

TRINSICON®

HEMATINIC CONCENTRATE
WITH INTRINSIC FACTOR/GLAXO

BRIEF SUMMARY OF PRODUCT INFORMATION TRINSICON®

(hematinic concentrate with intrinsic factor)

A Highly Potent Oral Antianemia Preparation

INDICATIONS AND USAGE: TRINSICON® is a multi-factor preparation effective in the treatment of anemias that respond to oral hematinics, including pernicious anemia and other megaloblastic anemias and also iron-deficiency anemia. Therapeutic quantities of hematopoietic factors that are known to be important are present in the recommended daily dose.

CONTRAINDICATIONS: Hemochromatosis and hemosiderosis are contraindications to iron therapy.

PRECAUTIONS: General: Anemia is a manifestation that requires appropriate investigation to determine its cause or causes.

Folic acid alone is unwarranted in the treatment of pure vitamin B₁₂ deficiency states, such as pernicious anemia. Folic acid may obscure pernicious anemia in that the blood picture may revert to normal while neurological manifestations remain progressive.

As with all preparations containing intrinsic factor, resistance may develop in some cases of pernicious anemia to the potentiation of absorption of physiologic doses of vitamin B₁₂. If resistance occurs, parenteral therapy, or oral therapy with so-called massive doses of vitamin B₁₂ may be necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential and are recommended.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Animal reproduction studies have not been conducted with TRINSICON®. It is also not known whether TRINSICON can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. TRINSICON should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TRINSICON is administered to a nursing woman.

Usage in Children: Safety and effectiveness in children below 10 years of age have not been established.

ADVERSE REACTIONS: Rarely, iron in therapeutic doses produces gastrointestinal reactions, such as diarrhea or constipation. Reducing the dose and administering it with meals will minimize these effects in the iron-sensitive patient.

In extremely rare instances, skin rash suggesting allergy has been noted following the oral administration of liver-stomach material. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

OVERDOSAGE: Symptoms: Those of iron intoxication, which may include pallor and cyanosis, vomiting, hematemesis, diarrhea, melena, shock, drowsiness, and coma.

Treatment: For specific therapy, exchange transfusion and chelating agents. For general management, gastric and rectal lavage with sodium bicarbonate solution or milk, administration of intravenous fluids and electrolytes, and use of oxygen.

DOSAGE AND ADMINISTRATION: One capsule twice a day. (Two capsules daily produce a standard response in the average uncomplicated case of pernicious anemia.)

HOW SUPPLIED: TRINSICON® capsules, dark pink and dark red (No. 2). Bottles of 60 (NDC 0173-0364-22), bottles of 500 (NDC 0173-0364-24), and unit dose packs of 100 capsules (NDC 0173-0364-27).

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LETTERS TO THE EDITOR

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.

AN IMPROVED TECHNIQUE FOR PAPANICOLAOU SMEAR SAMPLING IN POSTMENOPAUSAL WOMEN

To the Editor:

We have recently reported a study on Papanicolaou smear adequacy, comparing the yield of endocervical cells or squamous metaplasia cells with different techniques for four fertility states.¹ In brief, we learned that the best yield of endocervical cells and squamous metaplasia cells was obtained using a Milex spatula after swabbing the cervix free of excess mucus. However, even with this technique, the yield of endocervical cells and squamous metaplasia cells was only 43 percent in postmenopausal women. We have now added two additional techniques of obtaining Papanicolaou smears, with the goal of improving the yield of endocervical cells and squamous metaplasia cells in postmenopausal women.

Twelve hundred twenty consecutive Papanicolaou smear specimens were obtained from nonhysterectomized women from August 1, 1983, to June 30, 1984, among four practice groups in the Family Medicine Unit. Two of the four groups obtained Papanicolaou smears after swabbing the cervix free of visible mucus by sampling the endocervix first with a Milex spatula, then by a saline-soaked cotton swab. The other two practice groups also swabbed the cervix, but reversed the order of sampling, first using the saline-soaked cotton swab, then the Milex spatula.

