726,195.00	\$5,339.67	2.08%	44.3	0.03	\$4,809.24	\$160.45	\$54.35
Rebif interferon B1a 44mcg SC TIW	16	43	282	1320	\$244,983.00	\$213,605.00	\$10.50	\$211,314.00	\$4,914.28	0.61%	14.01	0.21	\$749.34	\$160.09	\$53.52
Rebif Rebidose	2	4	24	112	\$20,772.00	\$18,072.00	\$0.00	\$17,092.00	\$4,272.93	0.05%	1.3	0.21	\$712.16	\$152.61	\$245.00
Avonex interferon B1a 30mcg IM qW	14	35	45	1092	\$191,995.00	\$168,683.00	\$45.50	\$167,558.00	\$4,787.38	0.48%	11.4	0.04	\$3,723.52	\$153.44	\$33.44
Avonex Pen interferon B1a 30mcg IM qW	5	8	8	224	\$39,338.00	\$34,365.00	\$3.40	\$34,129.00	\$4,266.10	0.10%	2.61	0.04	\$4,266.10	\$152.36	\$29.93
Betaseron interferon B1b 0.25mg SC QOD	13	27	392	790	\$144,532.00	\$127,394.00	\$42.00	\$125,816.00	\$4,659.86	0.36%	8.79	0.5	\$320.96	\$159.26	\$60.00
Gilenya fingolimod 0.5mg cap daily	14	36	1008	1008	\$200,240.00	\$167,307.00	\$17.50	\$165,164.00	\$4,589.90	0.47%	11.73	1	\$163.85	\$163.85	\$60.01
Aubagio teriflunomide 7 or 14mg tab daily	7	12	336	336	\$54,370.00	\$46,758.00	\$0.00	\$46,393.00	\$2,866.08	0.13%	3.91	1	\$138.07	\$138.07	\$30.42
Tecfidera dimthyl fumarate 240mg DR cap BID	3	5	300	150	\$27,000.00	\$23,220.00	\$0.00	\$21,332.00	\$4,266.48	0.06%	1.63	2	\$71.11	\$142.22	\$377.60
Tecfidera Starter Pack	1	1	60	30	\$5,400.00	\$4,644.00	\$0.00	\$4,614.00	\$4,614.00	0.01%	0.33	2	\$76.90	\$153.80	\$30.00
Totals	137	307	2606	9588	\$1,762,964.00	\$1,537,461.00	\$292.90	\$1,519,607.00	\$4,949.86	4.35%	100.01				

Current Coverage Policies:

Drug	PA criteria
Avonex	1. Dx of multiple sclerosis.
Betaseron	1. Dx of multiple sclerosis.
Copaxone	1. Dx of multiple sclerosis.
Rebif	1. Dx of multiple sclerosis.
Gilenya (fingolimod)	1. Dx of relapsing multiple sclerosis. 2. Pt must have tried and shown intolerance to Betaseron, Rebif, or Extavia AND to Copaxone. 3. May NOT take concomitantly with interferon or w/ Copaxone.
Aubagio (teriflunomide)	1. Dx of relapsing form of multiple sclerosis. 2. Must have experienced at least 2 relapses in the previous 2 y or 1 relapse in the preceding 1y. QL of #31 d supply. Dose optimization should be applied. 1tab/1day.
Tecfidera (dimethyl fumarate)	1. Dx of relapsing form of MS. 2. Pt must have experienced at least 1 relapse over the previous y 0 had an MRI in the previous 6w showing at least 1 gadolinium-enhancing lesion at the time of initial request for the drug. 3. Baseline score of 0-5.0 on the Expanded Disability Status Scale. QL of #14 for the 120mg dosage form. Dose is 120mg BID X7d, then increased to 240mg BID. QL of #62 for each fill. NO more than a 31 d supply.

Filippini G, Del Giovane C, Vacchi L, D'Amico R, et al. Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD008933. DOI: 10.1002/14651858.CD008933.pub2.

