

National Guidelines for a Novel Therapy: Update on Clinical Trials and Experience Using Consensus Panel Recommendations for Incorporating Omalizumab into Asthma Management

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Educational Objectives

After reading this article, readers should be able to:

- Review the pathogenesis of allergic asthma and the mechanism of action of a novel treatment modality, IgE blockers.
- Review the outcomes from clinical trials of an IgE blocker, omalizumab.
- Review the role and results of new therapies, such as IgE blockers, and the potential to incorporate these treatments into established asthma guidelines.
- Review clinical studies and potential treatment strategies for specific populations, including suboptimally controlled asthma in patients with moderate-persistent to severe-persistent asthma.
- Discuss experts' experience with IgE blockers in treating patients with difficult-to-control asthma in accordance with Consensus Panel Guidelines.

Abstract

Omalizumab is a recombinant DNA-derived, humanized monoclonal antibody that inhibits the binding of IgE to the surface of mast cells and basophils, thereby limiting the release of mediators of the allergic response. In multiple studies, omalizumab has proved to be an effective treatment for moderate-persistent to severe-persistent asthma, improving symptoms as well as reducing exacerbations and health care utilization.

In June 2003, the Food and Drug Administration (FDA) approved omalizumab (Xolair, Genentech, Inc./Novartis Phar-

maceuticals) to treat moderate-persistent to severe-persistent asthma with an allergic component. A panel of experts in the specialties of allergy and pulmonology was convened on two occasions to discuss the use of omalizumab with respect to the asthma guidelines and to create an interim clinical practice guideline on the drug's appropriate use for practitioners and payers.

One compelling reason for pursuing the development of new modalities to treat the underlying causes of asthma is a growing awareness of the limitations of standard therapy. A plateau effect has been observed in the dose-response curve of inhaled corticosteroids whereby increasing the dose increases only the systemic effects and not the physiological improvement (i.e., pulmonary function and airway hyper-responsiveness measures.) This flat dose-response curve may be contributing to a rising number of asthmatic patients who are unable to achieve control. As a novel drug with dem-

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onstrated additive effects on maximal recommended therapy, omalizumab has the potential to increase the percentage of patients who achieve control when a skin or a radioallergosorbent test (RAST) confirms allergic asthma.

Although specialists in allergy and pulmonology have successfully incorporated omalizumab into treatment plans for their patients with difficult-to-control asthma, questions remain regarding the ideal use of this injectable biologic agent:

- Ideally, how should this agent be incorporated into existing National Asthma Education and Prevention Program (NAEPP) asthma treatment guidelines?
- For which types of asthma patients will the agent provide the most benefit?
- What are the most appropriate goals of therapy, markers of success, and endpoints in treatment?

Introduction

Asthma continues to place an enormous burden on the U.S. health care system. More than 31 million people have asthma, with the total cost of disease estimated to be \$12 billion in 1998.¹ Utilization of health care resources for asthma is disproportionately high among the 20% of patients with difficult-to-treat

asthma. These patients consume 80% of all asthma-related health care resources in the form of increased emergency visits, hospitalizations, and medication use. Indirect costs include absence from work or school and decreased potential earnings resulting from disability and death.² A large observational study highlighted the lack of control in patients with moderate-to-severe asthma and confirmed the increased use of health care resources and the reduced quality of life experienced by these patients.³

Role of Immunoglobulin E in the Pathogenesis of Asthma

In recent years, airway inflammation and atopy have become recognized as key factors in the pathogenesis of asthma. *Atopy*, the predisposition to form antibodies and to acquire allergies, is strongly correlated with the incidence of asthma.⁴ National statistics show that more than 70% of Americans with asthma also have allergies.⁴ The World Health Organization has suggested that allergic rhinitis is not a solitary disease but a complex syndrome that affects the upper and lower airways and that its presence may be a major risk factor in the development of asthma.⁵

Immoglobulin E (IgE)-dependent mechanisms are involved in many allergic responses at the level of the airway. Once IgE antibodies are produced, mast cells and other airway cells are sensitized and become activated when specific antigens are encountered (Figure 1).

