

TORADOL[®]™ and TORADOL[®] ORAL
(ketorolac tromethamine)

Carcinogenesis, Mutagenesis, and Impairment of Fertility

An 18-month study in mice at oral doses of ketorolac tromethamine equal to the parenteral MRHD (Maximum Recommended Human Dose) and a 24-month study in rats at oral doses 2.5 times the parenteral MRHD, showed no evidence of tumorigenicity. Ketorolac tromethamine was not mutagenic in Ames test, unscheduled DNA synthesis and repair, and in forward mutation assays. Ketorolac did not cause chromosome breakage in the *in vivo* mouse micronucleus assay. At 1590 µg/mL (approximately 1000 times the average human plasma levels) and at higher concentrations, ketorolac tromethamine increased the incidence of chromosomal aberrations in Chinese hamster ovarian cells. Impairment of fertility did not occur in male or female rats at oral doses of 9 mg/kg (53.1 mg/m²) and 16 mg/kg (94.4 mg/m²), respectively.

Pregnancy
Pregnancy Category C

Reproduction studies have been performed in rabbits, using daily oral doses at 3.6 mg/kg (42.35 mg/m²) and in rats at 10 mg/kg (59 mg/m²) during organogenesis. Results of these studies did not reveal evidence of fetotoxicity to the fetus. Oral doses of ketorolac tromethamine at 1.5 mg/kg (8.8 mg/m²), which was half of the human oral exposure, administered after gestation day 17 caused dystocia and higher pup mortality in rats. There are no adequate and well-controlled studies in pregnant women. Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

TORADOL is not recommended for use during labor and delivery (see INDICATIONS AND USAGE section of full prescribing information).

Lactation and Nursing

After a single administration of 10 mg of TORADOL[®]™ to humans, the maximum milk concentration observed was 73 ng/mL and the maximum milk-to-plasma ratio was 0.037. After one day of dosing (qid), the maximum milk concentration was 79 ng/mL and the maximum milk-to-plasma ratio was 0.025. Caution should be exercised when TORADOL[®]™ is administered to a nursing woman.

Pediatric Use

Safety and efficacy in children have not been established. Therefore, TORADOL is not recommended for use in children.

Use in the Elderly

Because ketorolac tromethamine is cleared somewhat more slowly by the elderly (see CLINICAL PHARMACOLOGY section of full prescribing information) who are also more sensitive to the renal effects of NSAIDs (see PRECAUTIONS—Renal Effects), extra caution and reduced dosages (see DOSAGE AND ADMINISTRATION section of full prescribing information) should be used when treating the elderly with TORADOL.

ADVERSE REACTIONS

Adverse reaction rates from short-term use of NSAIDs are generally from 1/10 to 1/2 the rates associated with long-term use. This is also true for TORADOL. Adverse reaction rates also may increase with higher doses of TORADOL (see WARNINGS, and DOSAGE AND ADMINISTRATION section of full prescribing information). TORADOL[®]™ is indicated for short-term use. Physicians using TORADOL[®]™ should be alert for the usual complications of NSAID treatment, and should be aware that with longer use (exceeding 5 days) of TORADOL[®]™, the frequency and severity of adverse reactions may increase. Physicians using TORADOL[®]™ should be alert to the relative risks associated with dose and dose duration as described in CLINICAL PHARMACOLOGY—Clinical Studies section of full prescribing information. Physicians using TORADOL should be alert for the usual complications of NSAID treatment. The adverse reactions listed below were reported in clinical trials with TORADOL in which patients received up to 20 doses, in 5 days, of TORADOL[®]™ 30 mg or up to 4 doses a day from long-term studies of TORADOL[®]™ 10 mg qid. In addition, adverse reactions that were reported from TORADOL[®]™ postmarketing surveillance are included in "Incidence 1% or Less." **Incidence Greater than 1%** (probably causally related): **Body as a Whole:** EDEMA^{*}; **Cardiovascular:** HYPERTENSION; **Dermatologic:** RASH, pruritus^{*}; **Gastrointestinal:** NAUSEA (12%), DYSPESIA (12%), GASTROINTESTINAL PAIN (13%), constipation, diarrhea^{*}, flatulence, gastrointestinal fullness, vomiting, STOMATITIS; **Hemic and Lymphatic:** purpura; **Nervous System:** drowsiness^{*}, dizziness^{*}, HEADACHE (17%), sweating. Injection site pain was reported by 2% of patients in multidose studies (vs. 5% for the morphine control group). **Incidence of reported reaction between 3% and 9%.** Those reactions occurring in less than 3% of the patients are unmarked. Reactions reported predominantly from long-term TORADOL[®]™ studies are CAPITALIZED. **Incidence 1% or Less** (probably causally related):

