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Issue Date
July-August
November-December

Closing Date June 1, 1993 October 1, 1993

Issue Date
September- October
January-February

Closing Date August 2, 1993 December 1, 1993

MIDWEST

CENTRAL MINNESOTA — Join a multi-specialty practice which includes three orthopedic surgeons. Outstanding compensation, takes region. Call 1-800-967-2711 or send C.V. to Delacore, 101 Park Place, Hutchinson, MN 55350, or fax (612) 587-7252.

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NORTHEAST

NEW HAMPSHIRE — **FAMILY PRACTICE** — Opportunity is available with the affiliated practices of Monadnock Community Hospital in Peterborough, NH. These satellite FP offices handle the primary care and non-urgent care needs of the area. Continuity of care is an essential part of these practices. Weekday office hours.

Located In the beautiful Southern Tier of New Hampshire — quaint New England villages and picturesque landscape. Area ofters a slow-paced lifestyle with easy access to the larger metro area of Boston (80 milles). For additional information, contact Denise Johnson, Spectrum Emergency Care, 1-800-325-3982, ext. 3017.

PACIFIC

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SOUTHEAST

PGY II POSITION — PGY II Position available at the oldest community hospital Family Practice Residency Program in Florida. LCME/AOA approved medical school graduates with first year PGY I FP or equivalent training in ACGME/AOA accredited program preferred. Particularly strong obstetical, procedural, and sports medicine experiences. Send letter and CV to R. Branoff, M.D., Hallfax Medical Center, PO Box 2830, Daytona Beach, Florida 32120-2830, (904) 254-4167.

CENTRAL VIRGINIA — Excellent opportunity for BC/BE family physician to join established group practice of four physicians in Chariottesville. Pleasant, well-equipped office. Superb community hospital. No obstetrics. Excellent university and school system. 30 mins. to Shenandoah National Park and other abundant recreational opportunities. Send CV to John Corpenter, MD, 3025 Berkmar Drive, Charlottesville, VA 22901 or call 1-800-525-9130.

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CLINICAL FACULTY — In the Heart of America, Health Midwest, a multi-hospital system in Kansas City, Missouri is actively recruiting Family Practice Faculty members to the Goppert Family Care Center, located in Kansas City, Missouri. Two faculty members who do OB are needed. Candidates must hold M.D. degrees, be Board Certified in Family Medicine and possess a strong clinical background.

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Please send a curriculum vitae to Marcia Cordell, Vice President, Physician Recruitment, 2316 E. Meyer Boulevard, Kansas City, Missouri 64132.

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East

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Southwest

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Southwest

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The Only Cardioselective Beta Blocker Indicated for PVC Control

Usual startina dose

200 ma RID

Optimal **PVC** response 600 mg to 1200 mg per day

Use in elderly

400 mg to 800 mg per day

Doses above 800 mg per day

should be avoided

(SECTRAL - Brief Summary of prescribing Information.)

CONTRAINDICATIONS: SECTRAL is contraindicated in: 1) persistently severe

CONTRAINDICATIONS: SECTRAL is contraindicated in: 1) persistently severe bradycardwa. 2) second- and third-degree heart block; 3) overt cardiac failure; 4) cardiogenic shock (See WARNINGS)
WARNINGS: Cardiac Failure: Sympathetic stimulation may be essential for support of circulation in patients with diminished myocardial contractility, and inhibition by 8-adrenergic receptor blockade may precipitate more severe failure. Although 8-blockers should be avoided in overticardiac failure. SECTRAL can be used cautiously when heart failure is controlled with digitals and/or diuretics. Digitalis and SECTRAL impair AV conduction. Withdraw SECTRAL if cardiac failure persists. In Patients Without a History of Cardiac Failure: In patients with acrtic or mitral valve disease or compromised left ventricular function, continued depression of the myocardium with 8-blockers over time may lead to cardiac failure. Digitalize patients at first signs of failure and/or nive a diuretic and observe closely. Withdraw SECTRAL if first signs of failure, and/or give a diuretic and observe closely. Withdraw SECTRAL if

cardiac failure persists.

Exacerbation of lachemic Heart Disease Following Abrupt Withdrawal: Abrupt discontinuation of some B-blockers in coronary artery disease patients may exacerbate angina; in some cases, myocardial infarction and death have been reported. Caution such patients against interruption of therapy without a physician's advice. Even in the absence of over ischemic heart disease, withdraw SECTRAL gradually over a period of about two weeks; observe carefully and advise patients to minimize physical activity during this time. (If desired, patients may be transferred directly to comparable doses of an alternative B-blocker without interruption of 8-blocking therapy). If exacerbation of angina occurs, restart full-dose anti-anginal therapy immediately and hospitalize patient until stabilized
Peripheral Vascular Disease: B-antagonists reduce cardiac output and can

precipitate/aggravate arterial insufficiency in patients with peripheral or mesenteric vascular disease. Exercise caution and observe such patients closely for progression of arterial obstruction

Bronchospestic Diseases: Patients with Bronchospestic Disease Should, in General, Not Receive a fi-Blocker. Because of its relative 6₁-selectivity, low doses of SECTRAL may be used cautiously in such patients who do not respond to, or cannot

Since B₁-selectivity is not absolute and is dose-dependent, use lowest possible dose of SECTRAL initially, preferably in divided doses. Make bronchodilator, e.g., theophylline, or a B₂-stimulant, available in advance with instructions for use.

or a 152-simpliant, available in advance with instructions for use.