Summary:

- High quality evidence shows natalizumab and IFNB-1a (Rebif) can reduce relapses and disability progression compared to placebo. They are more effective than IFNB-1a (Avonex) in RRMS. Natalizumab can induce progressive multifocal leukoencephalopathy, especially with more than 2 y of treatment.
- IFNB-1b (Betaseron), glatiramer acetate, and mitoxantrone may also prevent relapse and disability progression in people with RRMS. These treatments are associated with possible medium and long-term side effects, and the risk-benefit balance might be unfavorable.
- IFNB1a (Avonex), IV immunoglobulins, cyclophosphamide, and long-term corticosteroids have an unfavorable risk-benefit balance for RRMS patients.
- Azathioprine's risk-benefit balance evidence is insufficient.
- For PrMS, no study showed efficacy in preventing disability progression in PrMS with IFNB-1b (Betaseron), IFNB1a (Avonex and Rebif), glatiramer, mitoxantrone, methotrexate, cyclophosphamide, IV immunoglobulins, and long-term corticosteroids.
- Risk-benefit for all these treatments beyond 2 y is uncertain. Also 70% of the included studies were manufacturer-sponsored.

Fingolimod, teriflunomide, and dimethyl fumarate are too new to have been included in the systematic reviews to date.

Recommendation:

- 1. Provide incentive to MS patients to take Rebif.**
- 2. Consider step therapy with Rebif for subsequent access to glatiramer, fingolimod, teriflunomide, or dimethyl fumarate.**
- 3. Fingolimod (Gilenya): Require Dx of relapsing MS. Deny coverage for overlapping days supply with other MS therapy (interferon, natalizumab, glatiramer, mitoxantrone, immunoglobulins, corticosteroids/ACTH, fingolimod, or dimethyl fumarate. (Should not take both drugs concomitantly.)**

- QL of 1/1
 - limit to a 31 days supply
4. **Teriflunomide (Aubagio):** Require Dx of relapsing form of multiple sclerosis, must have experienced at least 2 relapses in the previous 2 y or 1 relapse in the preceding 1y, no overlapping days supply with other MS therapy (interferon, natalizumab, glatiramer, mitoxantrone, immunoglobulins, corticosteroids/ACTH, fingolimod, or dimethyl fumarate.
- Consider excluding the 14mg form. (The 14mg did not provide significant improvement over the 7mg in the clinical trial.) (O'Connor P, Wolinsky JS, Confavreux C, Comi G, et al. Randomized trial of oral teriflunomide for relapsing multiple sclerosis. N Engl J Med. 2011;365:1293-303.)
 - QL of 1/1
 - Limit to a 31 days supply
5. **Dimethyl fumarate (Tecfidera):** Require Dx of relapsing form of MS, must have experienced at least 1 relapse over the previous year OR had an MRI in the previous 6w showing at least 1 gadolinium-enhancing lesion at the time of initial request for the drug.
- QL of #14 for the 120mg dosage form. Dose is 120mg BID X7d, then increased to 240mg BID.
 - QL of #62 for each fill.
 - Limit to a 31 d supply.

Pharmacy Network	Pharmacy Type	Claim Count	Ing Cost MAC @ 100%	Ing Cost MAC @ 110%	Ing Cost Savings	Plan cost MAC @ 100%	Current Client Amount Due	Plan Cost Savings
AR	Retail	1,458,210	\$ 30,386,070.11	\$ 33,425,361.96	\$ 3,039,291.85	\$ 23,640,560.68	\$ 26,445,798.86	\$ 2,805,238.18
AR		1,458,210	\$ 30,386,070.11	\$ 33,425,361.96	\$ 3,039,291.85	\$ 23,640,560.68	\$ 26,445,798.86	\$ 2,805,238.18

Specialty Drug List

This is a listing by therapy of specialty medications that BrioVax Specialty Pharmacy can provide or facilitate access and is subject to change. Products all capitalized are preferred products on the Catamaran National Formulary, lower case products are generics, and capitalized products are specialty brands.