IgE is the initiator of the inflammatory cascade in the airways that produces the classic early-phase and late-phase airway responses to an inhaled allergen. Airway inflammation is initiated when an inhaled allergen forms a cross-link with a mast cell or basophil-bound IgE. Linking of the allergen and receptor-bound IgE provokes mast-cell and basophil degranulation and a release of inflammatory mediators, including histamine, prostaglandins, and leukotrienes. Together, these mediators are responsible for the mucosal edema and smooth muscle contraction that are the hallmarks of the early asthma response.⁶

IgE Blockers: A Novel Approach to Treating Asthma

Most patients with asthma have atopy and possess specific IgE antibodies to the allergens responsible for causing airway inflammation.⁴ Because of the central role of IgE in atopic disease, inhibiting IgE-mediated events with IgE blockers represents a novel approach to reducing the severity of asthma.

Omalizumab, a monoclonal antibody, forms complexes with circulating free IgE at the site of binding to mast cells. The formation of

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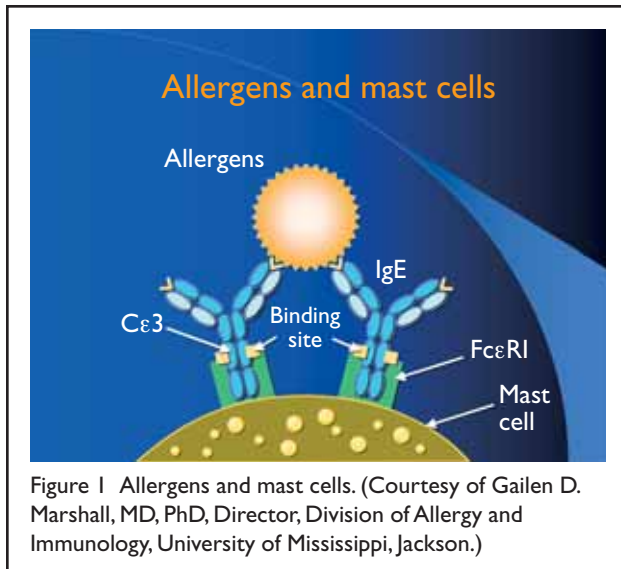


Figure 1 Allergens and mast cells. (Courtesy of Gailen D. Marshall, MD, PhD, Director, Division of Allergy and Immunology, University of Mississippi, Jackson.)

these complexes removes free IgE from circulation and inhibits the binding of IgE to mast cells, indirectly down-regulating IgE receptor expression on mast cells. Omalizumab also down-regulates Fcε receptor I on mast cells and basophils and on other cells involved in inflammatory responses, including type 1 and 2 dendritic cells.⁷ Treatment of allergic asthmatic patients with omalizumab prevents IgE from triggering the release of inflammatory mediators in response to an allergen, thereby inhibiting inflammation at its source rather than suppressing it after it has occurred.

Omalizumab has undergone extensive study in randomized, controlled trials. In phase 3 trials, the agent was tested in adolescents and adults, 12 to 75 years of age, with difficult-to-control, moderate-to-severe allergic asthma.⁸⁻¹¹ The primary endpoint of these trials was the number of exacerbations experienced by patients, defined as an episode severe enough to result in a doubling of the inhaled steroid dose or a course of systemic corticosteroids.

In the pooled phase 3 trials, omalizumab decreased asthma exacerbations by 50%, compared with the rate for placebo, and it improved asthma-related quality of life in all domains. Omalizumab reduced the use of health care resources, as manifested by lower rates of hospitalizations and emergency-department visits.¹²

A Consensus Panel Approach for Incorporating New Technologies into Established Guidelines

Despite the existence of internationally recognized, evidence-based guidelines for the management of asthma,¹³⁻¹⁶ the disease remains inadequately controlled in a significant number of patients.³ Several factors may play a role in this phenomenon, including access to care, comorbid conditions, and suboptimal adherence. Additional possibilities are that ideal treatment regimens have not been fully elucidated and national standards have yet to be updated to reflect knowledge of

recently approved treatment modalities. As newly discovered agents target different points in the asthma cascade, it is crucial to determine their appropriate place in treatment regimens.

