

#### Brief Summary:

**Contraindications:** Patients who have had allergic reactions to NAPROSYN<sup>®</sup>, ANAPROX<sup>®</sup> or ANAPROX<sup>®</sup> DS or in whom aspirin or other NSAIDs induce the syndrome of asthma, rhinitis, and nasal polyps. Because anaphylactic reactions usually occur in patients with a history of such reactions, question patients for asthma, nasal polyps, urticaria, and hypotension associated with NSAIDs before starting therapy. If such symptoms occur, discontinue the drug.

**Warnings:** Serious GI toxicity such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated chronically with NSAIDs. Remain alert for ulceration and bleeding even in the absence of previous GI tract symptoms. In clinical trials, symptomatic upper GI ulcers, gross bleeding or perforation occur in about 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. Inform patients of signs and/or symptoms of serious GI toxicity and what steps to take if they occur. Studies have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Except for a prior history of serious GI events and other risk factors associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (e.g., age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well and most spontaneous reports of fatal GI events are in this population. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity.

**Precautions:** DO NOT GIVE NAPROSYN<sup>®</sup> (NAPROXEN) CONCOMITANTLY WITH ANAPROX<sup>®</sup> OR ANAPROX<sup>®</sup> DS (NAPROXEN SODIUM) SINCE THEY CIRCULATE IN PLASMA AS THE NAPROXEN ANION. Acute interstitial nephritis with hematuria, proteinuria, and nephrotic syndrome has been reported. Patients with impaired renal function, heart failure, liver dysfunction, patients taking diuretics, and the elderly are at greater risk of overt renal decompensation. If this occurs, discontinue the drug. Use with caution and monitor serum creatinine and/or creatinine clearance in patients with significantly impaired renal function. Use caution in patients with baseline creatinine clearance less than 20 mL/minute. Use the lowest effective dose in the elderly or in patients with chronic alcoholic liver disease or cirrhosis. Borderline elevations of liver tests may occur in up to 15% of patients. Elevations of SGPT or SGOT occurred in controlled trials in less than 1% of patients. Severe hepatic reactions, including jaundice and fatal hepatitis, have been reported rarely. If liver disease develops or if systemic manifestations occur (e.g., eosinophilia or rash), discontinue therapy. If steroid dosage is reduced or eliminated during therapy, do so slowly and observe patients closely for adverse effects, including adrenal insufficiency and exacerbation of arthritis symptoms. Determine hemoglobin values periodically for patients with initial values of 10 grams or less who receive long-term therapy. Peripheral edema has been reported. For patients with restricted sodium intake, note that each tablet contains approximately 25 or 50 mg (1 or 2 mEq) sodium. Use with caution in patients with fluid retention, hypertension or heart failure. The drug may reduce fever and inflammation, diminishing their diagnostic value. Conduct ophthalmic studies if any change or disturbance in vision occurs. **Information for Patients:** Side effects can cause discomfort and, rarely, more serious side effects, such as GI bleeding, may result in hospitalization and even fatal outcomes. Physicians may wish to discuss with patients potential risks and benefits of NSAIDs, particularly when they are used for less serious conditions where treatment without NSAIDs may be acceptable. Patients should use caution for activities requiring alertness if they experience drowsiness, dizziness, vertigo or depression during therapy. **Laboratory Tests:** Because serious GI tract ulceration and bleeding can occur without warning symptoms, follow chronically treated patients and inform them of the importance of the follow-up. **Drug Interactions:** Use caution when giving concomitantly with coumarin-type anticoagulants; a hydantoin, sulfonamide or sulfonylurea; furosemide; lithium; beta-blockers; probenecid; or methotrexate. **Drug/Laboratory Test Interactions:** May decrease platelet aggregation and prolong bleeding time or increase urinary values for 17-ketogenic steroids. Temporarily stop therapy for 72 hours before adrenal function tests. May interfere with urinary assays of 5HIAA. **Carcinogenesis:** A 2-year rat study showed no evidence of carcinogenicity. **Pregnancy:** Category B. Do not use during pregnancy unless clearly needed. Avoid use during late pregnancy. **Nursing Mothers:** Avoid use. **Pediatric Use:** Single doses of 2.5-5 mg/kg (as naproxen suspension), with total daily dose not exceeding 15 mg/kg/day, are safe in children over 2 years of age.