Body as a Whole: hypersensitivity reactions such as anaphylaxis^{*}, bronchospasm, laryngeal edema, tongue edema, hypotension, and flushing, weight gain, fever; **Cardiovascular:** flushing, palpitation, pallor, hypotension, syncope; **Dermatologic:** Lyell's syndrome, Stevens-Johnson syndrome, exfoliative dermatitis, maculo-papular rash, urticaria; **Gastrointestinal:** peptic ulceration, GI hemorrhage, GI perforation (see WARNINGS and PRECAUTIONS), melena, rectal bleeding, gastritis, eructation, anorexia, increased appetite; **Hemic and Lymphatic:** postoperative wound hemorrhage rarely requiring blood transfusion (see WARNINGS and PRECAUTIONS), thrombocytopenia, epistaxis, anemia; **Nervous System:** convulsions, vertigo, tremors, abnormal dreams, hallucinations, euphoria; **Respiratory:** dyspnea, asthma, pulmonary edema; **Urogenital:** acute renal failure (see WARNINGS and PRECAUTIONS), flank pain with or without hematuria and/or azotemia, oliguria, nephritis.

^{*}Italics denote reactions reported from postmarketing experience.

Other Adverse Events (causal relationship unknown): **Body as a Whole:** asthenia; **Gastrointestinal:** pancreatitis; **Hemic and Lymphatic:** leukopenia, EOSINOPHILIA; **Nervous System:** paresthesia, depression, insomnia, nervousness, excessive thirst, dry mouth, abnormal thinking, inability to concentrate, hyperkinesia, stupor; **Respiratory:** RHINITIS, COUGH, dyspnea; **Special Senses:** abnormal taste, abnormal vision, blurred vision, tinnitus, HEARING LOSS; **Urogenital:** polyuria, increased urinary frequency.

[†]Reactions occurred under circumstances where the causal relationship to TORADOL treatment has not been clearly established; they are presented as alerting information for physicians. Reactions reported predominantly from long-term TORADOL[®]™ studies are CAPITALIZED.

See package insert for full prescribing information.

Caution: Federal law prohibits dispensing without prescription.

U.S. Patent No. 4,089,969 and others



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BOOK REVIEWS

Practical Dermatology

by Beth G. Goldstein and Adam O. Goldstein, 328 pages, 211 illus, \$51.95, ISBN 0-8151-3542-4, St Louis, Mo, Mosby-Year Book Inc, 1992.

Perhaps not a day goes by that a family physician does not encounter a patient with a rash. With common complaints of red spots, scaly skin, or terrible itching, dermatology is an intricate part of family medicine.

Practical Dermatology, by Beth and Adam Goldstein (she is a dermatologist and he, a family physician), is a book that will fill a void on many clinicians' bookshelves. The book is divided into four parts. Part I discusses the art of dermatology. This includes the dermatologic basics (terminology, differential diagnoses, and pitfalls in diagnoses), dermatologic therapies (topical agents, corticosteroid agents, patient-centered therapy, and pitfalls of treatment), diagnostic procedures (potassium hydroxide preparation, fungal culture, scabies test, Tzanck smear, Wood's light examination, cryosurgery, curettage, electrodesiccation, and shave and punch biopsies, as well as shave, punch, snip, elliptical, and cyst excisions), and preventive dermatology (occupational and environmental).

Discussions of the common skin dermatoses are found in part II. The authors also include discussions of 110 dermatologic disorders and 25 skin manifestations of systemic disease. The sections are logically arranged in outline order. Each in-

cludes classic description (distribution, primary, secondary), diagnosis, differential diagnosis, treatment, and prevention.

The authors have used more than 125 color illustrations and 200 figures to help the reader understand the physical presentation of the dermatologic findings associated with the clinical disorders.

The sections on treatment include common sense instructions to promote symptomatic relief and resolution of the problem. Pharmacologic options, techniques for surgical intervention, and preventive steps are presented in a straightforward manner.

In addition, this book contains special sections on skin disorders of pregnancy, geriatric patients, acquired immunodeficiency syndrome, the newborn, and the cutaneous manifestations of systemic diseases.

A thoughtful and useful addition is the appendix, which includes patient education handouts on 14 of the most commonly encountered dermatologic problems. The publisher has granted permission to reproduce these handouts for distribution to one's patients.

