



P I N A L ♦ C O U N T Y

Wide open opportunity

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DRUG REFORMULATIONS

Manufacturers frequently launch a "new and improved" formulation just before a drug gets generic competition.

Some are improvements...some are not.

Requip XL can be given once a day for Parkinson's...instead of TID for generic ropinirole. Requip XL may cause less on-off fluctuations...but it costs 3 times more than generic.

Moxatag will be a new once-daily amoxicillin for strep throat. But there's no proof it's better than a similar dose of regular amoxicillin dosed once a day.

Sular now comes in lower strengths that work the same as the old ones. But of course, nisoldipine generics are now not substitutable for the new Sular. Sound familiar?

Tricor has been reformulated several times...each time in different strengths...each time a step ahead of impending generics. Now no generic fenofibrates are substitutable for the current Tricor.

Explain how products are confused...especially when doses overlap.

Both Effexor and Effexor XR come in 37.5 and 75 mg tabs...both Depakote and Depakote ER come in 250 and 500 mg tabs. Note that the new divalproex generics match up with Depakote...NOT the ER version.

Explain that there is no standard meaning to all the "extended-release" suffixes...CR, SR, XL, ER, LA, etc. They don't indicate the release properties or dosing frequency.

Point out that Coreg CR is given once daily...Zyflo CR is BID. Ambien CR and Paxil CR are NOT longer-acting than their originals. Opana ER is given BID...Depakote ER once daily.

SUPPLEMENTS

There's confusion about the different oral iron products.

Many are promoted as better tolerated or absorbed...but not all of these claims can be substantiated.

Ferrous sulfate, ferrous gluconate, and ferrous fumarate contain different percentages of elemental iron. Efficacy and tolerability are similar for equal doses of elemental iron.

Carbonyl iron (Ferralet 90, Feosol Carbonyl Iron caplets, etc) is pure elemental iron that's absorbed slowly to reduce toxicity.

Recommend these if there are concerns about accidental ingestion by children.

Polysaccharide-iron complex (Niferex-150, etc) is iron bound to carbohydrates. It's promoted to improve tolerability, but there's no proof that there's a significant difference.

Heme iron polypeptide (Proferrin ES, etc) is derived from hemoglobin in animal red blood cells. It's better absorbed than the inorganic iron salts, especially when taken with food.

Recommend ferrous sulfate first-line...or carbonyl iron if toxicity is a concern.

Tell patients that GI tolerability is linked to the iron DOSE...not the salt. Enteric-coated and controlled-release preps might reduce nausea...but at the expense of lower absorption.

Vitamin C increases iron absorption, but most combo products don't contain enough. Over 200 mg is needed to increase absorption of 30 mg elemental iron.

Physician Detailing

A new code of conduct will change how companies market drugs.

You'll see fewer pens, mugs, notepads, and other giveaways...and more limits on restaurant meals and promotional events.

The new code is VOLUNTARY...self-imposed by the drug companies' own association, PhRMA. But most big drug companies will comply...to head off MANDATORY regulation.

Interestingly, most physicians think they aren't influenced by these gifts. Only 16% think reps influence their OWN prescribing...but 61% say it influences their colleagues.

Expect your reps to follow these new rules:

Gifts. Only educational items...textbooks, subscriptions, patient education materials, etc...worth up to \$100...are okay.

Meals. Modest meals along with education in the pharmacy, office, or facility will replace restaurant outings with reps.

Educational talks. Drug companies can still sponsor CE and educational programs at restaurants, but the CE provider or organizer will make the arrangements...not the drug company.

Drug samples. These are still okay. No new restrictions.

Literature. Reps still CAN'T talk about off-label uses...but they CAN hand you reprints of scientifically valid articles in many situations.

Even some experts who are antimarketing see value in reps distributing good published literature about off-label uses.

But beware. Literature might be cherry-picked to emphasize desirable outcomes and omit studies that show no benefit or even harm.

Expect to see more direct-to-consumer ads. They work. About a third of adults ask for an advertised drug...and nearly half get it.

[NoFreeLunch.org](#), [PrescriptionProject.org](#), and others are pushing legislation to rein in drug company influence. You'll also hear more about paying PharmDs to detail doctors to improve prescribing.

Keep in mind that *Pharmacist's Letter* and *Prescriber's Letter* never take advertising. If you want an objective analysis of a drug or therapy, ask us. We'll send you our published analyses...or consider the subject for future research and publication.

MEN'S HEALTH

GlaxoSmithKline reps will promote using *Avodart* (dutasteride) with *Flomax* (tamsulosin) for benign prostatic hyperplasia (BPH).

They'll cite new evidence that the combo improves BPH symptoms better than either drug alone. The FDA also just approved the combo for men with symptomatic BPH and an enlarged prostate.

