



Policosanol: A Non-Prescription Dietary Supplement to Control Hyperlipidemia

Learning Objectives

1. List the alternative medicines that have been used to lower serum lipids.
2. Explain the mechanism by which policosanol can improve a patient's lipid profile.
3. Summarize the primary evidence that demonstrates the effectiveness of policosanol.
4. Explain to a patient the dangers of discontinuing current therapy to try this alternative approach.

Introduction

The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) recommends aggressive low-density lipid (LDL) lowering therapy in patients with high risk of coronary heart disease.¹ Commonly used drugs to treat hypercholesterolemia are the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) inhibitors (statins), bile acid sequestrants, niacin, and fibric acid derivatives. The side effects of these agents may make them unacceptable therapy options in some patients. Additionally, some patients may be reluctant to be treated with chemically derived products.² Policosanol is a natural product which has been shown to have lipid lowering effects.

A number of alternative medications, or herbal products, have been reported to be useful in lowering serum lipids. Artichoke leaf, garlic, ginger, guggul, hawthorn, policosanol, red yeast rice, soy proteins, turmeric (*curcuma longa*) and viscous fiber have all been promoted for reducing cholesterol and triglycerides. There is limited safety and efficacy evidence, especially in humans, for most of these products. That evidence should be carefully reviewed before decisions are made to promote the regular use of these agents. This review will focus on one of those alternative medicines, policosanol.

Policosanol is a mixture of high-molecular-weight primary aliphatic alcohols obtained from sugar cane wax.³ The primary component of the mixture is octacosanol ($\text{CH}_3[\text{CH}_2]_{26}\text{CH}_2\text{OH}$). Octacosanol has been investigated as a possible treatment for

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Parkinsonism and amyotrophic lateral sclerosis.^{4,5} It has also been used by athletes seeking to enhance their performance.⁶⁻⁸ The policosanol mixture has been used as an anti-platelet agent, an anti-thrombic agent, an anti-ischemic agent, a protective or curative agent against drug-induced gastric ulcer, a treatment for hypercholesterolemia, and a treatment for the improvement of male sexual activity.³

The name policosanol is used by many supplement manufacturers for mixtures obtained from sugar cane wax, beeswax, rice wax, or wheat-germ oil.^{9,10} Most of the products do not contain, or do not consistently contain, the percentages of the aliphatic alcohols present in the policosanol that has been used in clinical trials.¹⁰

Dosage and Administration

In the early 1990's the National Center for Scientific Research in Havana, Cuba, began investigating the effects of policosanol on serum lipids.¹¹ The policosanol used in these studies had a composition of 1-octacosanol 60.0-70.0%, with 7 other high-molecular-weight aliphatic alcohols in lower concentrations.³ The Center created a company, Laboratorios Dalmer, to market policosanol. It sells policosanol as 5 and 10 mg film coated tablets in many countries under the trade names Ateromixol, PPG, MERCOL, LIPEX and DUPLA.¹² For the treatment of hyperlipidemia, policosanol has been used in doses of 1 to 40 mg/day. It is usually given either once daily with the evening meal or twice daily with meals. The most studied dose has been 10 mg/day.

Mechanism of Action

Policosanol has been shown to affect cholesterol levels in multiple ways. It reduces cholesterol biosynthesis at a step prior to the formation of mevalonate, but after acetate consumption. This is also the step at which HMG-CoA reductase inhibitors (statins) work. The exact mechanism by which policosanol effects this step has yet to be determined in humans. It has been suggested that it may interfere with the synthesis or degradation of HMG-CoA.