ACROMEGALY

octreotide acetate
Sandostatin
Sandostatin LAR
Somatuline Depot
Somavert*

ALPHA-1 ANTITRYPSIN DEFICIENCY

Aralast*
Glassia*
Prolastin*

BOTULINUM TOXINS

Botox
Dysport*
Myobloc
Xeomin

CROHN'S DISEASE

Cimzia
HUMIRA
Kineret
Remicade

CRYOPYRIN- ASSOCIATED PERIODIC SYNDROMES

Arcalyst*
Ilaris*

CYSTIC FIBROSIS

Cayston*
Kalydeco*
Pulmozyme
Tobi

ENZYME DEFICIENCY OR LYSOSOMAL STORAGE DISEASE

Adagen*
Aldurazyme*
Ceredase
Cerezyme
Cystadane*
Elaprase*
Elelyso*
Fabrazyme*
Lumizyme*
Myozyme*
Naglazyme*
Orfadin*
Sucraid*
Vpriv*
Zavesca*
Zemaira*

GROWTH HORMONE & RELATED DISORDERS

Genotropin
Humatrope
NORDITROPIN
NUTROPIN
Omnitrope
Saizen
Serostim
Tev-Tropin
Zorbtive

IGF-1 Deficiency

Increlex*

HEMATOPOIETICS

Aranesp
Epogen
Leukine
Mozobil
Neulasta
Neumega
Neupogen
Procrit

HEMOPHILIA & RELATED BLEEDING DISORDERS

Advate
Alphanate
Alphanine SD
Bebulin
Bebulin VH
Benefix
Corifact*
Feiba NF
Feiba VH
Helixate FS
Hemofil M
Humate-P
Koate-DVI
Kogenate FS
Monoclate-P
Mononine
Novoseven RT
Profilnine SD
Recombinate
Riastap
Stimate
Wilate
Xyntha

HEPATITIS B

Baraclude
Epivir HBV
Hepsera
Lamivudine
Tyzeka

HEPATITIS C

Copegus
INCIVEK
Infergen
PEGASYS
PEG-INTRON
Rebetol
Ribapak
Ribasphere
Ribatab
ribavirin
VICTRELIS

HEREDITARY ANGIOEDEMA

Berinert*
Cinryze*
Firazyr*
Kalbitor*

HIV

Aptivus
Atripla
Combivir
Complera
Crixivan
didanosine
Edurant
Egrifta*
Emtriva
Epzicom
Fuzeon

HIV (CONT.)

Intelence
Invirase
Isentress
Kaletra
Lexiva
Norvir
Prezista
Rescriptor
Retrovir
Reyataz
Selzentry
Stavudine
Stribild
Sustiva
Trizivir
Truvada
Videx
Viracept
Viramune
Viread
Zerit
Ziagen
zidovudine

HORMONAL THERAPIES

Eligard
Firmagon
leuprolide acetate
Lupron Depot
Lupron Depot-PED
Makena*
Supprelin LA*
Synarel
Trelstar
Vantas
Zoladex

IMMUNE DEFICIENCY & RELATED DISORDERS

Bivigam
Carimune NF
Flebogamma
Gamastan S/D
Gammagard
Gammaked
Gammaplex
Gamunex
Hizentra*
Octagam
Privigen
Winrho SDF

IMMUNE THROMBOCYTOPENIC PURPURA

Nplate*
Promacta*

INFERTILITY

Bravelle
Cetrotide
chorionic gonadotropin
Follistim AQ
ganirelix acetate
Gonal-F
Luveris
Menopur
Novarel
Ovidrel
Pregnyl
progesterone
Repronex

IRON DEFICIENCY

Ferrlecit
Nulecit

IRON OVERLOAD

Exjade*
Ferriprox*

MACULAR DEGENERATION

Eylea*
Lucentis*
Macugen*
Visudyne*

MULTIPLE SCLEROSIS

Ampyra*
Aubagio*

AVONEX

Betaseron

COPAXONE

Extavia
Gilenya*

REBIF

Tysabri*

ONCOLOGY - INJECTABLE

BriovaRx has access to various injectable oncology medications. Please contact the pharmacy for more information.