At the completion of the phase 3 trials for omalizumab, its developers (Genentech/Novartis) and the Department of Health Policy at Jefferson Medical College convened a panel of asthma experts to revisit the NAEPP Guidelines of 1997 and to review the potential role of IgE blocker therapy within the current asthma guidelines. The panel consisted of leaders in the fields of allergy and immunology, pulmonology, pediatrics, and pharmacology, as well as medical executives representing major managed care organizations (MCOs).¹⁷ The panel endorsed the 1997 NAEPP recommendations for mild-intermittent and mild-persistent asthma¹³ but recommended several additions to the remainder of the guidelines in light of the new technology (Table 1).

First, the panel addressed the problem of inadequate control of asthma in a high proportion of "persistent-asthma" categories and acknowledged the likely contribution of patient nonadherence to this lack of control in certain cases. The panel also recommended that guidelines include an aggressive and comprehensive education and evaluation program for patients who fall into the moderate-persistent and severe-persistent asthma categories, especially patients who are not able to achieve optimal control of their asthma. This program would include instruction on the use of devices, environmental control and avoidance measures, rescue action plans, and self-management and adherence techniques.

A second recommendation related to the actual treatment guidelines for patients with moderate-persistent and severe-persistent asthma. The panel agreed that distinguishing between these two states is difficult in clinical practice and questioned the value of making such a clinical distinction between these two suboptimally controlled groups. Further, differences in the treatment regimens associated with each were thought to be unnecessarily confusing, possibly contributing to lapses in patient adherence. Because of these concerns, the panel recommended eliminating the distinction between these categories, allowing for standardization of therapy among patients with suboptimally controlled asthma.

Finally, the panel encouraged a wider range of strategies for asthma management to supplement the current asthma guideline recommendations. The panel noted, on the basis of clinical trial data for omalizumab, that IgE-blocking therapy presents an attractive alternative for suboptimally controlled asthma after unsuccessful attempts with the established therapies. IgE-blocking therapy appears to reduce asthma exacerbation rates in patients who:

- are at least 12 years old.
- have evidence of reversible airway disease.
- have an IgE level of 30 IU/ml or more with an upper limit of 700 IU/ml in adults.

(Note: Attempts at therapy in patients with higher levels may be unsuccessful because of the inability to suffi-

Table 1 Consensus Panel Approach to Effective Asthma Management

Disease State	Daily Medication	Considerations for Anti-IgE Therapy						
Severe-persistent asthma	<p>Preferred Treatment:</p> <ul style="list-style-type: none"> High-dose inhaled corticosteroids <i>and</i> Long-acting inhaled beta₂ agonists <i>and</i> (if needed) Corticosteroid tablets or syrup long term (2 mg/kg per day, generally not exceeding 60 mg/kg per day). Repeated attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids. 	<ul style="list-style-type: none"> Patient at least 12 years of age Historical evidence of reversible disease (such as ≥12% improvement in FEV with at least a 200-ml increase or ≥20% improvement in PEF) IgE level > 30 IU/ml Historical evidence of specific allergic sensitivity (i.e., positive skin test or blood test for specific IgE) 						
Moderate-persistent asthma	<p>Preferred Treatment:</p> <ul style="list-style-type: none"> Low- to medium-dose inhaled corticosteroids <i>and</i> long-acting beta₂-agonists <p>Alternative Treatment (listed alphabetically):</p> <ul style="list-style-type: none"> Increase inhaled corticosteroids within medium-dose range <i>or</i> Low- to medium-dose inhaled corticosteroids <i>and</i> either a leukotriene modifier <i>or</i> theophylline (e.g., Theolair) 	<ul style="list-style-type: none"> Inadequately controlled* despite medium dose of inhaled corticosteroids for at least 3 months in combination with a trial of long-acting inhaled beta₂-agonists or leukotriene modifiers (or medication intolerance) Systemic corticosteroids or high-dose inhaled corticosteroids required to maintain adequate control May consider as directly observable therapy in patients not adhering to prescribed therapy 						
Patient evaluation and education	<p>All patients with persistent asthma require further evaluations and education, including identification of allergic triggers and comorbidities, and detailed advice regarding management of the condition.</p> <p style="text-align: center;">Types of Education:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; text-align: center;">Disease state</td> <td style="width: 50%; text-align: center;">Pharmacotherapy</td> </tr> <tr> <td style="text-align: center;">Environmental controls</td> <td style="text-align: center;">Immunotherapy</td> </tr> <tr> <td style="text-align: center;">Inhaler technique</td> <td style="text-align: center;">Action plan</td> </tr> </table>		Disease state	Pharmacotherapy	Environmental controls	Immunotherapy	Inhaler technique	Action plan
Disease state	Pharmacotherapy							
Environmental controls	Immunotherapy							
Inhaler technique	Action plan							
Mild-persistent asthma	<p>Preferred Treatment:</p> <ul style="list-style-type: none"> Low-dose inhaled corticosteroids <p>Alternative Treatment (listed alphabetically):</p> <ul style="list-style-type: none"> Cromolyn sodium (e.g., Intal Inhaler), leukotriene modifiers, nedocromil (e.g., Tilade) <i>or</i> Sustained-release theophylline (e.g., Theolair SR) to serum concentration of 5–15 mcg/ml 	None						
Mild-intermittent asthma	No daily medication needed. Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms; a course of systemic corticosteroids recommended.	None						
<p>* Examples of inadequate control: utilization of emergency department, hospitalization, or urgent-care visits; excessive use of short-acting beta₂-agonist or use of oral steroids; and impairment in activities of daily living, such as work, school, exercise, and sleep. FEV = forced expiratory volume; IgE = immunoglobulin E; PEF = peak expiratory flow.</p>								