Evidence for Beneficial Effect

Researchers have studied the lipid lowering effects of policosanol in a wide variety of subjects including healthy volunteers^{11,13} and patients with hypercholesterolemia.^{10,13-39} Trials comparing policosanol with simvastatin,³² pravastatin,^{19,40} lovastatin,^{24,29,41} probucol³⁷ and acipimox⁴² have shown policosanol to have equal or greater lipid-lowering effects. Policosanol has also been studied in combination with bezafibrate.⁴³ Most of these lipid-lowering studies in humans were conducted in Cuba. The results have not been independently confirmed and little data exists on the effects of policosanol in non-Cuban populations.⁴⁴ The length of the trials varied from 4 weeks to 5 years. Policosanol administered at a dose of 10 mg/day reduced LDL cholesterol by 20 to 27%.²⁶ Some of the trials have shown significant increases in high density lipids (HDL), while others have shown little or no increase. Results of some trials on policosanol's lipid-lowering effects are summarized in Table 1.

Precautions, Contraindications and Concerns

As with most herbal products, no research has been done in pregnant or lactating women to determine the safety profile.^{2,45} No teratogenic effects have been found in animal models.² Children should not take policosanol because there is a lack of data on safety in children.² Although policosanol has been given to children between the ages of 11 to 19 years of age in one study on adolescent type II hyperlipidemia, the number of participants in the experimental arm was too small (n=28) and the research lacked long term follow up to determine safety issues.²⁷ The researchers noted there was no increase in AST, ALT, blood pressure, creatinine, and blood glucose, but the cholesterol levels decreased while the children were taking policosanol.²⁷ It is recommended that patients not take policosanol concurrently with HMG-CoA reductase inhibitors.⁴⁵ Policosanol has been shown to have some additive effects with anticoagulants and antiplatelet drugs. It decreases thromboxane A₂ levels and may increase prostacyclin levels.⁴⁵ As a result, policosanol should be avoided or used cautiously in patients taking anticoagulants or anti-platelet drugs.

Castano and colleagues¹⁰ compared policosanol by the Laguna³ method to another product Octinol-60 by Garuda obtained from Australia. They

Table 1 Summary of policosanol efficacy studies.