ONCOLOGY – ORAL

Afinitor
Bosulif
Caprelsa*
cyclophosphamide
Erivedge*
etoposide
Gleevec
Hycamtin*
Inlyta*
Jakafi*

ONCOLOGY – ORAL (CONT.)

Matulane*
Myleran
Nexavar*
Revlimid*
Sprycel
Stivarga*
Sutent
Tarceva
Targretin
Tasigna
Temodar
Thalomid
tretinoin
Tykerb*
Votrient*
Xalkori*
Xeloda
Xtandi*
Zelboraf*
Zolanza
Zytiga*

ONCOLOGY – SUPPORTIVE CARE

Aredia
Elitek
pamidronate
Xgeva
Zometa

OSTEOARTHRITIS

Euflexxa
Hyalgan
Orthovisc
Supartz
Synvisc
Synvisc One

OSTEOPOROSIS

Forteo
Prolia
Reclast

PLAQUE PSORIASIS

Amevive
ENBREL
HUMIRA
Remicade
Stelara

PSORIATIC ARTHRITIS

ENBREL
HUMIRA
Remicade
Simponi

PULMONARY ARTERIAL HYPERTENSION

Adcirca
epoprostenol sodium*
Flolan*
Letairis*
Remodulin*
Revatio
Tracleer*
Tyvaso*
Veletri*
Ventavis*

RESPIRATORY SYNCYTIAL VIRUS

Synagis*

RHEUMATOID ARTHRITIS

Actemra*
Cimzia
ENBREL
HUMIRA
Kineret
Orencia
Remicade
Simponi
Xeljanz

TRANSPLANT

Cellcept
cyclosporine
Gengraf
mycophenolate mofetil
Myfortic
Neoral
Nulojix
Prograf
Rapamune
Sandimmune
tacrolimus
Zortress

OTHER THERAPIES

Acthar HP*
Benlysta
Korlym*
Krystexxa*
Kuvan*
Sabril*
Samsca*
Soliris*
Vivitrol*
Xenazine*
Xiaflex*
Xolair*

Additional Information:

General Questions
[1.855.4Briova](tel:18554Briova)
[\(1.855.427.4682\)](tel:18554274682)

Compounded Medication Questions
[1.800.951.0175](tel:18009510175)

