Numerous pregnant women suffer from allergic rhinitis, and particular attention is required when prescribing drugs to these patients. In addition, physiologic changes associated with pregnancy could affect the upper airways. Evidence-based guidelines on the management of allergic rhinitis have been published. Medication can be prescribed during pregnancy when the apparent benefit of the drug is greater than the apparent risk. Usually, there is at least one “safe” drug from each major class used to control symptoms. All glucocorticosteroids are teratogenic in animals but, when the indication is clear (for diseases possibly associated, such as severe asthma exacerbation), the benefit of the drug is far greater than the risk. Inhaled glucocorticosteroids (eg, beclomethasone or budesonide) have not been incriminated as teratogens in humans and are used by pregnant women who have asthma. A few H1-antihistamines can safely be used as well. Most oral decongestants (except pseudoephedrine) are teratogenic in animals. There are no such data available for intranasal decongestants. Finally, pregnancy is not considered to be a contraindication for the continuation of immunotherapy.

Introduction
Rhinitis is often a problem during pregnancy: 18% to 30% of nonselected pregnant women report symptoms of rhinosinusitis [1], which are not always of allergic nature. Persistent hormonal rhinitis, also called pregnancy rhinitis [2], is defined as nasal congestion present during the last 6 weeks or more of pregnancy without other sign of respiratory tract infection, and with no known allergic cause. Pregnancy rhinitis disappears completely within 2 weeks after delivery.

The incidence of atopy in pregnant women is 30%, and allergic rhinitis is estimated to affect up to 20% of pregnancies [3]. Pre-existing rhinitis usually remains stable during pregnancy [4,5]. But of those pregnant women with known allergies, some studies suggest that as many as 10% to 30% experience increasing allergic symptoms during their pregnancy [6–8], returning to their “normal state” after delivery. Active smoking and environmental tobacco smoke exposure increased the likelihood of allergic rhinitis in pregnant Japanese women [9]. And, in the same cohort of 1002 pregnant women, a high intake of soy and isoflavones was associated with a reduced prevalence of allergic rhinitis [10•]. In a retrospective cohort study [11], a total of 1755 nonsmoking women completed a questionnaire on reproductive history. The number of live births was inversely related to lifetime allergic rhinitis and allergic conjunctivitis: the odds-ratios for women with four or more children (in comparison with those having one or none) were 0.53 (95% CI, 0.27–1.04 for allergic rhinitis) and 0.42 (95% CI, 0.22–0.81 for allergic conjunctivitis). Mothers of preterm infants with very low birth weight (< 1000 g) had significantly less physician-diagnosed allergic rhinitis (P = 0.02) and vice versa: maternal allergic rhinitis was significantly associated (P = 0.03) with higher infant birth weight [12]. Any complication during pregnancy was shown to be a significant risk factor for hay fever later in life [13]. Additionally, a higher number of older siblings was protective for hay fever.

Nasal obstruction due to pre-existing allergic rhinitis may be aggravated by pregnancy itself [6–8]: postulated causes of increasing rhinitis symptoms included nasal vascular engorgement and hormonal influences on nasal mucosal secretions [1]. The rise of serum concentration of female sex hormones coincides with decreasing nasal airway patency [14].

The management of allergic rhinitis includes allergen avoidance, pharmacologic treatment, specific immunotherapy, and education. Evidence-based guidelines have been published, one of the most recent being the Allergic Rhinitis and Its Impact on Asthma (ARIA)—World Health Organization (WHO) workshop report [15]. Caution should always be taken when administering a drug to a pregnant woman, as most medications cross the placenta. The risk of malformation of the fetus represents a major fear and is highest during the first trimester. Concerning human teratogenicity, the following factors do not formally eliminate toxicity in a fetus: 1) the chemical structure
of a drug; 2) the animal reproductive studies; 3) the apparent safety of medication in healthy adults; and 4) the absence of case reports involving teratogenicity, even with drugs that have been on the market for a number of years. Moreover, for most available drugs, only limited studies on small groups without long-term analysis have been performed. However, for some drugs, it would appear that, based on birth registries and registries of congenital malformations, the possibility of fetal harm is remote. Nevertheless, prescribing a drug to a pregnant woman enlists the responsibility of the doctor, and it is always worth considering the benefit/risk ratio, for the mother and for the fetus.