| Reference | Study population | Number of participants | Treatment duration (weeks) | Policosanol dose | LDL change from baseline | TC change from baseline | HDL change from baseline | |
|---|--------------------------------------|------------------------|----------------------------|------------------|--------------------------|-------------------------|--------------------------|----------|
| Randomized single-blind placebo-controlled trials | | | | | | | | |
| Pons ³⁴ 1993 | Elderly, HC | 26 | 24 | 1 mg qd | n/a | -17% | n/a | |
| | | | | 10 mg qd | n/a | -22% | n/a | |
| Batista ¹⁸ 1996 | CHD, HC | 23 | 61 | 1 mg bid | -16% | -15% | -6% (ns) | |
| Randomized double-blind placebo-controlled trials | | | | | | | | |
| Hernandez ¹¹ 1992 | Healthy volunteers | 38 | 4 | 5 mg bid | -10% (ns) | -11% | 2% (ns) | |
| | | | | 10 mg bid | -22% | -11% | 24% | |
| Pons ³³ 1992 | HC II | 56 | 8 | 5 mg qd | -13% | -18% | -3% (ns) | |
| Aneiros ¹⁴ 1993 | HC II | 33 | 6 | 5 mg bid | -22% | -17% | 11% | |
| | | | | 10 mg bid* | -29% | -20% | 9% | |
| Pons ³⁵ 1994 | HC II | 59 | 52 | 5 mg qd | -24% | -15% | 2% (ns) | |
| Aneiros ¹⁶ 1995 | HC II | 45 | 6 | 5 mg bid | -22% | -16% | 14% (ns) | |
| Castano ²¹ 1995 | HC II | 74 | 52 | 5 mg bid | -26% | -17% | 14% | |
| Torres ³⁸ 1995 | HC, NIDDM | 29 | 12 | 5 mg bid | -22% | -18% | 11% (ns) | |
| Castano ¹⁵ 1995 | HC II, elderly | 62 | 52 | 5 mg bid | -23% | -16% | 8% (ns) | |
| Batista ¹⁷ 1995 | Mild CVA | 22 | 52 | 5 mg bid | -16% | -17% | 6% | |
| Zardoya ³⁹ 1996 | HC II, hepatic impairment | 46 | 12 | 5 mg qd | -19% | -14% | 12% | |
| | | | | 10 mg qd | -22% | -15% | 18% | |
| Castano ²² 1996 | HC II, HTN | 58 | 52 | 5 mg bid | -19% | -13% | 17% | |
| Crespo ²⁸ 1997 | NIDDM, HC | 21 | 12 | 5 mg bid | -44% | -29% | 24% | |
| Castano ²³ 1997 | HC II | 60 | 10 | 5 mg bid | -21% | -14% | 18% | |
| | | | | 10 mg qd | -23% | -15% | 29% | |
| Mas ³⁰ 1999 | HC II, coronary risk factors | 437 | 12 | 5 mg qd | -18% | -13% | 16% | |
| | | | | 10 mg qd* | -26% | -17% | 28% | |
| Menendez ¹³ 2000 | Healthy volunteers | 69 | 8 | 5 mg qd | -17% | -11% | 9% | |
| | | | | 10 mg qd | -20% | -12% | 15% | |
| Menendez ³¹ 2000 | HC II, high coronary risk | 20 | 12 | 5 mg qd | -20% | -16% | 5% | |
| Castano ²⁶ 2001 | HC II | 89 | 24 | 20 mg qd | -27% | -16% | 18% | |
| | | | | 40 mg qd | -28% | -17% | 17% | |
| Castano ²⁵ 2001 | HC II | 62 | 8 | 10 mg bid | -36% | -16% | 38% | |
| | | | | 20 mg qd | -38% | -20% | 39% | |
| Castano ²⁷ 2002 | Adolescents, HC II | 55 | 12 | 5-10mg qd | -33% | -22% | 10% | |
| Randomized double-blind trials comparing policosanol to other lipid-lowering medications | | | | | | | | |
| Pons ³⁷ 1997 | HC II | probuco | 30 | 8 | 5 mg bid | -23% | -18% | 3% (ns) |
| Ortensi ³² 1997 | Elderly, HC | simvastatin | 53 | 8 | 10 mg qd | -18% | -15% | -2% (ns) |
| Benitez ¹⁹ 1997 | HC II | pravastatin | 24 | 6 | 10 mg qd | -24% | -16% | 14% |
| Castano ²⁴ 2000 | HC II, high risk for coronary events | lovastatin | 59 | 12 | 10 mg qd | -32% | -22% | 14% |

* 10 mg dose was given following the 5 mg dose.

HC = hypercholesterolemia, HC II = Type II hypercholesterolemia

HTN = hypertension

(ns) = not statistically significant

found that Octinol-60 and policosanol differ in composition, lipid-lowering capabilities and adverse effects. The researchers were concerned products from beeswax sources and other sources claiming to have come from sugar cane wax contained higher aliphatic primary alcohols and varied more than the policosanol studied. According to Castano and colleagues¹⁰, products with higher aliphatic primary alcohols had more anti-inflammatory effects, anti-ulcer effects, and unwanted side effects. Also, these higher aliphatic alcohols had less cholesterol-lowering and antiplatelet effect compared to policosanol by the Laguna method³. The sugar-cane-derived policosanol described by these Cuban researchers is the one produced by Dalmer Laboratories. It is available in over 40 countries, but not in the U.S. due to the current trade embargo. Unfortunately, herbal manufacturing companies or distributors in the U.S. can associate the policosanol name with any product containing long-chain alcohols because no protection was requested for the name.