In summary, this book is very easy to use and will be quite helpful as a rapid reference source for most commonly and some not so commonly encountered dermatologic problems. Collected from the files of two medical schools and two practices, the photographs are excellent. The common-sense approaches to therapy and prevention contain many of the practical pearls of dermatology that can make a family physician's practice more successful and rewarding. This book would make an excellent basic text and/or reference text for medical students, residents, faculty, and prac-

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Manual of Otolaryngology: Diagnosis and Therapy

edited by Marshall Strome, James H. Kelly, and Marvin P. Fried, 287 pp, with illus, \$27.50, ISBN 0-316-81968-9, Boston, Mass, Little Brown & Co, 1992.

This second edition of the *Manual of Otolaryngology* covers most common ear, nose, and throat problems and many otolaryngologic emergencies. The text has eight contributing authors and was written to provide concise, timely information that can be applied to the medical care of patients. The information is organized in a functional manner for the practicing physician.

This pocket-sized text is similar to others but is more detailed. The eight chapters are arranged primarily by anatomic division (ear, larynx, etc). There is also a chapter that focuses on emergencies, and the final chapter addresses otolaryngologic manifestations of acquired immunodeficiency syndrome.

All chapters provide concise and current information and are well written. Family physicians will find the overview of the ear and larynx to be of particular benefit. In the review of the ear, most common problems are discussed, including vertigo, otitis media, serous otitis, otitis externa, and other diseases of the external canal. Diseases are discussed in a pragmatic manner, providing useful signs and symptoms for diagnostic purposes and a clear plan for treatment. The overview of vertigo provides a list of common nonvestibular causes of dizziness and schematic representations of the clinical spectrum of dizziness. Tympanometry is briefly reviewed; unfortunately, graphs of the

different curves generated and an explanation of how to interpret the tympanogram are not included. Cholesteatoma is reviewed and a clear, useful definition is presented.

The chapter on the larynx includes a thorough review of the anatomy and evaluation of the larynx. The overview of stridor is one of the best I have ever reviewed. Hoarseness, including acute and chronic causes, with appropriate diagnostic and therapeutic recommendations for the primary care practitioner, is also discussed. The latter part of this chapter gives an overview of neoplasms of the larynx and of respiratory obstruction. This section is quite detailed and much of the diagnostic information is more appropriate to the otolaryngologist. This chapter also contains an appendix entitled "Voice Evaluation and Rehabilitation," which provides a detailed review of speech and voice therapy that could be useful in making appropriate referrals to speech pathology.

In the chapter on the head and neck, the ethics of head and neck surgery are discussed, as well as therapeutic interventions. The statement,

... it is the mature physician's responsibility to lucidly present all the available data and to assist a fellow human being in reaching a decision that is most appropriate for a given psychologic and social set,

shows an ethical concern for the patient not appreciated in many such texts. Head and neck surgery can impact negatively, both psychologically and cosmetically, regardless of the therapeutic triumph. The authors of this section are to be commended for their caring approach to the patient, an approach that is familiar to the family physician.

In summary, the *Manual of Otolaryngology* is an inexpensive, well-written, informative, pocket-sized book. It is a handy reference for the office setting and in the pocket of the learner on the wards. Although many chapters contain information beyond the scope of ambulatory family medicine, all chapters contain use-

ful primary care information. I recommend this book as a good reference manual on otolaryngology. It is easy to read and is a good resource for quick, clear, and thorough information about common otolaryngologic problems.

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Conn's Current Therapy 1993

45th ed, edited by Robert E. Rakel, 1274 pp, \$55, ISBN 0-7216-6745-7, Philadelphia, Pa, WB Saunders Co, 1993.

Most primary care physicians are already acquainted with *Conn's Current Therapy 1993*. Now in its 45th edition, this textbook has a well-deserved reputation as a useful reference of up-to-date treatment strategies for the practicing physician. The 1993 edition tackles 286 clinical problems and also includes an appendix of important laboratory values and a thorough index. Subject matter is arranged according to organ systems, with the exception of an introductory section on the symptomatic care of the patient and a closing section on physical and chemical injuries that also includes an extensive discussion of acute poisonings. While the format of most of the topics presented includes a brief introduction, etiology, description of signs and symptoms, and diagnosis, the emphasis is clearly on treatment. The writing is remarkably crisp, clear, and consistent, given the fact that 369 authors have contributed to this book. Over 500 tables and figures further distill concise treatment methods into nicely packaged units of information such as an analgesic ladder for the management of cancer pain, an endocarditis prophylaxis regimen, a dosage schedule for antiemetic therapy, and guidelines for the treatment of calcium stone disease.

Conn's Current Therapy 1993 teems not only with novel but occasionally