The criteria for selecting women

and their fertility states as well as cytopathologic interpretations have been described in the previous study.¹ The yield of endocervical cells and squamous metaplasia cells by the two additional techniques was compared first with the other, for each fertility state and second, for all fertility states collectively. The difference between the two techniques was not significant for the entire set of smears or for those from nonpregnant premenopausal, pregnant, or postpartum women. However, the yield of endocervical cells and squamous metaplasia cells in smears from postmenopausal women was significantly higher (63 percent to 49 percent) in the groups that used the Milex spatula prior to the saline-tipped applicator.

This latest study demonstrates that the yield of endocervical cells and squamous metaplasia cells from postmenopausal women can be improved by sampling the endocervix first with a Milex spatula followed by a saline-soaked cotton swab. A possible explanation for this finding is that the serrated edges of the Milex spatula loosen adherent endocervical cells and squamous metaplasia cells, which are then collected on the saline-soaked cotton swab. It is noteworthy that this 63 percent yield of endocervical cells and squamous metaplasia cells in smears from postmenopausal women is greater than that from other published reports² as well as that reported in our previous study.¹ The order of sampling did not affect the yield of endocervical cells and squamous metaplasia cells in the other fertility states studied; however, the yield

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Brief Summary

Tavist®

(clemastine fumarate) tablets, USP 2.68 mg

INDICATIONS: TAVIST Tablets 2.68 mg are indicated for the relief of symptoms associated with allergic rhinitis such as sneezing, rhinorrhea, pruritus, and lacrimation. TAVIST Tablets 2.68 mg are also indicated for the relief of mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

CONTRAINDICATIONS: *Use in Nursing Mothers:* Because of the higher risk of antihistamines for infants generally and for newborns and premature infants in particular, antihistamine therapy is contraindicated in nursing mothers.

Use in Lower Respiratory Disease: Antihistamines should not be used to treat lower respiratory tract symptoms including asthma.

Antihistamines are also contraindicated in the following conditions:

Hypersensitivity to TAVIST (clemastine fumarate) or other antihistamines of similar chemical structure.

Monoamine oxidase inhibitor therapy (see Drug Interaction Section).

WARNINGS: Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy and bladder neck obstruction.

Use in Children: Safety and efficacy of TAVIST have not been established in children under the age of 12.

Use in Pregnancy: Experience with this drug in pregnant women is inadequate to determine whether there exists a potential for harm to the developing fetus.

Use with CNS Depressants: TAVIST has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).

Use in Activities Requiring Mental Alertness: Patients should be warned about engaging in activities requiring mental alertness such as driving a car or operating appliances, machinery, etc.

Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

PRECAUTIONS: TAVIST (clemastine fumarate) should be used with caution in patients with: history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, and hypertension.

Drug Interactions: MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

ADVERSE REACTIONS: Transient drowsiness, the most common adverse reaction associated with TAVIST (clemastine fumarate), occurs relatively frequently and may require discontinuation of therapy in some instances.

Antihistaminic Compounds: It should be noted that the following reactions have occurred with one or more antihistamines and, therefore, should be kept in mind when prescribing drugs belonging to this class, including TAVIST. The most frequent adverse reactions are underlined>.

1. *General:* Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat.

2. *Cardiovascular System:* Hypotension, headache, palpitations, tachycardia, extrasystoles.

3. *Hematologic System:* Hemolytic anemia, thrombocytopenia, agranulocytosis.

4. *Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.

5. *GI System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

6. *GU System:* Urinary frequency, difficult urination, urinary retention, early menses.

7. *Respiratory System:* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

DOSAGE AND ADMINISTRATION: DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND RESPONSE OF THE PATIENT.

TAVIST Tablets 2.68 mg: The maximum recommended dosage is one tablet three times daily. Many patients respond favorably to a single dose which may be repeated as required, but not to exceed three tablets daily.

HOW SUPPLIED: TAVIST Tablets: 2.68 mg clemastine fumarate. White, round compressed tablet, embossed "78/72" and scored on one side. "TAVIST" on the other. Packages of 100.