Many prescribers already use *Avodart* or *Proscar* (finasteride) with an alpha-blocker (*Flomax*, *Cardura*, *Hytrin*).

Alpha-blockers provide rapid symptom relief...*Proscar* and *Avodart* reduce prostate size and prevent disease progression.

Suggest combo therapy for men at high risk for BPH progression. These are men 50 and over with urinary symptoms...PSA level of 1.5 ng/mL or greater...and an enlarged prostate.

Watch for tamsulosin generics later next year...plus eventually a combo *Avodart*/tamsulosin tablet.

ANTITHROMBOTICS

New recommendations will finally clarify what to do about aspirin, clopidogrel, NSAIDs, and warfarin when patients need surgery.

These are the first comprehensive guidelines for perioperative management of these drugs from the Amer College of Chest Physicians.

They address various scenarios. But it always comes down to weighing the risk of bleeding if the drug is continued...compared to the risk of thrombosis if it's stopped.

Aspirin can be continued before and after surgery for patients with a high thrombosis risk...such as a recent stent or heart attack.

Also continue it for procedures with a low risk of bleeding...such as minor dental, dermatologic, or cataract surgeries.

If aspirin is held, recommend stopping it 7 to 10 days prior to surgery instead of just 5 days...to minimize antiplatelet effects.

Clopidogrel is tough. It should be stopped 7 to 10 days before surgery...BUT many stent patients should continue it to prevent clots. Surgeons and internists will debate whether it's safer to delay surgery until the patient is finished taking clopidogrel or take the chance of increased bleeding.

NSAIDs should be stopped about 5 half-lives before surgery. This is just one day for ibuprofen...and 10 days for nabumetone.

Recommend not restarting any antiplatelet drugs until the next morning...or about 24 hours after surgery.

Warfarin can be continued for minor dental or derm procedures.

For more invasive procedures, stop warfarin about 5 days prior...to normalize INR and decrease bleeding.

Suggest restarting warfarin 12 to 24 hours after surgery...it takes about 5 days to take full effect.

Bridge therapy with one of the heparins can be used to bridge the gap between when warfarin is stopped and restarted.

Suggest therapeutic doses of a low-molecular-weight heparin (LMWH) for patients at moderate or high risk of thrombosis.

Suggest low-dose LMWH, or NO therapy, for low-risk patients.

In general, start bridge therapy about 2 days after stopping warfarin...hold it for surgery...then resume it 24 to 72 hours after surgery until warfarin is restarted and becomes therapeutic.

For more info, see our *Detail-Document, Managing Warfarin and Antiplatelet Drugs Perioperatively.*

Restless Legs Syndrome

Requip is the first drug approved for restless legs syndrome.

About 10% of Americans get these overpowering urges to move their legs...especially when at rest.

Ropinirole (*Requip*) is a dopamine agonist...similar to pramipexole and pergolide. They're thought to help by boosting dopamine, a neurotransmitter responsible for controlling movement.

These are often effective for moderate to severe symptoms.

Advise patients to start with a low dose and increase slowly.

For *Requip*, suggest starting with 0.25 mg/day, then increase weekly as needed up to 4 mg/day.

Caution patients about nausea... dizziness... and hypotension.

Levodopa/carbidopa can help intermittent symptoms because it's short-acting. But its effects can wear off before morning...or it can cause worse symptoms early the next day.

Benzodiazepines (clonazepam, etc) can be used occasionally... to help patients sleep in spite of their restless legs.

Gabapentin helps some patients who have pain along with their restless legs.

Opiates are sometimes used before bed...but daytime drowsiness and constipation limit their usefulness.

Recommend avoiding SSRIs...tricyclic antidepressants...sedating antihistamines...and lithium. These drugs worsen symptoms.

Remind patients that symptoms can also be exacerbated by caffeine...smoking...and alcohol.

If you need, get our chart that compares medications and dosing for restless legs syndrome at www.pharmacistsletter.com.

RUMOR VS TRUTH

RUMOR: Hyoscyamine (*Levsin, Levbid, etc*) is going off the market

TRUTH: All hyoscyamine products are unapproved. They came on the market before FDA approval was required. The FDA hasn't taken any action against these products...yet. But several companies have voluntarily withdrawn their products.

This has put a squeeze on the few remaining companies, creating a drug shortage.

There are only a handful of hyoscyamine products currently marketed. But these are either not available through some wholesalers and/or the cost of these may be prohibitive for some patients.

Ethex has all hyoscyamine products on long-term back order with no release date. Alaven's *Levsin* and *Levbid* are expected to be available by the end of June 2008.

In the meantime, encourage patients using one of these products to discuss other options with their provider.

Suggest dicyclomine, *Donnatal*, or *Librax* for stomach cramps or spasms.

RUMOR: Eating chia seeds is heart healthy.