**Adverse Reactions:** In a study, GI reactions were more frequent and severe in rheumatoid arthritis patients on 1650 mg/day naproxen sodium than in those on 825 mg/day. In children with juvenile arthritis, rash and prolonged bleeding times were more frequent, GI and CNS reactions about the same, and other reactions less frequent than in adults. Incidence Greater Than 1%: Probable Causal Relationship: GI: The most frequent complaints related to the GI tract: constipation,\* heartburn,\* abdominal pain,\* nausea,\* dyspepsia, diarrhea, stomatitis. CNS: headache,\* dizziness,\* drowsiness,\* light-headedness, vertigo. Dermatologic: itching (pruritus),\* skin eruptions,\* ecchymoses,\* sweating, purpura. Special Senses: tinnitus,\* hearing disturbances, visual disturbances. Cardiovascular: edema,\* dyspnea,\* palpitations. General: thirst. \*Incidence of reported reaction 3%-9%. Where unmarked, incidence less than 3%. Incidence Less Than 1%: Probable Causal Relationship: GI: abnormal liver function tests, colitis. GI bleeding and/or perforation, hematemesis, jaundice, melena, peptic ulceration with bleeding and/or perforation, vomiting. Renal: glomerular nephritis, hematuria, hyperkalemia, interstitial nephritis, nephrotic syndrome, renal disease, renal failure, renal papillary necrosis. Hematologic: agranulocytosis, eosinophilia, granulocytopenia, leukopenia, thrombocytopenia. CNS: depression, dream abnormalities, inability to concentrate, insomnia, malaise, myalgia and muscle weakness. Dermatologic: alopecia, photosensitive dermatitis, skin rashes. Special Senses: hearing impairment. Cardiovascular: congestive heart failure. Respiratory: eosinophilic pneumonitis. General: anaphylactoid reactions, menstrual disorders, pyrexia (chills and fever). Causal Relationship Unknown: Hematologic: aplastic anemia, hemolytic anemia. CNS: aseptic meningitis, cognitive dysfunction. Dermatologic: epidermal necrolysis, erythema multiforme, photosensitivity reactions resembling porphyria cutanea tarda and epidermolysis bullosa, Stevens-Johnson syndrome, urticaria. GI: non-peptic GI ulceration, ulcerative stomatitis. Cardiovascular: vasculitis. General: angioneurotic edema, hyperglycemia, hypoglycemia.

**Overdosage:** May have drowsiness, heartburn, indigestion, nausea, vomiting. A few patients have had seizures. Empty stomach and use usual supportive measures. In animals 0.5g/kg of activated charcoal reduced plasma levels of naproxen.

**Dosage and Administration for Mild to Moderate Pain, Dysmenorrhea and Acute Tendinitis and Bursitis:** Recommended starting dose is 550 mg, followed by 275 mg every 6 to 8 hours. Total daily dose should not exceed 1375 mg.

**Dosage and Administration for Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis:** Recommended dose in adults is 275 mg or 550 mg twice daily. In patients who tolerate lower doses well, the dose may be increased to 1650 mg per day for limited periods when a higher level of anti-inflammatory/analgesic activity is required. At this dosage, physicians should observe sufficient increased clinical benefits to offset potential increased risk.

**Caution:** Federal law prohibits dispensing without prescription. See package insert for full Prescribing Information.

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## Letters to the Editor

### LEEP

To the Editor:

The article on the loop electro-surgical excisional procedure<sup>1</sup> is informative, but the authors' statement that "Pregnancy rates after LEEP are comparable to laser therapy and better than rates for conization" is a major overstatement unsupported by the literature. The reference for this statement is a letter to the editor that noted that 48 of 1000 women who received the LEEP procedure got pregnant.<sup>2</sup> There appeared to be no abnormally high rate of pregnancy complications. However, neither this letter to the editor nor the articles referenced by this letter actually determined the rate of infertility in women after any of the ablative cervical procedures. For example, this letter<sup>2</sup> did not state the number of women who wished to conceive, the age of the women, or the dropout rate in follow-up.

I continue to believe that the potential for reduced fertility exists after ablative procedures of the cervix, and that we must further study this issue.

Marjorie A. Bowman, MD, MPA  
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The Bowman Gray School of Medicine  
Wake Forest University  
Winston-Salem, North Carolina

### References

1. Mayeaux EJ Jr, Harper MB. Loop electro-surgical excisional procedures. *J Fam Pract* 1993;36:214-9.
2. Bigrigg MA, Codling BW, Pearson P, Read MD, Swingler GR. Pregnancy after cervical loop diathermy [letter]. *Lancet* 1991;337:119.

The preceding letter was referred to Drs Mayeaux and Harper, who respond as follows:

Dr Bowman is correct in stating that no prospective studies on pregnancy

The Journal welcomes letters to the editor. If found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with Journal style. All letters that reference a recently published Journal article are sent to the original authors for their reply. If no reply is published, the authors have not responded by date of publication. Send letters to Paul M. Fischer, Editor, The Journal of Family Practice, Department of Family Medicine, Medical College of Georgia, Augusta, GA 30912, or Fax (706) 855-1107.

rates after LEEP are currently available. The cited study by Bigrigg et al<sup>1</sup> primarily addressed the low rate of pregnancy complications. However, they do reference a prospective study that examines pregnancy rates after diathermy treatment of the cervix.<sup>2</sup>

Hollyock and colleagues followed 109 patients after diathermy treatment who did not practice contraception and were not postmenopausal to establish their pregnancy rates. Of the 109 patients followed, 96 conceived during the 3-year follow-up period. Their findings suggest that diathermy causes minimal adverse effects on fertility, parturition, and menstrual function. This procedure is similar to LEEP in that it uses electrical current to fulgurate and destroy dysplastic tissue but differs in that straight wires and ball electrodes were used instead of the wire loop used in LEEP. Diathermy is considered by many physicians to be a more destructive therapy than the newer LEEP approach.