CAUTION: Federal law prohibits dispensing without prescription.

LETTERS TO THE EDITOR

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of endocervical cells and squamous metaplasia cells was acceptable in either order.

As a consequence of this and our previous study, the technique described in this report is now used routinely in this Family Medicine Unit.

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Steven M. Ornstein, MD

Laurann Litchfield, RN

Department of Family Medicine

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Charleston, South Carolina

References

1. Hamblin JE, Brock CD, Litchfield L, Dias J: Papanicolaou smear adequacy: Effect of different techniques in specific fertility states. *J Fam Pract* 1985; 20:257-260
2. Allingham JD, King A: Patient characteristics and endocervical cell recovery on Papanicolaou smears. *J Fam Pract* 1985; 20:185-190

PROTEINURIA IN ADOLESCENTS

To the Editor:

Concerning the article by Peggs et al (Peggs JF, Reinhardt RW, O'Brien JM: Proteinuria in adolescent sports physical examinations. *J Fam Pract* 1986; 22:80-81), the common finding of proteinuria should not be all that surprising. However, the conclusion that such a common occurrence does not warrant the use of routine urine screening is a dangerous one. A point to be raised is that the preseason examination done may represent the only such physical examination done in these adolescents since early childhood. Certainly proteinuria is not always a sign of more overt conditions such as renal disease or adolescent hypertension, but the use of dipstick urinalysis followed by repeated urinalyses on those proved to be spilling protein is not a high price to pay for the possible uncovering of such pathologic disorders.

I would bring up two possible

reasons why the incidence of proteinuria may have been high: (1) the possibility of exercise-induced proteinuria, and (2) testing equipment aging or storage problems.

It would have been interesting to have learned what the results were on the follow-up testing, which was obviously done on the 62 percent of students who exhibited proteinuria on the first screening. Furthermore, it would have been very helpful to have learned whether any of the proteinuric youngsters eventually ended up having either sustained hypertension or renal pathology.

Douglas B. McKeag, MD

Associate Professor of

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Director of Research

Coordinator of Sports Medicine

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The preceding letter was referred to Dr. Peggs, who responds as follows:

I appreciate Dr. McKeag's comments and believe that they only further point out the lack of justification for doing such routine urine testing on a mass screening basis. Certainly all physicians in primary care recognize that preparticipation sports physical examinations may be one of the few medical evaluations obtained by their patients in the adolescent years. However, the high occurrence of such false negatives argues against the screening value of the routine urine testing at the time of the sports physical. Both the American Academy of Family Physicians and the American Academy of Pediatrics have recommended that urine testing no longer be included in the routine sports examination.

As to the possible reasons for the incidence of proteinuria being so high in our reported population, I agree with the possibility of exercise-induced proteinuria. The likelihood that any of us could

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Norgesic[®] Forte TABLETS

(orphenadrine citrate, 50 mg; aspirin,
770 mg; caffeine, 60 mg)

Stops the pain, not the patient.

Brief Summary

Indications:

1. Symptomatic relief of mild to moderate pain of acute musculo-skeletal disorders.
2. The orphenadrine component is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute painful musculo-skeletal conditions.

The mode of action of orphenadrine has not been clearly identified, but may be related to its analgesic properties. Norgesic and Norgesic Forte do not directly relax tense skeletal muscles in man.

Contraindications:

Because of the mild anticholinergic effect of orphenadrine, Norgesic or Norgesic Forte should not be used in patients with glaucoma, pyloric or duodenal obstruction, achalasia, prostatic hypertrophy or obstructions at the bladder neck. Norgesic or Norgesic Forte is also contraindicated in patients with myasthenia gravis and in patients known to be sensitive to aspirin or caffeine.

The drug is contraindicated in patients who have demonstrated a previous hypersensitivity to the drug.

Warnings:

Norgesic Forte may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; ambulatory patients should therefore be cautioned accordingly.