ciently reduce free IgE to the levels required for reducing Fcε receptor 1 expression. A few clinicians have reported positive results in patients with borderline total IgE levels of less than 30 IU/ml.)

- show evidence of specific allergic sensitivity by positive skin or blood tests for a specific IgE.

The panel recommended that IgE blockers be used as an

alternative treatment in patients with inadequately controlled asthma who are using high-dose inhaled corticosteroids or who require frequent courses of systemic corticosteroids. The panel suggested that IgE blockers could also be considered in patients whose disease is inadequately controlled despite a three-month trial of medium-dose inhaled corticosteroids and long-acting beta agonists or leukotriene receptor agonists. The panel's recommended additions to the current asthma guidelines are listed in Table 1.

Approximately six months following the FDA's approval of omalizumab, in January 2004, a second consensus panel was convened to evaluate the first six months of real-world experience with the drug, to revisit the panel's previous recommendations regarding clinical practice guidelines, and to address unanswered questions related to managing allergic asthma and the remaining barriers to acceptance as well as to implementing updates to the guidelines.

The panel endorsed the previously released asthma guideline recommendations (i.e., the inclusion of criteria for consideration of IgE-blocker therapy and a comprehensive education and evaluation program). The panel also acknowledged several barriers to the appropriate dissemination of the updated asthma guidelines. These challenges included the problems of patient adherence as well as confusion related to the unclear definitions of "optimal control" and "allergic asthma."

Unanswered questions specific to IgE blocker therapy included the duration and characteristics of the optimal drug trial with an IgE blocker, the definitions of the appropriate end-points of therapy, and the most appropriate mechanisms of payment for the drug.

Panel members also voiced general concerns about the difficulty of distributing new medical information and guidelines into the community of clinical practitioners.

Current Patterns of Use: Anti-IgE Therapy

Direct information about the patterns of use of anti-IgE therapy is not readily available. An indirect method of assessing patterns of use is to analyze the prior authorization strategies of MCOs associated with this particular therapy. The use of biologic injectables, such as omalizumab, is frequently subjected to prior authorization procedures that ensure medical appropriateness. A review of these prior authorization procedures, available as published documents, provides insight into patterns of use via the criteria that must be met for coverage of the drug. Because of the high costs associated with biologic injectables, criteria for coverage have a strong influence on patterns of clinical use.

An assessment of prior authorization procedures for 40 commercial health plans covering more than 30 million members determined that plans representing almost 90% of these covered lives had prior authorization procedures consistent with the clinical practice guideline updates recommended by the expert panel, the FDA package insert guidelines, or a less restrictive procedure.¹⁸

The survey findings show that most patients in these plans

have access to omalizumab in the clinical situations deemed "appropriate" by the expert panel of clinicians. The findings also suggest that the intellectual process of formulating these guidelines may have a positive effect on the clinical practice standards supported by commercial health plans as well as by clinicians.