TRUTH: Chia seeds are well known for sprouting the fast-growing "hair" on little clay *Chia Pets*. Now people are eating the nutty-flavored grains in hopes of reducing their risk of heart disease.

Chia reportedly contains more omega-3 fatty acids than flaxseed, more fiber than bran, and more protein than soy. It also contains calcium, magnesium, iron, and antioxidants.

The whole grain is harvested from *Salvia hispanica*, a member of the mint family that grows in Mexico and South America.

Preliminary data shows that type 2 diabetes patients who eat 37 grams/day of a variety of chia called Salba for 3 months will see drops in blood pressure, A1c, and other cardiovascular risk factors.

The chia craze is really taking off since its recent debut on Oprah. Some people take chia oil supplements...others eat the seeds whole or use them to make bread, muffins, drinks, and more. There's even a chia cookbook available on the internet.

Expect to see chia pop up in nutrition bars, baked goods, and snack foods. Salba Smart Natural Products already has a line of foods made from ground Salba...including salsa, chips, tortillas, and pretzels.

Tell people chia is a good alternative to replace other grains in a balanced diet...and to look for the Salba variety.

But caution people with high triglycerides to keep tabs on their lipid levels. Chia contains a high concentration of alpha-linolenic acid...which MIGHT increase triglyceride levels and potentially worsen hypertriglyceridemia.

Vytorin Update:

On September 3, 2008, results from The Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trial and a meta-analysis looking at the link between ezetimibe and cancer were both published in the New England Journal of Medicine (NEJM). An Issues Document was developed in order to summarize the findings from these studies.

Early Communication About an Ongoing Safety Review of Ezetimibe/Simvastatin (marketed as Vytorin), Simvastatin (marketed as Zocor) and Ezetimibe (marketed as Zetia) FDA Investigates a Report from the SEAS Trial

This information reflects FDA's current analysis of available data concerning these drugs. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug product and the emerging safety issue. Nor does it mean that FDA is advising health care professionals to discontinue prescribing this product. FDA is considering but has not reached a conclusion about whether this information warrants any regulatory action. FDA intends to update this document when additional information or analyses become available.

FDA is investigating a report from the SEAS trial (Simvastatin and Ezetimibe in Aortic Stenosis) of a possible association between the use of Vytorin (a combination of simvastatin plus ezetimibe) and a potentially increased incidence of cancer. Simvastatin (Zocor), a "statin" class drug approved in 1991, decreases production of cholesterol by the liver and is indicated to reduce LDL-cholesterol levels and reduce the risk of cardiovascular events such as heart attack and stroke. Ezetimibe (Zetia), approved in 2002, inhibits the absorption of cholesterol in the intestine and is indicated to reduce LDL-cholesterol levels. Vytorin, the combination product approved in 2004, is indicated to reduce LDL-cholesterol levels.

Recently, FDA obtained preliminary results from the SEAS trial. This clinical trial tested whether lowering LDL-cholesterol with Vytorin would reduce the risk of major cardiovascular events, including aortic valve replacement, congestive heart failure, and ischemic cardiovascular events in individuals with aortic stenosis (a tight heart valve). A lower overall cardiovascular risk was not found with Vytorin. However, there was an additional observation that a larger percentage of subjects treated with Vytorin were diagnosed with and died from all types of cancer combined (including skin cancer) when compared to placebo during the 5-year study.

Interim data from two large ongoing cardiovascular trials of Vytorin – the Study of Heart and Renal Protection (SHARP) and the Improved Reduction in High-Risk Subjects Presenting with Acute Coronary Syndrome (IMPROVE-IT) – show no increased risk of cancer with the combination of simvastatin plus ezetimibe. The SHARP trial is expected to be completed in 2010. The IMPROVE-IT trial is scheduled for completion around 2012. Safety data from both of these trials are being evaluated on a regular basis by independent data safety monitoring boards. FDA has determined that, to date, these findings in the SEAS trial plus the interim data from ongoing trials should not prompt patients to stop taking Vytorin or any other cholesterol lowering drug. FDA is aware of previous reports suggesting a link between low on-treatment cholesterol levels and an increased risk of cancer. A 2007 pooled analysis of 16 studies with 23 statin drug arms, published in the *Journal of the American College of Cardiology*, reported an association between the level of LDL-cholesterol achieved and incident cancer in patients receiving a statin.

However, most large prospective studies of statin drugs have reported no difference in cancer incidence between the active and placebo arms. For simvastatin, the Heart Protection Study randomized 20,000 patients to a daily dose of simvastatin 40 mg or placebo for up to 5 years. The incidence rate for cancer was 7.9% in the simvastatin group and 7.8% in the placebo group, and the deaths from cancer occurred at similar rates in both groups.

FDA anticipates receiving a final SEAS study report from the sponsors in about 3 months. Once FDA receives the final study report, it will likely take 6 months to fully evaluate the clinical trial data and other relevant information. As soon as this review is complete, FDA will communicate our conclusions and recommendations to the public.