Conclusion

There appears to be evidence that policosanol does reduce LDL cholesterol and may increase HDL. The problem is that it is difficult to know whether or not products promoted as containing policosanol actually possess the same combination of primary aliphatic alcohols as the products that have shown efficacy. In addition, policosanol has not been studied in comparison to other herbal products for lowering cholesterol. Many of the policosanol products are sold in combination with herbal/vitamin products such as garlic, guggulsterones, niacin, plant sterols, soy, fiber, and artichoke (list not

inclusive). Patients may also buy multiple herbal products to “maximize” the cholesterol-lowering potential. It is unknown what additive or inhibitory effects these combinations may have. As a result, if this therapy is to be recommended to patients, care should be taken to use those products that have policosanol that has been shown to be effective.

There are some general counseling tips that should be kept in mind for all herbal or natural products. Make sure the patient understands the risks associated with using products not regulated by the FDA. Encourage the patient to use the same brand and ensure that it is from a reputable manufacturer to help limit possible inconsistencies. Products should list the ingredients and the amounts on the container. Check for a quality-control seal by an independent laboratory or certified chemist. Dissolution profiles, chromatographic analysis, and demonstrations that the product is free of contaminants is desirable. Be wary of combination products containing multiple herbal products to treat the same disease. Be cautious of products that have broad claims about what they are able to do.

Make sure that the patient’s physician is aware that they are using this herbal product, especially if their primary physician is treating them for hyperlipidemia. A patient should not discontinue prescribed medications or add this alternative medication without the primary care physician’s knowledge.

Expanded Database Coverage – Newly Approved Drugs

Effective with the May 2004 *IDIS* Update, our coverage of drugs newly approved by the FDA will be expanded. Relevant clinical studies and case reports for new molecular entities that appear in the manufacturer’s bibliography at the time the new product is released, and are from journals not indexed by *IDIS*, will be added to the database. The first drug highlighted will be Tiotropium Bromide in the May 2004 Update.

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CE REGISTRATION

ACPE # 020-000-04-019-H01

VOLUME: 15 ISSUE: 2 JUNE 2004

TITLE OF EDUCATIONAL ACTIVITY (ARTICLE)

POLICOSANOL: A NON-PRESCRIPTION DIETARY SUPPLEMENT TO CONTROL HYPERLIPIDEMIA

NAME _____

ADDRESS _____

CITY _____ STATE _____ ZIP _____

SOCIAL SECURITY NUMBER (OPTIONAL) _____

PHARMACY LICENSE NUMBER(S) _____

I HEREBY CERTIFY THAT I HAVE TAKEN THIS TEST:

Signature/Date _____

(circle the correct answer)

1. Which one of the following has **NOT** been promoted heavily for lowering serum lipids?
 - a. artichoke leaf
 - b. garlic
 - c. ginseng
 - d. guggul
 - e. red yeast rice

2. Policosanol is obtained from:
 - a. artichokes
 - b. chrysanthemum pollen
 - c. dogwood leaves
 - d. sugar cane wax
 - e. yeast extract

3. The primary ingredient of the mixture of aliphatic alcohols that make up policosanol is:
 - a. ethanol
 - b. octosanol
 - c. polyoctanol
 - d. red policose
 - e. tetracosanol

4. Policosanol has been recommended in many doses, but the most common total daily dose is:
 - a. 1 mg
 - b. 10 mg
 - c. 50 mg
 - d. 100 mg
 - e. 500 mg

5. Statins inhibit the activity of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. Which of the following is not true about policosanol? It may:
 - a. inhibit this enzyme activity
 - b. interfere with the synthesis of this enzyme
 - c. interfere with the degradation of this enzyme
 - d. increase liver uptake of LDL
 - e. improve metabolism of LDL receptor fibroblasts

6. Policosanol when compared with simvastatin, pravastatin, lovastatin, probucol, and acipimox, has been shown to:
 - a. have superior lipid-lowering effects
 - b. decrease LDL and HDL significantly
 - c. have inferior lipid-lowering effects
 - d. increase LDL and HDL significantly
 - e. have equal or greater lipid-lowering effects