We also have an active infertility service at our hospital. To date, no patients have presented or been referred after LEEP for infertility evaluation in the 3 years in which LEEP has been performed here.

We do agree that there is a need for prospective cohort studies to establish post-LEEP pregnancy rates. However, we cannot find any support in the literature for Dr. Bowman's concern that there is reduced fertility after this procedure.

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Michael B. Harper, MD  
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### References

1. Bigrigg MA, Codling BW, Pearson P, Read MD, Swingler GR. Pregnancy after cervical loop diathermy [letter]. *Lancet* 1991; 337:119.
2. Hollyock VE, Chanan W, Wein R. Cervical function following treatment of intraepithelial neoplasia by electrocoagula-

tion diathermy. *Obstet Gynecol* 1983; 61: 79-81.

## CLARITHROMYCIN vs PENICILLIN

To the Editor:

Dr Schrock has certainly shown that clarithromycin is as effective as penicillin in the treatment of streptococcal pharyngitis (*Schrock CG. Clarithromycin vs penicillin in the treatment of streptococcal pharyngitis. J Fam Pract* 1992; 35:622-6). However, there is information missing from the study that would certainly be important if we as family physicians are to use this agent as primary therapy. What would be the cost of such a decision?

While Schrock's study found that clarithromycin was marginally better in bacteriologic cure rates, the clinical success rates of the two drugs seemed identical. In an era of cost-containment, providing information on the cost consequences of a change in therapy would be most useful.

What would be the dollar cost if we treated all patients with group A  $\beta$ -hemolytic streptococcal pharyngitis with clarithromycin as a first-line agent? What would be the cost if we treated only those who did not respond to penicillin therapy? What would be the cost if the penicillin VK were administered only as 250 mg bid for children with streptococcal pharyngitis?

When the answers to questions such as these are included in research studies,

their clinical value to practicing family physicians will increase.

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To the Editor:

Schrock's study comparing clarithromycin with penicillin for the treatment of streptococcal pharyngitis (*Schrock CG. Clarithromycin vs penicillin in the treatment of streptococcal pharyngitis. J Fam Pract* 1992; 35:622-6) was interesting in its content, but very disturbing by its omissions. A quick telephone call to a local pharmacy revealed that the cost of penicillin V 250 mg tid for 10 days is \$5 while the cost of clarithromycin 250 mg bid for 10 days is \$65, more than 10 times the cost!

Schrock states that \$300 million is spent yearly on the diagnosis and treatment of streptococcal pharyngitis. How would the cost change if clarithromycin was used to treat all these cases? Clearly, because of its cost, clarithromycin should not be a first-line drug for this illness and the author should have stated this. The author states that "... clarithromycin twice daily is as effective and as well tolerated as penicillin..." By "well tolerated," I assume that the author is referring to the safety analysis, but had the patients purchased the medication themselves, they might not have tolerated the price tag!

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## Manuscript Submission

### The Journal of Family Practice

Submit Manuscripts to the Editor

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# YOCON<sup>®</sup> Yohimbine HCl

**Description:** Yohimbine is a 3a-15a-20B-17a-hydroxy Yohimbine-16a-carboxylic acid methyl ester. The alkaloid is found in Rubiaceae and related trees. Also in Rauwolfia Serpentina (L) Benth. Yohimbine is an indolalkylamine alkaloid with chemical similarity to reserpine. It is a crystalline powder, odorless. Each compressed tablet contains (1/12 gr.) 5.4 mg of Yohimbine Hydrochloride.

**Action:** Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

**Indications:** Yocon<sup>®</sup> is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1-3</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1-3</sup>

**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1-3-4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>1</sup>

**How Supplied:** Oral tablets of YOCON<sup>®</sup> 1/12 gr. 5.4mg in bottles of 100's NDC 53159-001-01, 1000's NDC 53159-001-10 and Blister-Paks of 30's NDC 53159-001-30

#### References:

1. A. Morales et al., *New England Journal of Medicine*: 1221, November 12, 1981.
2. Goodman, Gilman — *The Pharmacological basis of Therapeutics* 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. *Weekly Urological Clinical letter*, 27:2, July 4, 1983.
4. A. Morales et al., *The Journal of Urology* 128: 45-47, 1982.



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