Aspirin should be used with extreme caution in the presence of peptic ulcers and coagulation abnormalities.

Usage in Pregnancy:

Since safety of the use of this preparation in pregnancy, during lactation, or in the childbearing age has not been established, use of the drug in such patients requires that the potential benefits of the drug be weighed against its possible hazard to the mother and child.

Usage in Children:

The safe and effective use of this drug in children has not been established. Usage of this drug in children under 12 years of age is not recommended.

Precautions:

Confusion, anxiety and tremors have been reported in few patients receiving propoxyphene and orphenadrine concomitantly. As these symptoms may be simply due to an additive effect, reduction of dosage and/or discontinuation of one or both agents is recommended in such cases.

Safety of continuous long term therapy with Norgesic Forte has not been established; therefore, if Norgesic Forte is prescribed for prolonged use, periodic monitoring of blood, urine and liver function values is recommended.

Adverse Reactions:

Side effects of Norgesic or Norgesic Forte are those seen with aspirin and caffeine or those usually associated with mild anticholinergic agents. These may include tachycardia, palpitation, urinary hesitancy or retention, dry mouth, blurred vision, dilatation of the pupil, increased intraocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, drowsiness and rarely, urticaria and other dermatoses. Infrequently an elderly patient may experience some degree of confusion. Mild central excitation and occasional hallucinations may be observed. These mild side effects can usually be eliminated by reduction in dosage. One case of aplastic anemia associated with the use of Norgesic has been reported. No causal relationship has been established. Rare G.I. hemorrhage due to aspirin content may be associated with the administration of Norgesic or Norgesic Forte. Some patients may experience transient episodes of lightheadedness, dizziness or syncope.

Caution:

Federal law prohibits dispensing without prescription. NG-7

References: 1. Colket T, Mann LB: Electromyographic data presented at the following scientific meetings: American Academy of General Practice, Atlantic City, NJ, Apr 1964; American Academy for Cerebral Palsy, Dallas, Tex, Nov 1963; Loma Linda University School of Medicine, Scientific Assembly, Los Angeles, Calif, Alumni Postgraduate Convention, Mar 1964. 2. Masterson JH, White AE: Electromyographic validation of pain relief: Pilot study in orthopedic patients. *Am J Orthop* 1966;8:36-40. 3. Perkins JC: Orphenadrine citrate: Clinical and electromyographic controlled study in patients with low back pain. Data on file, Medical Department, Riker Laboratories, Inc. 4. Gold RH: Treatment of low back syndrome with oral orphenadrine citrate. *Curr Ther Res* 1978;23:271-276.

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St. Paul, Minnesota 55144-1000



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examine a large number of junior and senior high school student athletes who have abstained from exercise prior to the examination is very low. The exercise, as well as the warm summer temperatures, may be factors that explain the results, but also serve as factors that are very difficult to control. As regards the testing equipment at the time of the studies, the quality control checks were performed on separate batches of reagent strips in view of the findings from the first-year studies. Similar fresh supplies of equipment from separate batches were utilized during the second year's examination as well. The staff performing the tests were also cross-checked for their reliability.

In reference to those 214 students who were examined in both years reported, 61 of them (28 percent) had urine test results that were positive for protein on both occasions. Unfortunately our follow-up information is incomplete, since a number of the students are cared for by family physicians in surrounding communities. To our knowledge thus far, none of the students has yet been diagnosed as suffering either renal disease or significant hypertension.

The cost of an initial urine screening test is minimal; the price paid in repeat evaluations and anxiety on the part of the patient and the family is more difficult to calculate. Our desire to maximize the opportunity to evaluate adolescents must be tempered by our concern for cost effectiveness. I feel there is insufficient evidence to continue routine screening of urines in this age group.

James F. Peggs, MD
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OCCUPATIONAL MEDICINE

To the Editor:

Dr. Schusterman's excellent dis-

ussion of work-aggravated illness in three patients (*Schusterman D: Problem-solving techniques in occupational medicine. J Fam Pract* 1985; 21:195-199) is consistent with *The Journal's* policy of keeping physicians ever alert to occupational hazards.