7. When used in conjunction with antiplatelet medications, policosanol can:
 - a. increase platelet aggregation
 - b. decrease platelet aggregation
 - c. increase thromboxane A₂ levels
 - d. decrease prostacyclin levels
 - e. increase INR by two-fold

8. Based on the potential interaction in question 7, it would be wise to:
 - a. decrease the policosanol dose by 50%.
 - b. double the dosing interval
 - c. increase the antiplatelet dose by 50%
 - d. give the antiplatelet drug twice as often
 - e. avoid using these drugs together

9. Policosanol can be used:
 - a. safely in pregnant or lactating women
 - b. safely in children
 - c. for long periods of time
 - d. when taking HMG-CoA reductase inhibitors
 - e. safely with anticoagulants

10. Comparison of various policosanol products has shown:
 - a. consistent content of the main ingredients
 - b. higher aliphatic alcohols lower cholesterol better
 - c. consistent lipid lowering among the products
 - d. higher aliphatic alcohols have more side effects
 - e. consistent rate of adverse effects

PROGRAM EVALUATION

| | Excellent | | | | Poor | |
|-------------------------------------|-----------|---|---|---|----------|--|
| Overall quality | 5 | 4 | 3 | 2 | 1 | |
| Relevance to practice | 5 | 4 | 3 | 2 | 1 | |
| Value of content | 5 | 4 | 3 | 2 | 1 | |
| Important to pharmacists | Agree | | | | Disagree | |
| Increased my knowledge | 5 | 4 | 3 | 2 | 1 | |
| Achieved stated objectives | 5 | 4 | 3 | 2 | 1 | |
| Was educational and not promotional | 5 | 4 | 3 | 2 | 1 | |

It took me _____ hours and _____ minutes to read this article and complete the assessment questions.

QUICK GUIDE

TO DDIS PRODUCTS AND SERVICES

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FDA APPROVAL PACKAGES

SUMMARY AND ANALYSIS OF PIVOTAL CLINICAL DRUG TRIALS, PHARMACOLOGY, TOXICOLOGY AND PHARMACEUTICAL INFORMATION IN ONE COMPREHENSIVE DOCUMENT
PIVOTAL STUDIES WITHIN APPROVAL PACKAGES IDENTIFIED AND ABSTRACTED
ORGANIZED INTO STANDARD FORMAT WITH TABLE OF CONTENTS
RAPID RESPONSE TO ALL REQUESTS

DRUG VOCABULARY AND THESAURUS

COMPREHENSIVE CONTROLLED VOCABULARY OF PROPRIETARY AND NON-PROPRIETARY NAMES
US AND INTERNATIONAL DRUG SYNONYMS CROSS-REFERENCED
OVER 8,000 GENERIC TERMS
OVER 21,800 DRUG TERMS
CONTINUALLY UPDATED
UNIQUE NUMERIC INDICATOR FOR EACH DRUG

CUSTOMIZED DRUG INFORMATION INSTRUCTION

BASIC OR ADVANCED INSTRUCTION IN DRUG INFORMATION AND INFORMATICS FOR PRACTICING PHARMACISTS
PROGRAM FACULTY INCLUDE MEMBERS OF THE UNIVERSITY OF IOWA COLLEGE OF PHARMACY
UNIVERSITY AND COMMUNITY HOSPITAL EXPERIENCES AVAILABLE

PHARMACEUTICAL INFORMATION RETRIEVAL AND EVALUATION SERVICE

SPECIALIZING IN:

DRUG INFORMATION
CLINICAL PHARMACEUTICS
FORMULARY REVIEWS
MEDICAL-LEGAL QUESTIONS

COMMITTED TO:

RAPID RESPONSE
EVIDENCE BASED EVALUATION

DDIS Selected As Contractor for USP-AMCP Joint Project

The Academy of Managed Care Pharmacy (AMCP) and the U.S. Pharmacopeia (USP) are working jointly to understand the use of drug-drug interaction alerts by pharmacists through the Drug-Drug Interaction Initiative (DDII). The current system provides information that sometimes can be redundant, irrelevant or outdated, causing concern among pharmacists, patients and researchers.