Various Drugs Available for the Control of Allergic Rhinitis

Glucocorticosteroids

All glucocorticosteroids [16] are teratogenic in animals ( prin cipally hare lip but also cardiovascular malformations), and, although a significant risk of abnormalities regarding systemic glucocorticosteroids has been found in humans, some debates exist. When considering systemic glucocorticosteroids administered during the first trimester, there is an increased risk of approximately 3 to 5 for hare lip (with or without cleft palate). The power of such studies remains poor, and many confounding factors persist [17]. Nevertheless, when the indication is clear (not for allergic rhinitis but for diseases possibly associated, such as severe asthma exacerbation), the benefit of the drug is far greater than the risk. There is no other increased risk of teratogenicity. In the case of prolonged systemic corticotherapy, the increased risk of growth retardation in utero, first demonstrated by Reinisch et al. [18], seems to be more related to a severe underlying maternal pathology than to the corticotherapy itself [19]. However, the increased risk for preeclampsia is observed even after controlling for other potential confounders [4,19]. The risk described initially for adrenal insufficiency in newborns in the perinatal period has not been confirmed [20]. As an example, in 36 pregnant asthmatic women treated with prednisone, Snyder and Snyder [21] did not notice any pathologic pregnancy or medical problem in the children born and observed during a 2-year period.

Intranasal glucocorticosteroids (beclomethasone dipropionate, budesonide, flunisolide, fluticasone propionate, mometasone furoate, and triamcinolone acetonide) are currently the most potent medications available for treating allergic [15,21] and nonallergic rhinitis [15], with a few exceptions, including pregnancy rhinitis [22]. Conversely, a treatment with fluticasone propionate aqueous nasal spray in 53 women with pregnancy rhinitis was ineffective [22].

Intranasal glucocorticosteroids can suppress many stages of the allergic inflammatory process. The rationale for using intranasal glucocorticosteroids (instead of systemic glucocorticosteroids) in the treatment of allergic rhinitis is that high drug concentrations can be achieved at receptor sites in the nasal mucosa, with minimal risk of adverse systemic effects. Systemic absorption may occur following the nasal administration of glucocorticosteroids, but, although more data are required, clinically relevant side effects do not generally occur at therapeutic doses [15,23]. Nevertheless, inhaled glucocorticosteroids (eg, beclomethasone or budesonide) have not been incriminated as teratogens in humans and are used by pregnant women who have asthma. Greenberger and Patterson [24] did not find any maternofetal side effects in 40 pregnant asthmatic women who were treated with beclomethasone. The Michigan Medicaid registry did not find any excess of risk for congenital malformation in 395 newborns who were exposed to beclomethasone during the first trimester [25]. Three-hundred ninety-six pregnant asthmatic women exposed to inhaled steroids and enrolled in the Registry for Allergic and Asthmatic Pregnant Patients of the American College of Allergy Asthma and Immunology and the American Academy of Allergy Asthma and Immunology did not show any increased risk for small for gestational age infants or mean birth weight [26•]. Beclomethasone was the most commonly used inhaled steroids. The US Food and Drug Administration (FDA) recently approved a revised labeling for budesonide inhalation powder that upgrades its pregnancy rating to category B. All other inhaled glucocorticosteroids are classified as pregnancy category C (Table 1). Several studies (retrospective epidemiologic studies and a randomized placebo-controlled multicenter trial) [27–30] found no statistically significant effects on fetal outcomes among more than 6600 infants [31•] whose mothers were exposed to inhaled or intranasal budesonide during pregnancy. However, a marginally increased risk for cardiovascular defects (OR 1.58; 95% CI, 1.02–2.46) was observed with intranasal budesonide in one analysis [29]. The rate of cesarean births was higher among mothers who used asthma medication (inhaled budesonide) during their pregnancy than among a control group [30].

Chromones

The action of these drugs (disodium cromoglycate and sodium nedocromil) is linked to the cell wall of the mast cell [32] and/or to the intracellular events that follow the allergen binding to IgE [33]. However, the mechanisms of action remain unclear. In regard to pharmacokinetics, cromoglycate and nedocromil are virtually not absorbed through mucosal surfaces. The swallowed portion is also poorly absorbed from the gastrointestinal tract and excreted in the feces.
Rhinitis

No teratogenic effect has been found in animals. To date, no side effects have been found in humans [34], but there are no prospective studies available. However, neither the Michigan Medicaid registry [25] nor Schatz et al. [19] found any excess of risk for congenital malformation in 191 and 151 women with asthma who were exposed to inhaled cromoglycate during the first trimester. Consensus and several publications [3,19,35] then proposed the use of cromoglycate as a first-line treatment for allergic rhinitis in pregnant women.