An informal poll of the expert clinicians who helped to develop the guidelines for omalizumab sheds light on prescribing patterns and how allergists and pulmonologists are addressing some of the unanswered questions. Most experts assigned high priority to "high doses of other medications ineffective in controlling symptoms" (80%) and "reducing dependence on steroids" (100%) in their decisions to prescribe anti-IgE therapy. When asked at which steroid dosage levels they considered prescribing anti-IgE therapy when patients' symptoms failed to be controlled, the experts most frequently indicated "salmeterol/fluticasone 50/500 mcg" (e.g., Advair Diskus, GlaxoSmithKline) (33.3% of the time) and "trial of corticosteroids" (33.3% of the time).

While questions remain—for instance, a reasonable end-point for a successful course of therapy has yet to be established—the respondents believed that the process of developing an interim guideline in the absence of national standards or extensive experience is helpful in determining appropriate patterns of the use of a novel agent.

Anti-IgE Profile

In clinical trials contributing a total of more than 2,037 patients with mild-to-severe allergen-mediated asthma, anti-IgE therapy was well tolerated, and no complications associated with reduced circulating IgE or antibodies against the drug were observed. The incidence of adverse drug events (ADEs) was similar among treatment groups, and no drug-related serious ADEs were reported. In general, treatment with anti-IgE was well tolerated, and both patient and physician assessments of the treatment were positive.

As with any protein, there is a potential for local or systematic reactions to occur. Patients should be advised to seek prompt medical attention in the event of an allergic reaction. Parasitic infections may result in elevated serum IgE concentrations, and the effects of anti-IgE in the presence of known concurrent parasitic infections are being studied.

Investigations are ongoing to identify any association between anti-IgE treatment and the incidence of malignancies. Current long-term data do not indicate such an association.

Source

Walker S, Monteil M, Phelan K, et al. Anti-IgE for chronic asthma in adults and children. Cochrane Database of Systematic Reviews 2005, Issue 2. Available at: www.cochrane.org/reviews/english/ab003559.html.

What Is Considered “Optimal” Control of Asthma?

The goal of asthma management is to achieve and maintain control of the disease while minimizing the occurrence or severity of adverse drug events (ADEs) from the therapies used. We know from multiple, large, community-based studies that despite the promulgation of an international effort and guidelines to standardize the assessment and management of asthma, most asthma patients continue to experience a high rate of symptoms and functional impairment from their illness.^{19–21}

Strategies to improve asthma control can lead to socioeconomic gains in terms of improved school attendance; fewer absences from work; and, by implication, a smaller burden on families.²²

Most clinical studies of asthma therapies focus on the incremental improvements in individual endpoints obtained with fixed doses of medication. Although these studies are helpful in assessing an incremental benefit of a particular medication, they usually do not compare how groups of medications work together as a regimen. Consensus treatment guidelines—reference tools frequently used by practicing physicians—must rely on the results of these individual efficacy trials, combined with the consensus judgment of expert panels. As consensus documents based on individual drug trials, consensus treatment guidelines in their totality—such as the Global Initiative for Asthma/National Institutes of Health (GINA/NIH) guidelines—are rarely themselves subject to rigorous scientific validation (e.g., patient outcomes using guideline care versus baseline care).

The Gaining Optimal Asthma controL (GOAL) study²³ addressed the issue of efficacy of the asthma treatment guidelines, subjecting more than 3,000 patients with documented, suboptimally controlled asthma to rigorous adherence with predefined, stepwise increases in either salmeterol/fluticasone, or fluticasone propionate (e.g., Flonase, Flovent, GlaxoSmith-Kline). Under the study protocols, dosage acceleration continued until the patients reached a defined state of asthma control or the maximum dose of medication. For patients receiving salmeterol/fluticasone, 41% achieved total control of their asthma and 71% achieved good control. Both of these values were significantly higher, compared with the baseline of 28% and 59%, respectively, prior to guideline-directed dose escalation.

The authors concluded that for most asthma patients, comprehensive guideline-defined control can be achieved and maintained. On the basis of this study, they further suggested that total control should be the aim of treatment for all patients with asthma. This aggressive approach runs counter to a conventional belief held by many experts—that full control of asthma is an unrealistic goal for most of these patients. Factors promoting these conventional beliefs include limitations of current treatments, problems with treatment strategies, lowered physician and patient expectations regarding outcomes, and concerns about adherence to treatment.