Aneafheais and Major Surgery: The necessity/desirability of withdrawing.

B-blockers prior to major surgery is controversial; the heart's impaired ability to respond to 3-adrenergically mediated reflex stimuli may enhance the risk of excessive myocardial depression during general anesthesia. Difficulty in restarting and maintaining the heartbeat also has been reported with beta-blockers. If treatment is continued to the control of the provided with the control of the provided in the control of the provided with the development of the provided with the control of the provided in the control of the provided provided in the provided with the provided provided in the provided pro in the second of the second of

Diabetes and Hypoglycemia: B-blockers may potentiate insulin-induced hypoglycemia and mask some symptoms such as tachycardia; dizziness and sweating are usually not significantly affected. Warn diabetics of possible masked

Thyrotoxicosis: ß-adrenergic blockade may mask some clinical signs (tachycardia) of hyperthyroidism. Abrupt withdrawal of SECTRAL may precipitate a thyroid storm in patients suspected of developing thyrotoxicosis.

PRECAUTIONS: Impaired Renal or Hepatic Function: While there are no U.S.

PHEGAUTIONS: Impaired Henal or nepatic Function: While there are no U.S. studies, foreign published experience shows that acabutolol has been used successfully in chronic renal insufficiency. Acebutolol is excreted via the G.f. tract, but the active metabolite, diacetolol, is eliminated mainly by the kidney. A linear relationship exists between renal clearance of diacetolol and creatinine clearance (Cl_{Ct}); reduce daily dose of acebutolol by 50% when Cl_{Ct} is less than 50 mL/min and by 7% when it is less than 25 mL/min. Use cautiously in patients with impaired hepatic function.

SECTRAL has been used successfully and without problems in elderly patients in

U.S. clinical trials without specific dosage adjustment. However, in the elderly, low maintenance doses may be required because bioavailability of SECTRAL and its

metabolite are approximately doubled.

Information for Patients: Warn patients, especially those with evidence of coronary artery disease, against interruption or discontinuation of SECTRAL without physician supervision. Although cardiac failure rarely occurs in properly selected patients, advise patients to consult a physician if signs or symptoms suggestive of impending CHF, or unexplained respiratory symptoms, develop.

Warn patients of possible severe hypertensive reactions from concomitant use of

lpha-adrenergic stimulants, e.g., nasal decongestants used in OTC cold medicines and

Aradrenergic stimulants, e.g., has a decongestant uses in 10 to a discontinuation of the continuation of the continuation of the continuation of the continuation of antinuctear antibodies (ANA). In prospective clinical trials, patients receiving SECTRAL had a dose-dependent increase in the development of positive ANA liters. Symptoms related to this faboratory abnormality were infrequent. Symptoms and ANA titers were reversible upon discontinuation of SECTRAL.

Drug Interactions: Catecholamine-depleting drugs may have additive effects when given with β-blockers. Observe patients treated with both agents closely for evidence of marked bradycardia or hypotension which may present as vertigo, syncope/ presyncope, or orthostatic changes in blood pressure without compensatory tachycardia. Exaggerated hypotensive responses have been reported from use of β-adrenergic antagonists with α-adrenergic stimulants, including those in OTC cold remedies and vasoconstrictive nasal drops. Nonsteroidal anti-inflammatory drugs may blue astifycentersize effects of heats plockers.

B-adrenergic antagonists with re-adrenergic stimulants, including those in OTC cold remedies and vasoconstrictive nasal drops. Nonsteroidal anti-inflammatory drugs may blunt antihypertensive effects of beta-blockers.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Chronic oral toxicity studies in rats and mice, at doses 15 times the maximum recommended (60 kg) human dose, did not indicate carcinogenic potential for SECTRAL. Diacetolot, the major metabolite in man, was without carcinogenic potential in rats at doses up to 1800 mg/kg/d.

SECTRAL and diacetolot also had no mutagenic potential in the Ames Test. No significant impact on reproductive performance or fertility was found in rats following SECTRAL or diacetolot doses of up to 240 or 1000 mg/kg/d, respectively.