Fibric Acid Derivatives - June 1, 2013 through August 31, 2013

Label Name	Util Members	# of Rxs	Quantity	Days Supply	Ingred Cost	Disp Fee	Total Rx Cost	Plan Paid	Member Paid	Plan Paid/Unit	RP/Unit	Savings/Unit	Total Savings
<i>gemfibrozil 600mg</i>	586	1151	78788	41248	\$31,797.00	\$4,886.00	\$36,683.00	\$21,920.00	\$14,763.00	\$0.28			
Tricor 145mg	26	38	1320	1320	\$8,084.00	\$128.50	\$8,212.50	\$4,785.00	\$3,427.50	\$3.63	\$0.28	\$3.35	\$4,415.40
Tricor 48mg	3	6	180	180	\$378.00	\$21.00	\$399.00	\$225.00	\$174.00	\$1.25	\$0.28	\$0.97	\$174.60
<i>fenofibrate 145mg Tab</i>	386	837	28692	28631	\$114,903.00	\$3,587.50	\$118,490.50	\$107,242.00	\$11,248.50	\$3.74	\$0.28	\$3.46	\$99,208.24
<i>fenofibrate 130mg Cap</i>	39	79	2550	2550	\$15,416.00	\$318.50	\$15,734.50	\$14,707.00	\$1,027.50	\$5.77	\$0.28	\$5.49	\$13,993.00
<i>fenofibrate 160mg Tab</i>	596	1362	46659	46509	\$92,902.00	\$5,876.00	\$98,778.00	\$80,242.00	\$18,536.00	\$1.72	\$0.28	\$1.44	\$67,177.48
<i>fenofibrate 48mg Tab</i>	31	63	2220	2130	\$3,046.00	\$263.00	\$3,309.00	\$2,544.00	\$765.00	\$1.15	\$0.28	\$0.87	\$1,922.40
<i>fenofibrate 54mg Tab</i>	51	116	3993	3843	\$2,789.00	\$472.50	\$3,261.50	\$1,780.00	\$1,481.50	\$0.45	\$0.28	\$0.17	\$661.96
<i>fenofibrate 43mg Cap</i>	2	5	150	150	\$314.00	\$20.50	\$334.50	\$285.00	\$49.50	\$1.90	\$0.28	\$1.62	\$243.00
<i>fenofibrate 134mg Cap</i>	174	377	13240	13240	\$22,721.00	\$1,617.50	\$24,338.50	\$19,753.00	\$4,585.50	\$1.49	\$0.28	\$1.21	\$16,045.80
<i>fenofibrate 200mg Cap</i>	41	91	3090	3090	\$8,123.00	\$383.50	\$8,506.50	\$7,486.00	\$1,020.50	\$2.42	\$0.28	\$2.14	\$6,620.80
<i>fenofibrate 67mg Cap</i>	6	12	450	360	\$260.00	\$54.00	\$314.00	\$194.00	\$120.00	\$0.43	\$0.28	\$0.15	\$68.00
Antara 130mg Cap	19	37	1172	1172	\$7,958.00	\$125.50	\$8,083.50	\$6,109.00	\$1,974.50	\$5.21	\$0.28	\$4.93	\$5,780.84
Lipofen 150mg Cap	24	51	1530	1530	\$6,784.00	\$174.50	\$6,958.50	\$3,929.00	\$3,029.50	\$2.57	\$0.28	\$2.29	\$3,500.60
Fenoglide 120mg Tab	6	10	420	420	\$3,651.00	\$35.00	\$3,686.00	\$2,846.00	\$840.00	\$6.78	\$0.28	\$6.50	\$2,728.40
	1404	members affected						\$274,047.00	\$9,271.50			Savings/Qtr	\$222,540.52
												Annualized	\$890,162.08

Convenience Kit Policy:

As new drugs are released to the market through Medispan, those drugs described as “kits” will not be considered for inclusion in the plan and will therefore be excluded products unless the product is available solely as a kit. Kits typically contain, in addition to a pre-packaged quantity of the featured drug(s), items that may be associated with the administration of the drug (rubber gloves, sponges, etc.) and/or additional convenience items (lotion, skin cleanser, etc.). In most cases, the cost of the “kit” is greater than the individual items purchased separately.

Medical Food Policy:

Medical foods will be excluded from the plan unless two sources of peer-reviewed, published medical literature supports the use in reducing a medically necessary clinical endpoint.

A medical food is defined below:

A medical food, as defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is “a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”

FDA considers the statutory definition of medical foods to narrowly constrain the types of products that fit within this category of food. Medical foods are distinguished from the broader category of foods for special dietary use and from foods that make health claims by the requirement that medical foods be intended to meet distinctive nutritional requirements of a disease or condition, used under medical supervision, and intended for the specific dietary management of a disease or condition. Medical foods are not those simply recommended by a physician as part of an overall diet to manage the symptoms or reduce the risk of a disease or condition, and all foods fed to sick patients are not medical foods. Instead, medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in a natural state) for a patient who is seriously ill or who requires use of the product as a major component of a disease or condition’s specific dietary management.

Cough & Cold Policy:

As new cough and cold products enter the market, they are often simply re-formulations or new combinations of existing products already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new cough and cold products are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new cough and cold products to “excluded” unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.