The GOAL study results generate several interesting questions for the future of asthma treatment guidelines:

1. Should total control of symptoms be the target for all asthmatic patients, regardless of the initial severity of disease?
2. If total control is a realistic goal for many patients, are the current asthma treatment recommendations adequate to meet this challenge? Considering that more than 30% of patients did not achieve a well-controlled state despite systematic and rigorous adherence to current guidelines, what other modalities should be factored into the equation to increase the percentage of patients achieving control?

There are clearly limits to the efficacy of standard asthma therapy. As a result of the GOAL study, many patients continued taking higher doses of inhaled fluticasone (1,000 mcg/day) without achieving the level of symptom control sought by the researchers. The maximum effect of inhaled corticosteroids is typically reached at doses in the low-to-medium range. Higher doses do not typically improve efficacy measures but do have an impact on systemic effect measures, causing a plateau effect.²⁴

In addition, the use of high doses of fluticasone over prolonged periods presents an unknown risk. The GOAL results suggest an algorithm in which omalizumab is prescribed when patients do not respond adequately to salmeterol/fluticasone 50/500 mcg twice daily—an approach that may increase the probability of reaching GOAL endpoints without using high-dose steroids over prolonged periods.

As a nontraditional agent targeting IgE-mediated allergic asthma, omalizumab is a strong candidate to fill the void between maximal standard therapy and total control. In the INNOVATE trial,²⁵ omalizumab was tested in a subpopulation of severe-persistent asthmatic patients who had not achieved adequate control despite maximal standard treatment (GINA step 4).^{14,22}

As an add-on therapy in this challenging population, omalizumab significantly reduced the rate of severe asthma exacerbations by 50%, reduced emergency department visits by 44%, and improved asthma-related quality of life. These improvements occurred without an increase in overall ADEs, a burdensome aspect of step 4 treatment, and any ADEs were generally well tolerated.

It was the large numbers of patients with inadequately controlled symptoms, despite maximum conventional therapy, coupled with the belief that total or adequate control is an attainable goal for most asthma patients, that prompted the Asthma Consensus Panels I and II to recommend consideration of omalizumab as an add-on medication to maximal standard therapy in patients with moderate-persistent to severe-persistent asthma.

Conclusion

The growing awareness of the limitations of standard therapy is one of the most compelling reasons for pursuing the development of new modalities to treat the underlying causes of asthma.

A plateau effect has been observed in the dose–response

curve of inhaled corticosteroids, whereby increasing the dose increases only the systemic effects but not physiological improvement. With the FDA's approval of omalizumab, a panel of experts in the fields of allergy and pulmonology proposed additions to the NAEPP clinical guidelines and recommended that IgE blockers be used as an alternative treatment in patients with moderate-persistent to severe-persistent asthma whose disease is suboptimally controlled with high-dose inhaled corticosteroids or in patients who need systemic corticosteroids.

IgE blockers can also be considered in patients whose asthma is inadequately controlled despite a three-month trial of medium-dose inhaled corticosteroids and long-acting beta agonists or leukotriene receptor agonists. The panel also advised that specific patient education recommendations be added to the guidelines for all levels of severity.

Although a cure for asthma has not yet been discovered, novel treatment modalities, such as IgE blockers, represent a new and unique opportunity for improved control in many asthma patients. Predicting the response of patients with severe, intensely treated asthma to omalizumab will be an important issue for future study.²⁶

With the advent of new technologies and treatment modalities, many asthma experts now believe that total control is a realistic goal that can and should be achieved and maintained for the majority of patients with asthma.

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Jefferson Medical College of Thomas Jefferson University, as a member of the Consortium for Academic Continuing Medical Education, is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. All faculty/authors participating in continuing medical education activities sponsored by Jefferson Medical College are expected to disclose to the activity audience any real or apparent conflict(s) of interest related to the content of their article(s). Full disclosure of these relationships appears on the last page of the article.

Continuing Medical Education Credit

This CME activity is designed to assist physicians and other health care professionals who are P&T committee members in making formulary decisions. Its goal is to increase participants' ability to recognize and treat important medical problems.