In case 3 (headaches, vertigo, and gastrointestinal distress) the symptoms were not characteristic of either nitrophen (herbicide) poisoning or organophosphate poisoning.¹ Fortunately a job-site visit by Shusterman provided the clue that led him to the correct diagnosis of metal fume fever.

This confirms our experience in Charleston that often the patient cannot give the physician the important facts in the office that the physician needs to make the diagnosis. As with a well-planned home visit to a family, a job-site visit can help patient and physician work out the chain of events together. This can be done in the urban or the rural setting for industrial or agricultural exposures.

The routine office-based occupational history has a very low yield unless supported by onsite investigation.² One wonders why the routine work history is over-emphasized when, in fact, it is so limited and unproductive. Perhaps it can be justified as a minimal first step for the keen clinician who knows that he may have to make further observations at the workshop or farm site.

Stanley H. Schuman, MD, DPH
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Charleston, South Carolina

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1. Hays WJ: Pesticides Studied in Man. Baltimore, Williams & Wilkins, 1985
2. Larsen ME, Schuman SH, Hainer BL: Workplace observation key to a meaningful office history. *J Fam Pract* 1983; 16:1179-1184

BOWEL PREPARATION FOR FLEXIBLE SIGMOIDOSCOPY

To the Editor:

In the October issue of *The Journal of Family Practice*, Weiss and Watkins¹ discussed their experience in bowel preparation for 35-cm flexible proctosigmoidoscopy, concluding that one enema is adequate preparation for a bowel (vs a two-enema technique). Although I do not disagree with their conclusions, I was distressed by their seemingly high incidence of poor preparation in both groups (12.9 percent in the one-enema group; 20.0 percent in the two-enema group). Perhaps they, and others, should review their technique of bowel preparation instead of the quantity required.

In their paper they stated, "all patients received verbal and written instructions on administration of enemas. . . ." But they did not elucidate upon a time interval for holding the enema. According to the package instructions of the Fleet enema, the patient is to "maintain position until urge to evacuate is strong (usually 2 to 5 minutes)."²

My training and practice involve use of a 60-cm sigmoidoscope. I limit the patient's bowel preparation to a single Fleet enema one hour prior to the procedure, requesting patients to hold it in the colon for 10 to 15 minutes. Certainly not all patients can hold a Fleet enema 15 minutes; patient interview prior to the examination has revealed that one third of patients can hold the enema for 5 to 10 minutes, one third for up to 10 minutes, and the remainder for 15 minutes. Although my present study population is small (51 subjects), failure to complete an adequate 60-cm examination (secondary to fecal obstruction) has been encountered in only six cases (11.8 percent). Of these cases, one required a total of four enemas to clear stool palpable within the rectal vault (and then lead to a clear procedure), two patients demon-

strated spastic colon during the examination (which could also be expected to occur during the enema process, minimizing its efficacy), one had significant sigmoid diverticular disease and a tortuous sigmoid colon, one simply had a poor preparation result, and the last patient was requested to hold the enema only to urgency as he was bleeding from radiation proctitis. Excluding the four-enema "clean-out" examination, I was still able to visualize an average of 40-cm (range 35 to 40 cm) and in only one examination was unable to visualize all of the sigmoid colon. Therefore, if I were to relate my experience to a 35-cm examination, my failure rate would be only 2.0 percent.

I do not wish to take issue with Dr. Weiss' protocol for bowel preparation prior to sigmoidoscopy, but to offer data from a slightly different technique that might yield a higher successful outcome to an important diagnostic procedure. His efforts are timely and appreciated as they mark the need to respect the comfort of the patient and at the same time to facilitate the value of this procedure.

Jeffrey H. Baker, MD
State College, Pennsylvania

References

1. Weiss BD, Watkins S: Bowel preparation for flexible sigmoidoscopy. *J Fam Pract* 1985, 21:285-287
2. Fleet instruction leaflet. Lynchburg, Va. CB Fleet, 1985

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