

BioDrugsTM

Clinical Immunotherapeutics, Biopharmaceuticals and Gene Therapy

2001, Vol. 15, No. 7 (pp. 419-489)

ISSN: 1173-8804

Adis Drug Evaluation
Silymarin: A Review

Leading Article
Pegylated Interferons for Chronic Hepatitis C

Review Articles
Molecular Biology of Pancreatic Cancer
Anti-Allergy Drugs for Young Children
Therapeutic Advances in Cutaneous T-Cell Lymphoma

Available Online

PHARMACY LIBRARY
UNIVERSITY OF WISCONSIN

AUG 28 2001

Madison, WI 53705

adis
INTERNATIONAL

A Wolters Kluwer Company

AUCKLAND • BARCELONA • BUENOS AIRES • CHESTER • HONG KONG • MADRID
MILAN • MUNICH • OSAKA • PARIS • PHILADELPHIA • SÃO PAULO • SYDNEY

Contents

Leading Article	Development of Pegylated Interferons for the Treatment of Chronic Hepatitis C <i>A Kozlowski, SA Charles, JM Harris</i>	419-429
Review Articles	Therapeutic Advances in Biological Response Modifiers in the Treatment of Cutaneous T-Cell Lymphoma <i>CC Vittorio, AH Rook, LE French, M Shapiro, MS Lehrer, JM Junkins-Hopkins</i>	431-437
	Molecular Biology of Pancreatic Cancer: Potential Clinical Implications <i>GH Sakorafas, GG Tsiotos</i>	439-452
	Clinical Prescribing of Allergic Rhinitis Medication in the Preschool and Young School-Age Child: What are the Options? <i>SP Galant, R Wilkinson</i>	453-463
Adis Drug Evaluation	Silymarin: A Review of its Clinical Properties in the Management of Hepatic Disorders <i>K Wellington, B Jarvis</i>	465-489

PHARMACY LIBRARY
UNIVERSITY OF WISCONSIN
AUG 28 2001
Madison, WI 53705

BioDrugs is indexed in *Index Medicus*, *Medline*, *Chemical Abstracts*, *EMBASE/Excerpta Medica*, *Current Contents/Clinical Medicine*, *Science Citation Index*[®], *SciSearch*[®], *Research Alert* and the *Medical Documentation Service*TM. Individual articles are available through the ADONIS document delivery system and are available on-line via the World Wide Web through Ingenta. Further details are available from the publisher.

International Editorial Board

L. Bergmann, *Frankfurt, Germany*
J. Bousquet, *Montpellier, France*
J. Brostoff, *London, England*
E. De Clercq, *Leuven, Belgium*
G.D. Demetri, *Boston, MA, USA*
R.D. deShazo, *Mobile, AL, USA*
R. Feld, *Toronto, ON, Canada*
C.J. Fisher Jr, *Cleveland, OH, USA*
T.R. Flotte, *Gainesville, FL, USA*
Ø. Førre, *Oslo, Norway*
A. Ganser, *Hannover, Germany*
F. Guilhot, *Poitiers, France*
J.W. Hadden, *Tampa, FL, USA*
B.D. Kahan, *Houston, TX, USA*
S.L. Lightman, *London, England*
R.F. Lockey, *Tampa, FL, USA*
V.J. Marder, *Los Angeles, CA, USA*
T.C. Merigan Jr, *Stanford, CA, USA*
W.J. Metzger, *Greenville, NC, USA*
H.W. Murray, *New York, NY, USA*
J.L. Murray, *Houston, TX, USA*
C. Picado, *Barcelona, Spain*
A.J. Pinching, *London, England*
T.A.E. Platts-Mills, *Charlottesville, VA, USA*
C. Ponticelli, *Milan, Italy*
A.L. Sheffer, *Chesnut Hill, MA, USA*
C.A. Stein, *New York, NY, USA*
A.-M. Svennerholm, *Gothenburg, Sweden*
P.C. Tugwell, *Ottawa, ON, Canada*
J.W.M. van der Meer, *Nijmegen, The Netherlands*
S.A. Watson, *Nottingham, England*
D.A. Willoughby, *London, England*

Aim and Scope: *BioDrugs* provides healthcare decision makers with a regular programme of peer reviewed articles covering issues in the clinical application of biotechnological and immunological knowledge to the treatment of human disease.