Drug Interaction Team, Left to right: Jeff Zear, Hazel Seaba, ThaiBinh Ton-That, Brad Gilchrist, Nickie Sarrazin, Mary Ann Cull, Ron Herman, Pam Mollenhauer, Vicki Kee

One goal of the DDII is to provide pharmacists with reliable drug interaction messaging, based on agreed-upon industry standards. Spearheading the creation of the new methodology is the USP Therapeutic Decision Making (TDM) Expert Committee. Chaired by Elizabeth Chrischilles, Ph.D., professor of epidemiology in the University of Iowa College of Public Health, the committee was tasked with identifying and classifying drug-drug and drug-class interactions that posed the greatest risk of serious and/or life threatening drug-induced illness for patients.

The overall goals of the initiative are to:

- Establish an evidence-based, clinically significant method to classify drug-drug interactions with a high probability of causing harm to patients, and
- Facilitate collaboration between health care providers and drug information publishers to ensure this methodology is applied and the results integrated into the DUR components of systems used at the point of care.

The Division of Drug Information Service (DDIS) has been chosen to test and assess the new methodology for evaluating interactions that the TDM Committee has developed in order to determine which types of evidence to consider regarding drug-drug interactions. Led by Professor Hazel H. Seaba, R.Ph., M.S., Director of the Division of Drug Information Service and colleagues, a new database and reports are being developed that will compile relevant literature and summarize the level of evidence for a drug interaction to evaluate their validity and relevance.

The evaluation of USP's Expert Committee criteria by DDIS is expected to be completed by September 2004.

New Drugs: Key References

This new drug bibliography provides a selection of key critical studies and reviews of new drugs approved by the FDA January 2004 through March 2004. An *IDIS* search retrieved articles relevant to the new drugs and their approved uses.

Bevacizumab

Kabbinavar F, Hurwitz HI, Fehrenbacher L, Meropol NJ, et al. Phase II randomized trial comparing bevacizumab plus fluorouracil (FU)/leucovorin (LV) with FU/LV alone in patients with metastatic colorectal cancer. *J Clin Oncol.* 2003; 21:60-65. (*IDIS* Article Number 495428) **Investigators conducted a Phase II randomized trial of 104 patients with metastatic colorectal cancer who were randomized to FU (500 mg/m²)/LV(500 mg/m²) alone, FU/LV plus low-dose bevacizumab (5 mg/kg every 2 weeks), and FU/LV plus high-dose bevacizumab(10 mg/kg every 2 weeks) and found a higher response rate at both doses of bevacizumab compared with FU/LV control arm (control arm 17%, low-dose arm 40%, and high-dose arm 24%).**

Cetuximab

Ma BBY, Bristow RG, Kim J, Siu LL. Combined-modality treatment of solid tumors using radiotherapy and molecular targeted agents. *J Clin Oncol.* 2003; 21:2760-2776. (*IDIS* Article Number 503164)

The authors of this in-depth review integrate preclinical data and focus on molecular mechanisms, efficacy and applicability of molecular targeted agents, including cetuximab, combined with radiotherapy, and they conclude that these molecular targeted agents can directly effect cytoprotective and cytotoxic pathways in the cellular response to ionizing radiation making this a promising therapy for solid tumors.