Jefferson Medical College designates this continuing medical education activity for a maximum of one Category 1 credit toward the Physician's Recognition Award (PRA) of the American Medical Association. Each physician should claim only those credits that he/she actually spent in the educational activity.

This credit is available for the period of one year from the date of publication.

Although forms will be processed when received, certificates for CME credits will be issued every six months, in February and August. Interim requests for certificates can be made by contacting the Jefferson Office of Continuing Medical Education at (215) 955-6992 or by going online to <http://jeffline.tju.edu/jeffcme/>.



Continuing Pharmacy Education Credit

The Department of Health Policy, Thomas Jefferson University Hospital, is approved by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education and complies with the

Criteria for Quality for continuing pharmaceutical education programming. This program (079-999-06-017-H01) is acceptable for 1.0 hour of continuing education credit (0.1 CEUs) in states that recognize ACPE-approved providers. Statements of Credit indicating hours/CEUs will be mailed within six to eight weeks to participants who completed this activity and submitted a completed evaluation with payment.

How to Apply for CE Credit

1. Each CE article is prefaced by learning objectives for participants to use to determine whether the article relates to their individual learning needs.
2. Read the article carefully, paying particular attention to the tables and other illustrative materials.
3. Complete the questions and fill in the answers on the evaluation form on the next page.
4. Complete the CE Registration and Evaluation Form. Type or print your full name and address in the space provided, and evaluate the activity as requested. In order for the form to be processed, all information must be complete and legible.
5. Payment of \$10 per exam is required for processing and maintenance of records. Make checks payable to P&T®. This processing fee is non-refundable.
6. Send the completed form, answer sheet, and \$10 payment to:

Department of Health Policy
Thomas Jefferson University
Attn: Continuing Education Credit
1015 Walnut Street, Suite 115
Philadelphia, PA 19107
7. Be sure to mail the Registration, Evaluation Form, and \$10 payment within one year of the date of publication. After that date, this article will no longer be designated for credit and forms cannot be processed.

Continuing Education Questions for Physicians and Pharmacists

TOPIC: National Guidelines for a Novel Therapy: Update on Clinical Trials and Experience Using Consensus Panel Recommendations for Incorporating Omalizumab into Asthma Management

APCE Program #079-999-06-017-H01

CE Evaluation: Select the one best answer to each of the following questions, and record your response on the examination answer sheet. Complete the additional requested information. Forward the answer sheet, with appropriate payment, to the Department of Health Policy, Thomas Jefferson University Hospital, at the address indicated. A certificate of completion will be mailed within six to eight weeks of receipt of your exam/payment. (A minimum test score of 70% is required.)

Multiple Choice

Select the one correct answer.