The Journal includes:

- Leading/current opinion articles providing an overview of contentious or emerging issues
- Definitive reviews on a broad range of topics in biopharmaceuticals, gene therapy and clinical immunology, including the development and optimum therapeutic use of agents based on biotechnological and immunological principles and the treatment of disorders with an immunological component
- Therapy in Practice reviews including recommendations for specific clinical situations
- Adis Drug Evaluations reviewing the properties and place in therapy of both newer and established drugs
- Adis New Drug Profiles with expert commentary
- Original research articles on the human clinical pharmacology, clinical development and therapeutic optimisation of relevant drugs will also be considered for publication.

All manuscripts are subject to peer review by international experts. Letters to the Editor are welcomed and will be considered for publication.

Editor: Anne Bardsley-Elliott

Publication Manager: Hera C. Millard

Editorial Office and Inquiries: Adis International Ltd., 41 Centorian Drive, Private Bag 65901, Mairangi Bay, Auckland 10, New Zealand. Information on the preparation of manuscripts will be provided to authors.

E-mail: biodrugs@adis.co.nz

<http://www.adis.com>

BioDrugs (ISSN 1173-8804) is published as 1 volume with 12 monthly issues by Adis International Limited. Annual 2001 subscription price: \$US1095; Japan ¥167 792. Personal subscription rate: \$US165; Japan ¥24 750. Online only available for the same price as print subscription; print and online available for an additional 20%. (Further subscription information is given at the back of each issue.)

Policy Statement: Although great care has been taken in compiling the content of this publication, the publisher and its servants are not responsible or in any way liable for the currency of the information, for any errors, omissions or inaccuracies, or for any consequences arising therefrom. Inclusion or exclusion of any product does not imply its use is either advocated or rejected. Use of trade names is for product identification only and does not imply endorsement. Opinions expressed do not necessarily reflect the views of the Publisher, Editor or Editorial Board.

Copyright: © 2001 Adis International Ltd. All rights reserved throughout the world and in all languages. No part of this publication may be reproduced, transmitted or stored in any form or by any means either mechanical or electronic, including photocopying, recording, or through an information storage and retrieval system, without the written permission of the copyright holder.

The appearance of the code at the top of the first page of an article in this journal indicates the copyright owner's consent that copies of the article may be made for the personal or internal use of specific clients. This consent is given provided that the fee of \$US22 per copy is paid directly to the Copyright Clearance Center Inc., 222 Rosewood Drive, Danvers, Massachusetts 01923, USA, for copying beyond that permitted by sections 107 or 108 of the US Copyright Law. This consent does not extend to other kinds of copying such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale.

Clinical Prescribing of Allergic Rhinitis Medication in the Preschool and Young School-Age Child

What are the Options?

Stanley P. Galant¹ and Robert Wilkinson²

1 Department of Paediatric Allergy/Immunology, University of California, Irvine, California, USA

2 Department of Pharmacy, St Joseph Hospital, Orange, California, USA

Contents

Abstract	453
1. Aetiology, Epidemiology and Impact of Allergic Rhinitis (AR) in Children	454
2. Evaluation and Diagnosis	454
3. Pathogenesis	455
4. Treating AR in the Child	455
4.1 Histamine H ₁ Receptor Antagonists (Antihistamines)	456
4.2 Decongestants	458
4.3 Intranasal Corticosteroids	458
4.4 Mast Cell Stabilisers	461
4.5 Anticholinergic Agents	461
5. Conclusions and Recommendations	461

Abstract

Allergic rhinitis (AR) is the most common chronic condition in children and is estimated to affect up to 40% of all children. It is usually diagnosed by the age of 6 years. The major impact in children is due to co-morbidity of sinusitis, otitis media with effusion, and bronchial asthma. AR also has profound effects on school absenteeism, performance and quality of life.