Pregnancy: Taratogenic Effects: Pregnancy Category B: No teralogenic effects were seen in rat or rabbit reproduction studies utilizing SECTRAL doses that were, respectively, approximately 31.5 and 6.8 times the maximum recommended human dose. At this dose in the rabbit, slight tetal growth retardation was noted; this was considered to be a result of maternal toxicity (evidenced by reduced food intake, lowered rate of body weight gain, mortality). Diacetoloid studies (doses up to 450 mg/kg/d in rabbits and up to 1800 mg/kg/d in rats) showed no evidence of fetal harm other than a significant elevation in postimplantation loss with 450 mg/kg/d, a level at which food consumption and body weight gain were reduced in rabbit dams; there was a nonstatistically significant increase in incidence of bilateral cataract in rat feluses from dams treated with 1800 mg/kg/d. There are no adequate and well-controlled trials in pregnant women: SECTRAL should be used during pregnancy only if potential benefit justifies risk to the felus.

Nonteratogenic Effects: Human studies indicate thal acebutolol during pregnancy have seeded with deceased the deceased well-controlled during pregnancy have

the placenta. Neonates of mothers who received acebutolol during pregnancy have reduced birth weight, decreased blood pressure, and decreased heart rate. **Labor and Delivery:** Effect on labor and delivery in pregnant women is unknown. Animal studies have shown no effect of SECTRAL on the usual course of tabor and

Nursing Mothers: Acebutolol and discetolol appear in breast milk (milk:plasma ratio NUTsing Mothers: Accountion and discessors appear in preast milk (nuts, present at a of 7.1 and 12.2, respectively). Use in nursing mothers is not recommended.

Pediatric Use: Safety and effectiveness in children have not been established. ADVERSE REACTIONS: SECTRAL is well tolerated in properly selected patients. Most adverse effects have been mild, not required therapy discontinuation, and

tended to decrease as treatment duration increases.

The incidence of treatment-related side effects (volunteered and elicited) derived

The incidence of treatment-related side effects (volunteered and elicited) derived from U.S. controlled clinical trials in patients with hypertension, angina and arrhythmia follows. Numbers represent percentage incidence for SECTRAL (N=1002) versus placebo (N=314), respectively.

Cardiovascular Chest pain 2%,1%; Edema 2%,1%. CNS: Depression 2%,1%; Dizziness 6%,2%; Fatigue 11%, 4%; Headache 5%, 4%; Insomnia 3%,1%; Abnormal dreams 2%,1%. **Dermatologic: Rash 2%,1%: Gastrointestinal: Constripation 4%,0%; Diarrhea 4%,1%; Dysopsia 4%,1%: Elatulence 3%,1%; Nausea 4%, 0%

**Genitourinary: Mictunition (frequency) 3%,<1%. **Musculoskeletal. Arthralgia 2%,2%, Myalgia 2%,0%. **Respiratory: Cough 1%,0%; Dysopea 4%,2%; Rhinnils 2%,<1%. **Special Senses: Abnormal Vision 2%,0%.

The following selected (potentially important) side effects were seen in up to 2% of SECTRAL patients: **Cardiovascular:* hypotension, bradycardia, heart failure. CNS: anxiety, hyper/hypoesthesia, impotence. **Skri: pruntlus. **Gastrointestinal:* vomiting, abdominal pain. **Genitourinary:* dysuria, nocturia. **Liver and Bitiary:* small number of reported cases of liver abnormalities (increased SGOT, SGPT. LDM). In some cases, increased bilirubin or alkaline phosphatase, fever, malaise, dark unne, anorexia, nausea, headache, and/or other symptoms have been reported. In some cases, symptoms and signs were confirmed by rechallenge. Abnormalities were reversible symptoms and signs were confirmed by rechallenge. Abnormalities were reversible upon drug cessation. Musculoskeletal: back and joint pain. Respiratory: pharyngitis. wheezing. Special Senses: conjunctivitis, dry eye, eye pain. Autoimmune: extremely rare reports of systemic lupus erythematosis.

Incidence of drug-related adverse effects (volunteered and solicited) based on SECTRAL dose is shown below. (Data from 266 hypertensive patients freated for 3 months on a constant dose.)

Body System	400 mg/day (N=132)	800 mg/day (N=63)	1200 mg/day (N=71)
Cardiovascular	5%	2%	1%
Gastrointestinal	3%	3%	7%
Musculoskeleta!	2%	3%	4%
Central Nervous System	9%	13%	17%
Respiratory	1%	5%	6%
Skin	1%	2%	1%
Special Senses	2%	2%	6%
Genitourinary	2%	3%	1%

Potential Adverse Effects: Certain adverse effects not listed above have been reported with other B-blocking agents and should be considered as potential adverse cts of SECTRAL

CNS: Reversible mental depression progressing to catatonia, an acute syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuro-psychometrics.

Cardiovascular: Intensification of AV block (see CONTRAINDICATIONS).

Allergic: Enythematous rash, fever with aching and sore throat, laryngospasm, respiratory

Hematologic: Agranulocytosis, nonthrombocytopenic and thrombocytopenic purpura. Gastrointestinal: Mesentenc arterial thrombosis, ischemic colitis.

Miscellaneous: Reversible alopecia, Peyronie's disease. The oculomucocutaneous

syndrome associated with practolof has not been reported with SECTRAL Keep at room temperature. Approximately 25°C (77°F).

1. Data on file, Wyeth-Ayerst Laboratories.



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