Multivitamin Policy:

As new vitamin products enter the market, they are often simply re-formulations or new combinations of vitamins/multivitamins in similar amounts already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new vitamins are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new vitamin/multivitamin products to “excluded” unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.

Oral Contraceptives (OC) Policy:

OCs which are new to the market may be covered by the plan with a zero dollar, tier 1, 2, or 3 copay, or may be excluded. If a new-to-market OC provides an alternative product not similarly achieved by other OCs currently covered by the plan, the DUEC will consider it as a new drug. IF the drug does not offer a novel alternative or offers only the advantage of convenience, it may not be considered for inclusion in the plan.

DUEC Jul 22-Sept 30 2013								
DRUG NAME	Generic	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	Connie Notes	Jill's Notes	DUEC Vote Nov 4, 2013	IB Vote
Lo Minastrin Pak FE	10mcg EE, 1mgNorethindrone. 24 active, 4 Fe(without therapeutic use).	\$99/28 days	Oral contraceptive			OC policy. Could exclude. 10mcg EE, 1mgNorethindrone. 24 active, 4 Fe(without therapeutic use).		
Mirvaso gel	brimonidine 0.33%	\$296/30gm	For topical treatment of the facial erythema(redness) of rosacea in adults 18 years or older	Metronidazole 0.75% cm = \$181/45gm		T3. QL: 1 tube/month. Available strength 0.33% of brim free base. For topical non transient facial erythema of rosacea in adults 18 and older. Apply pea- so/ize amount QD to each of 5 areas of the face avoid eyes and lips.		
Tivicay 50mg tabs (SPECIALTY)	Dolutegravir 50mg tablet	50mg daily = \$1,410. Max dose = 100mg/day	Tx of HIV infection	Raltegravir		T3PA. Efficacy in INSTI-resistant cases of HIV.T3PA; Must be taken in combination with HAART therapy.		
Simponi Aria Sol 50mg/4ml(SPECIALTY DRUG)	Golimumab	\$1,380/50mg	New dosage form given by 30 minute IV infusion by a HCP every 8 weeks, after 2 starter dose, given 4 weeks apart for moderate to severe RA, taken w/methotrexate	Simponi 50mg/0.5ml for subq inj = \$3,042	Most likely covered under medical benefit	Added to PA criteria.		
Astagraf XL capsules 0.5, 1, or 5mg capsules (SPECIALTY DRUG)	Tacrolimus XR	\$71 - \$713/30 days	Extended-release form (given once daily) of tacrolimus for transplant rejection prophylaxis	Tacrolimus 5mg immediate release twice daily = \$1380/30 days		Exclude. No benefit over immediate-release, which is generically available.		
Brisdelle 7.5mg	Paroxetine	\$161/30 days	7.5mg po at bedtime for moderate to severe hot flashes associated w/menopause	AWP generic paroxetine 10mg = 2.53/10mg		Exclude. Generics available.		
Butrans	buprenorphine patch		chronic pain. 1 patch every 7 days	generic & brand fentanyl patch		Exclude. Cheaper alternatives exist		
Enteragam Powder 5GM		\$60/5gm	Prescription medical food product for management of diarrhea - predominant irritable bowel syndrome.			Exclude. SERUM-DERIVED BOVINE IMMUNOGLOB/PROTEIN ISOLATE 5 GM PACKET. For enteropathy. Only clinical trial was open-label with 8 pts on the manufacturer's website.		
Epaned Solution	enalapril 1mg/ml enalapril for oral solution	\$342/150ml bottle	Tx of heart failure or hypertension	Enalapril tabs: 2.5mg/\$0.80 5mg/\$1.02 10mg/\$1.07		Exclude. Tablets able to be crushed.		