Pharmacotherapy for AR should be based on the severity and duration of signs and symptoms. For mild, intermittent symptoms lasting a few hours to a few days, an oral second-generation antihistamine should be used on an as-needed basis. This is preferable to a less expensive first-generation antihistamine because of the effect of the latter on sedation and cognition. Four second-generation antihistamines are currently available for children under 12 years of age: cetirizine, loratadine, fexofenadine and azelastine nasal spray; each has been found to be well tolerated and effective. There are no clearcut advantages to distinguish these antihistamines, although for children under 5 years of age, only cetirizine and loratadine are approved. Other agents include pseudoephedrine, an oral vasoconstrictor, for nasal congestion, and the anticholinergic nasal spray ipratropium bromide for rhinorrhoea. Sodium cromoglycate, a mast cell stabiliser nasal spray, may also be useful in this population.

For patients with more persistent, severe symptoms, intranasal corticosteroids

are indicated, although one might consider azelastine nasal spray, which has anti-inflammatory activity in addition to its antihistamine effect. With the exception of fluticasone propionate for children aged 4 years and older, and mometasone furoate for those aged 3 years and older, the other intranasal corticosteroids including beclomethasone dipropionate, triamcinolone, flunisolide and budesonide are approved for children aged 6 years and older. All are effective, so a major consideration would be cost and safety. For short term therapy of 1 to 2 months, the first-generation intranasal corticosteroids (beclomethasone dipropionate, triamcinolone, budesonide and flunisolide) could be used, and mometasone furoate and fluticasone propionate could be considered for longer-term treatment. Although somewhat more costly, these second-generation drugs have lower bio-availability and thus would have a better safety profile.

In patients not responding to the above programme or who require continuous medication, identification of specific triggers by an allergist can allow for specific avoidance measures and/or immunotherapy to decrease the allergic component and increase the effectiveness of the pharmacological regimen.

1. Aetiology, Epidemiology and Impact of Allergic Rhinitis (AR) in Children

Allergic rhinitis (AR) is currently the most common of all chronic conditions in children. The disease can be classified as seasonal or perennial, depending on when the child appears to have symptoms most predominantly. Those children with seasonal allergic rhinitis (SAR) have symptoms predominantly in the spring and fall generally due to tree, grass and weed pollen, and occasionally mold spores, whereas those with perennial allergic rhinitis (PAR) have symptoms all year long secondary to year-round indoor allergens, such as the housedust mite, animal danders, mould spores and cockroach allergens (the latter particularly in the inner city). PAR generally occurs in younger children and is frequently associated with otitis media with effusion and sinusitis, while the SAR pattern is usually seen in older children and adults. The 2 conditions can occur together and are not different diseases; therefore treatment is the same.

A 1988 US survey found AR to be present in 59.7 cases per 1000 children up to the age of 18 years.^[1] This probably is an underestimate, since it included only those with SAR or hayfever. A prospective study of 747 children in Tucson, Arizona, found that 42% of families interviewed had a physician diagnosis of AR by the age of 6 years, and half of these children developed this condition in

the first year of life.^[2] The prevalence of AR worldwide appears to be similar to that of the United States.^[3] The estimated direct expenditure for AR and allergic conjunctivitis in children 12 years of age or less was estimated to be \$2.3 billion in the US in 1996.^[4] Risk factors for developing AR include a family history of atopy, serum immunoglobulin (Ig) E levels ≥ 100 IU/ml before the age of 6 years, higher socioeconomic class, exposure to indoor allergens, and a positive skin test indicating specific IgE antibodies.^[5]

AR can have a profound effect on a child's quality of life. Children with AR more likely to demonstrate shyness, depression, anxiety, fearfulness and fatigue compared with nonallergic peers.^[6] Furthermore, these children miss 2 million days of school each year in the US, and even when they attend school their ability to learn and process cognitive input is significantly impaired.^[7] If left untreated, AR can exacerbate and contribute to symptoms of asthma, sinusitis and otitis media with effusion.^[8]

2. Evaluation and Diagnosis

The diagnosis of AR is highly dependent on obtaining a comprehensive history from an older child or from the parent of a younger child. Signs and symptoms in older children with SAR include a history of paroxysmal sneezing, nasal itching, clear rhinorrhoea and red, itchy, watery eyes, par-

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.