1. **How many people in the U.S. have a diagnosis of asthma?**
 - a. 15 million
 - b. 31 million
 - c. 49 million
 - d. 84 million
2. **Which of the following statements is incorrect?**
 - a. Airway inflammation and atopy are key factors in the pathogenesis of asthma.
 - b. More than 70% of Americans with asthma also have allergies.
 - c. The prevalence of asthma has been shown to be associated with decreased levels of total immunoglobulin E (IgE).
 - d. The World Health Organization has suggested that allergic rhinitis is a complex syndrome, the presence of which may be a major risk factor for asthma.
3. **Which of the following is the mechanism by which omalizumab inhibits IgE from triggering the release of inflammatory mediators?**
 - a. forming complexes with the mast cell receptors
 - b. forming complexes with circulating free IgE at the site of binding to the mast cell
 - c. forming complexes with mast cell-bound IgE
 - d. none of the above
4. **According to this article, patients with the greatest number of unmet needs are those with:**
 - a. moderate asthma that is suboptimally controlled.
 - b. mild asthma that is suboptimally controlled.
 - c. severe asthma that is suboptimally controlled.
 - d. both a and c
5. **All of the following play a role in keeping asthma inadequately controlled in a significant number of patients except:**
 - a. access to care
 - b. comorbid conditions
 - c. adherence issues
 - d. lack of evidence-based guidelines
6. **According to the Consensus Panel Recommendations, which of the following considerations may support the use of IgE blockers in the treatment of patients with severe-persistent and moderate-persistent asthma?**
 - a. patients who are at least 12 years of age
 - b. patients who have evidence of specific allergic sensitivity by a positive skin test or a blood test for specific IgE
 - c. patients who have evidence of reversible airway disease
 - d. all of the above
7. **All of the following are features of suboptimally or inadequately controlled asthma except:**
 - a. frequent usage of the emergency department
 - b. low rates of hospitalizations
 - c. impaired ability to work, attend school, exercise, or sleep
 - d. excessive use of rescue medications and/or oral steroids
8. **According to the Consensus Panel Recommendations, all of the following are potential treatment options for severe-persistent asthma except:**
 - a. high-dose corticosteroids
 - b. long-acting inhaled beta₂ agonists
 - c. ipratropium
 - d. IgE blockers
9. **The INNOVATE trial included patients with severe-persistent asthma and not at adequate control despite maximal standard therapy. The addition of omalizumab in these patients reduced the severe asthma exacerbation rate by what amount?**
 - a. 10%
 - b. 25%
 - c. 50%
 - d. 70%
10. **According to the article, IgE blockers may be considered as an alternative treatment in patients whose asthma is inadequately controlled with which of the following treatment regimens?**
 - a. high-dose inhaled corticosteroids
 - b. frequent courses of systemic steroids
 - c. three-month trial of medium-dose inhaled corticosteroids plus long-acting beta agonists or leukotriene receptor agonists
 - d. all of the above

CE Registration and Evaluation Form

Date of publication: May 2006

Title: **National Guidelines for a Novel Therapy: Update on Clinical Trials and Experience Using Consensus Panel Recommendations for Incorporating Omalizumab into Asthma Management**

Authors: **Mark J. Baumel, MD, Lawrence Du Buske, MD, Stanley J. Szeffler, MD, Lanny Rosenwasser, MD, and David B. Nash, MD, MBA**

Submission deadline: **May 31, 2007**

ACPE Program #079-999-06-017-H01

Registration

Name: _____ Degree: _____

Street address: _____ Last 4 Digits of Social Security No. (Web ID): _____

City: _____ State: _____ Zip: _____ Telephone: _____

E-mail Address: _____ Check one: Physician Pharmacist Other

Time needed to complete this CE activity in hours: 0.5 hr 1 hr 1.5 hr 2 hr Other _____

Certification: I attest to having completed this CE activity. _____

Signature (required) _____ Date _____

Answer Sheet

Please fill in the box next to the letter corresponding to the correct answer

- | | | | | | | | |
|-------------------------------|----------------------------|----------------------------|----------------------------|--------------------------------|----------------------------|----------------------------|----------------------------|
| 1. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> | 6. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> |
| 2. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> | 7. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> |
| 3. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> | 8. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> |
| 4. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> | 9. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> |
| 5. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> | 10. a <input type="checkbox"/> | b <input type="checkbox"/> | c <input type="checkbox"/> | d <input type="checkbox"/> |

Evaluation

Rate the extent to which:

	Very High	High	Moderate	Low	Very Low
1. Objectives of this activity were met	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. You were satisfied with the overall quality of this activity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Content was relevant to your practice needs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Participation in this activity changed your knowledge/attitudes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. You will make a change in <i>your practice</i> as a result of participation in this activity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. This activity presented scientifically rigorous, unbiased, and balanced information	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Individual presentations were free of commercial bias	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Adequate time was available for Q&A	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Which ONE of the following best describes the impact of this activity on your performance:					
<input type="checkbox"/> This program will not change my behavior because my current practice is consistent with what was taught.					
<input type="checkbox"/> This activity will not change my behavior because I do not agree with the information presented.					
<input type="checkbox"/> I need more information before I can change my practice behavior.					
<input type="checkbox"/> I will immediately implement the information into my practice.					
10. Will you take any of the following actions as a result of participating in this educational activity (check all that apply)					
<input type="checkbox"/> Discuss new information with other professionals					
<input type="checkbox"/> Discuss with industry representative(s)					
<input type="checkbox"/> Other _____					
<input type="checkbox"/> Consult the literature					
<input type="checkbox"/> Participate in another educational activity					
<input type="checkbox"/> None					

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