An elevated LDL-cholesterol level is an established risk factor for heart disease and lowering cholesterol reduces the risk of death from heart disease and stroke. Patients should not stop taking Vytorin or other cholesterol lowering medications and should talk to their doctor if they have questions about whether to continue to take the medication. Until further information is available, healthcare professionals and caregivers should continue to monitor patients taking Vytorin as outlined in the prescribing information.

The FDA urges both healthcare professionals and patients to report side effects from the use of Vytorin to the FDA's MedWatch Adverse Event Reporting program

- on-line at www.fda.gov/medwatch/report.htm
- by returning the postage-paid FDA form 3500, available in PDF format at www.fda.gov/medwatch/getforms.htm to 5600 Fishers Lane, Rockville, MD 20852-9787
- faxing the form to 1-800-FDA-0178
- by phone at 1-800-332-1088

Price Comparisons

FENOFIBRATES					
Drug	Generic or Brand	FORM	STRENGTH	Brand Cost	Generic Cost
ANTARA (Fenofibrate-micronized)	Brand	CAPS	43MG	\$44.70	N/A
		CAPS	130MG	\$134.40	N/A
LOFIBRA (Fenofibrate-micronized)	BRAND--Generic	CAPS	67	\$29.70	\$25.20
		CAPS	134	\$57.30	\$48.90
		CAPS	200	\$89.10	\$76.20
		TABS	54	\$29.70	\$23.70
		TABS	160	\$89.10	\$71.10
TRICOR (Fenofibrate)	Brand	TABS	48	\$42.90	N/A
		TABS	145	\$129.00	N/A
GEMFIBROZIL		TABS	600MG		\$6.60
SULAR (Nisoldipine)					
Drug	Generic or Brand	FORM	STRENGTH	Brand Cost	Generic Cost
SULAR (Nisoldipine)		legally substitute nidoldipine tabs for Sular tabs.			
	Brand	TABS	8MG	\$57.00	N/A
	Brand	TABS	10MG	\$63.00	N/A
	Brand	TABS	17MG	\$72.00	N/A
	Brand-Generic	TABS	20MG	\$72.00	\$65.00
	Brand	TABS	25MG	\$79.00	N/A
	Brand-Generic	TABS	30MG	\$79.00	\$70.00
	Brand	TABS	34MG	\$79.00	N/A
	Brand-Generic	TABS	40MG	\$79.00	\$70.00
AMLODIPINE		TABS	5MG		\$3.90
REQUIP (Ropinerole)					
Drug	Generic or Brand	FORM	STRENGTH	Brand Cost	Generic Cost
REQUIP (Ropinerole)	Brand-Generic	TABS	0.25MG	\$230.00	\$72.00
T.I.D.	Brand-Generic	TABS	0.5MG	\$230.00	\$72.00
	Brand-Generic	TABS	1MG	\$230.00	\$72.00
	Brand-Generic	TABS	2MG	\$230.00	\$72.00
	Brand-Generic	TABS	30MG	\$230.00	\$72.00
	Brand-Generic	TABS	4MG	\$230.00	\$72.00
	Brand-Generic	TABS	5MG	\$230.00	\$72.00
REQUIP XL	Brand	TABS	2MG	\$69.00	N/A
QD			4MG	\$162.00	N/A
			8MG	\$207.00	N/A

Price Comparisons

EFFEXOR AND EFFEXOR XR					
Drug	Generic or Brand	FORM	STRENGTH	Brand Cost	Generic Cost
EFFEXOR (Venlafaxine) T.I.D.	Brand-Generic	TABS	25MG		\$72.00
	Brand-Generic	TABS	37.5MG		\$81.00
	Brand-Generic	TABS	50MG		\$81.00
	Brand-Generic	TABS	75MG		\$85.50
	Brand-Generic	TABS	100MG		\$90.00
EFFEXOR XR QD	Brand	TABS	37.5MG XR	\$100.47	N/A
			75MG XR	\$112.71	N/A
			150MGXR	\$122.66	N/A
Prostate Drugs					
Drug	Generic or Brand	FORM	STRENGTH	Brand Cost	Generic Cost
5-alpha-reductase inhibitors					
PROSCAR (finasteride) QD	Brand-Generic	TABS	5MG		\$42.00
AVODART (dutasteride)	Brand	CAPS	0.5MG	\$92.00	N/A
Alpha-adrenergic blockers					
FLOMAX (Tamsulosin)	Brand	CAPS	0.4MG	\$87-\$175	
CARDURA (Doxazosin)	Brand-Generic	TABS	1mg-8mg		\$10.00
HYTRIN (Terazosin)	Brand-Generic	CAPS	1mg		\$5.70
			2mg		
			5mg		
			10mg		

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