Cinacalcet

Shoback DM, Bilezikian JP, Turner SA, McCary LC, et al. The calcimimetic cinacalcet normalizes serum calcium in subjects with primary hyperparathyroidism. *J Clin Endocrinol Metab.* 2003; 88:5644-5649. (*IDIS* Article Number 509227)

This randomized, double-blind study included 22 patients with primary hyperparathyroidism who received oral cinacalcet doses of 30, 40 or 50 mg, or placebo, twice daily for 15 days and found that calcium serum concentrations in the cinacalcet treated patients decreased from baseline by 11.0%, 18.7% and 18.5% in the 30, 40 and 50 mg dose groups respectively, compared with placebo, (p = 0.09 for the 30 mg arm, p = 0.03 for the 40 mg arm and p = 0.06 for the 50 mg arm), and that the calcium serum concentrations were brought to within the normal range for all dose groups but remained at baseline for the placebo group. The combined data from all cinacalcet dosed groups resulted in a mean reduction of serum calcium of 16.0% (p = 0.004).

Pemetrexed

Vogelzang NJ, Rusthoven JJ, Symanowski J, Denham C, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol.* 2003; 21:2636-2644. (*IDIS* Article Number 503150) (Pivotal Study)

In this randomized Phase III study, 448 patients with malignant pleural mesothelioma received either intravenous pemetrexed 500 mg/m² plus cisplatin 75 mg/m² on day 1, or cisplatin alone at 75 mg/m² on day 1 every 21 days for 1-12 cycles resulting in a median survival time in the pemetrexed/cisplatin group of 12.1 months compared with 9.3 months in the cisplatin alone group (p = 0.02), and response rates of 41.3% in the pemetrexed/cisplatin group compared with 16.7% in the cisplatin alone group (p = <.0001).

Paz-Ares L, Bezares S, Tabernero JM, Cortes-Funes H. Review of a promising new agent – pemetrexed disodium. *Cancer.* 2002; 97:2056-2063. (*IDIS* Article Number 496731)

Many preclinical, Phase I and Phase II studies are included in this review with summaries of pemetrexed use, as a single agent and in combination with other agents, in patients with solid tumors, and pharmacokinetic information as well as the mechanism of action of pemetrexed are also included.

Tiotropium Bromide

Van Noord JA, Bantje TA, Eland ME, Korducki L, et al. A randomized controlled comparison of tiotropium and ipratropium in the treatment of chronic obstructive pulmonary disease. *Thorax.* 2000; 55:289-294. (*IDIS* Article Number 445951)

This double-blind, double dummy, randomized, controlled trial included 288 patients with chronic obstructive pulmonary disease from 14 centers and compared the safety and efficacy of 18 mcg inhaled tiotropium once daily with inhaled ipratropium 40 mcg 4 times a day for 13 weeks, and found that compared to ipratropium, tiotropium achieved significantly greater improvement in trough, average and peak FEV₁ (forced expiratory volume in 1 second) levels, and in trough and average FVC (forced vital capacity) levels (p<0.05) while having a safety profile similar to ipratropium.

Donohue JF, Van Noord JA, Bateman ED, Langley SJ, et al. A 6-month, placebo-controlled study comparing lung function and health status changes in COPD patients treated with tiotropium or salmeterol. *Chest.* 2002; 122:47-55. (*IDIS* Article Number 484065)

A total of 623 patients with chronic obstructive pulmonary disease (COPD) were included in a 6-month, randomized, double-blind, placebo- controlled study compared the safety and efficacy of 18 mcg inhaled tiotropium once daily, 50 mcg inhaled salmeterol twice daily or placebo and found that after 6 months of therapy, compared with placebo, the mean morning predose FEV₁(forced expiratory volume in 1 second) increased significantly more with tiotropium (0.14L) than with salmeterol (0.09L), (p<0.01).



About the Author:

Nicola Sarrazin is a 1984 graduate of the University of Iowa (B.A. in Anthropology and Asian Studies) and a 1997 graduate of the University of Iowa College of Pharmacy (Pharm.D.). Since that time she has been a pharmacist in the College of Pharmacy's Division of Drug Information Service. Nickie's responsibilities include indexing articles for the *IDIS* database, overseeing the Drug and Descriptor vocabulary and contributing articles for the *World of Drug Information* newsletter.