Fabior Aer 0.1%	TAZAROTENE (ACNE) FOAM 0.1%	\$340/50gm can; \$6.816/gram, 100g & 50g can	Tazarotene (acne) foam	Tazorac Cream 0.05% 60gm tube = \$558 Tazorac Gel 0.05% 30gm tube = \$279		Exclude. Cheaper alternatives exist.		
Fioricet cap w/Cod	butalbital/APAP/Caffeine/Codeine 50/300/40/30mg	\$5.70/capsule	Treatment of headache	Multiple generic versions of butalbital/APAP/Caffeine/Cod (50/325/40/30). Cost - \$1.49/cap		Exclude. Reformulated for APAP. Generic available.		
Gilotrif (20,30, & 40mg tabs)	AFATINIB DIMALEATE TAB 20 MG, 30, 40mg (BASE EQUIVALENT)	\$6,660/30 days.	Approved for first-line tx of metastatic non-small cell lung cancer whose tumors have epidermal growth factor exon 19 deletions or exon21 substitution mutations as detected by an FDA- approved test.		All strengths are \$222/cap. If coverage is elected, QL of 30/30 days would be recommended	Exclude. No OS data benefit. PFS about 3m > than placebo. QoL improvements vs. placebo, but not beneficial (cough, dyspnea, pain).		
Injectafer injection 750mg/15ml.	Ferric Carboxymaltose IV solution	\$958/750mg dose	For iron-deficiency anemia (2 - 750mg dose given slow IV push or IV infusion separated by at least 7 days)		Most likely covered under medical benefit	Medical infusion.		
Naftin Gel 2% (new strength)	NAFTIFINE HCL GEL 2%	\$340/45gm	Antifungal	Clotrimazole 1% 45gm - \$48. Ketoconazole cream 60gm - \$43. Tolnaftate 1% cream 30gm - \$10		Exclude. Cheaper alternatives exist. Naftifine comes in 1 & 2% gel and cream as Naftin brand. Alternatives are not naftin.		
Podiarn Capsules		\$34/bottle of 60	Dietary management product (medical food)		L-methylfolate-B-12-B-6-Alpha lipoic AC Capsules	Exclude. No data		
Riax 5.5 or 9.5%	(benzoyl peroxide foam)	\$330/can	Treatment of acne	Benzoyl peroxide 5% gel = \$13/60 gm. 10% = \$21/60gm	Benzoyl peroxide foam 5.3% and 9.8% currently set to reject	Exclude OTC.		
Selrx Shampoo	2.3% (selenium sulfide-pyrithione zine-urea shampoo)	\$360/180ml bottle	Tx of dandruff, seborrheic dermatitis, tinea versicolor	Generic strengths of 2.25% available		Exclude. Cheaper alternative exists. Selenium sulfide generic shampoo 1% is OTC. AlsoDandrex. This is 2.3% and is Rx only.		
Tretin-X crean	tretinoin cream 0.075% - new strength	\$284/35gm tube	Tx of acne			Exclude		

Trokendi XR	topiramate oral extended release caps 25,50,100, or 200mg -	Dose of extended release is 200-400mg/day = \$684-\$1,367/30 days	Oral antiepileptic	generic immediate release topiramate 200mg = \$477		Cheaper alternatives exist. Exclude.		
Utopic Cream	urea cream 41%	\$420/227 gm bottle	Treatment of Xerosis plus pruritus, irritation, or inflammation, keratolytic and dry skin.	Generic strengths of 10-50% available.	Plan currently has urea cream 39,43, and 45% set to reject	Exclude. Cheaper alternative exists.		
Vitafol caps ultra		\$26/30 caps	Prenatal vitamins	various generics available		Exclude. Vitamin Policy.		
Vytone 1-1.9% cream	hydrocortisone 10mg/iodoquinol 10mg/g of cream	\$200/box of 30	Topical antifungal			Exclude. only possibly effective. Unusual prescribing info: "INDICATIONS AND USAGE Based on a review of a related drug by the National Research Council and subsequent FDA classification for that drug, the indications are as follows: "Possibly" Effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis, bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis, intertrigo. Final classification of the less-than-effective indications requires further investigation."		