FDA DRUG/BIOLOGIC APPROVALS

| Generic Name (FDA Therapeutic Classification) Trade Name | Sponsor (Approval Date) | IDIS Drug Term Drug Number (IDIS Citations)* | Indication/Use | IDIS Disease Term Modified ICD-9-CM Number |
|--|--|---|--|--|
| Bevacizumab (BIOL) <i>Avastin</i> | Genentech (Feb. 26, 2004) | BEVACIZUMAB 82000423 (11 citations) | Metastatic colorectal cancer. | Neop, Mgn-Intestine, LG NEC 153. Neop, Mgn-Rectum/Anus NEC 154. Neop, Mgn-Rectosigmoid Junct 154.0 |
| Cetuximab (BIOL) <i>Erbix</i> | Bristol-Myers Squibb/ImClone (Feb. 12, 2004) | CETUXIMAB 82000459 (37 citations) | Metastatic colorectal cancer. | Neop, Mgn-Intestine, LG NEC 153. Neop, Mgn-Rectum/Anus NEC 154. Neop, Mgn-Rectosigmoid Junct 154.0 |
| Cinacalcet Hydrochloride (1P)***** <i>Sensipar</i> | Amgen (Mar. 8, 2004) | CINACALCET 92000409 (2 citations) | Treatment of secondary hyperparathyroidism in patients with chronic kidney failure on dialysis and hypercalcemia in patients with parathyroid carcinoma. | Failure, Renal 586. Hyperparathyroidism 252.0 Disorder, Calcium Metabolism 275.4 |
| Pemetrexed Disodium (1PV)**** <i>Alimta</i> | Eli Lilly (Feb. 4, 2004) | PEMETREXED 10081209 (18 citations) | Malignant mesothelioma. | Neop, Mgn-Pleura 163. |
| Tiotropium Bromide (1S)*** <i>Spiriva handihaler</i> | Boehringer Ingelheim (Jan. 30, 2004) | TIOTROPIUM BROMIDE 12080059 (34 citations) | Chronic obstructive pulmonary disease COPD (including chronic bronchitis and emphysema) | Obstruction, Air, Chr NEC 496. Emphysema NEC 492. Bronchitis, Obstructive, Chr 491.2 |

* Through April 2004 Update. Complete bibliographic citations will be provided upon request.

** Not applicable.

*** New molecular entity given standard review by FDA.

**** Designated orphan drug.

***** New molecular entity given priority review.

+ Accelerated Approval.

Additional information on these newly approved drugs will be available in the FDA Approval Package [an official United States Food and Drug Administration (FDA) document] that is compiled for new drugs following approval. This document includes reviews of the pivotal and supportive clinical studies conducted during the approval process. These studies are often not published elsewhere. FDA Approval Packages are selectively indexed and included as part of the *IDIS* database as they become available. Use descriptor *155 FDA APPROVAL PACKAGE* in combination with the valid drug term to retrieve these documents from the database.

IDIS/Web Enhancements Now Available

Effective April 2004, the Email Results and Print Results functions have been improved. These functions now return results much faster than before. You can use the Email function to send selected search results to yourself or someone else. The Print function can be used to create printer-friendly pages you can send to your printer. Additionally, *IDIS/Web* has been loaded onto a new larger, faster server in June.

2004 EXHIBIT SCHEDULE

American Association of Colleges of Pharmacy (AACP)
Grand America Hotel, Salt Lake City, UT
July 10-14, 2004
Booth #41

Federation International Pharmaceutique (FIP) 2004
Pharmacy and Pharmaceutical Sciences World Congress
Hyatt Regency, New Orleans, LA
September 4-9, 2004

American College of Clinical Pharmacy (ACCP)
Hyatt Regency by Reunion, Dallas TX
October 24-27, 2004
Booth #113

39th American Society of Health-System Pharmacists (ASHP)
Midyear Meeting and Exhibit
Orange County Convention Center, Orlando FL
December 5-9, 2004



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