Antihistamines

Antihistamines, or H1-blockers or H1-antihistamines, block the effect of the major mediator involved in the pathophysiology of allergic rhinitis—histamine. First-generation antihistamines provoke sedation and are no longer recommended in developed countries [15]. The new generation of compounds is mostly devoid of central nervous system side effects [35], and is, therefore, a first-choice treatment for allergic rhinitis in these countries [15].

Some first-generation antihistamines (eg, azelastine, chlorpromazine, diphenhydramine, hydroxyzine, and promethazine) were shown to be teratogenic in animals [36–38]. Because they have been on the market for more than 50 years, dexchlorpheniramine [39,40] and tripelennamine [3,41•,42] are favored by some authors, but they are sedative and no longer recommended by guidelines on allergic rhinitis [15]. Second-generation antihistamines do not appear to be teratogenic in animal reproductive studies. Once again, the absence of controlled trials in humans and the crossing of the placental barrier make the avoidance of their prescription necessary during pregnancy. However, a small, prospective, matched-case control study of hydroxyzine and cetirizine was conducted in 33 pregnant women, and no side effects were found [43]. No increased risk for total congenital malformations was found with loratadine in infants of 292 exposed mothers from the Swedish Medical Birth Registry [44]. No causal relationship could be confirmed nor excluded from that registry concerning the risk of hypospadia. Other studies on antihistamines used during the first trimester in nearly 500 women (65% taking loratadine) [45–47] revealed no increase in the number of complications of pregnancy nor that of congenital abnormalities. Although there are differences in regulations between countries, examples of the FDA categories for antihistamines are given in Table 1.

Anticholinergic agents

Intranasal ipratropium bromide, a quaternary derivative of isopropyl noratropine, is poorly absorbed by the nasal mucosa because of a low lipid solubility and does not cross the blood-brain barrier [48]. It acts on rhinorrhea by blocking the muscarinic receptors of the seromucinous glands [48]. It is effective in controlling watery nasal discharge, but it does not affect sneezing or nasal obstruction.

There is no existing teratogenicity in animals with this class of drugs. Atropine passes through the placenta and can be prescribed to pregnant women. The prescription of its derivatives also seems to be without danger, but once again, it is advisable, owing to a lack of extensive studies, to avoid these during the first trimester.

Table 1. US Food and Drug Administration pregnancy rating for allergic rhinitis medications

<table>
<thead>
<tr>
<th>Categories</th>
<th>Description of the risk</th>
<th>Interpretation</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Animal studies and well-controlled human studies exclude teratogenicity.</td>
<td>No risk</td>
<td>Budesonide, cetirizine, loratadine, dexchlorpheniramine, diphenhydramine, cromoglycate, nedocromil, ipratropium bromide, pseudoephedrine, tripelennamine</td>
</tr>
<tr>
<td>B</td>
<td>Animal studies do not show teratogenicity but no well-controlled human studies are available, or animal studies show teratogenicity but well-controlled human studies exclude teratogenicity.</td>
<td>No evidence of risk</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Animal studies show teratogenicity or are not available, and no well-controlled human studies are available. However, potential benefits may justify the potential risk.</td>
<td>Risk cannot be ruled out</td>
<td>Other glucocorticosteroids, azelastine, fexofenadine, brompheniramine, hydroxyzine, all other decongestants</td>
</tr>
<tr>
<td>D</td>
<td>Well-controlled human studies show teratogenicity, but apparent benefit of the drug may be greater than the risk in certain circumstances.</td>
<td>Evidence of risk</td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>Well-controlled human studies show an increased risk of teratogenicity that always exceeds that of the clinical benefit.</td>
<td>Contraindication</td>
<td></td>
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</table>
Decongestants
The decongestant (or vasoconstrictor) drugs affect the sympathetic tone regulation of blood vessels by acting on adrenergic receptors and provoking vasoconstriction [49]. They may be administered topically or systemically. In both allergic and nonallergic rhinitis, intranasal decongestants, such as oxymetazoline, xylometazoline, and naphazoline, are very effective in the treatment of nasal obstruction in the short term [50]. Their prolonged use (> 10 days) may lead to tachyphylaxis, a rebound swelling of the nasal mucosa, and to rhinitis medicamentosa [51]. Oral decongestants, such as ephedrine, phenylephrine, and especially pseudoephedrine, are the most commonly used systemic nasal decongestants [52]. They act on nasal obstruction only. In many countries, combinations of oral antihistamines and decongestants (pseudoephedrine) are marketed and frequently available over the counter.

Most oral decongestants (except pseudoephedrine) are teratogenic in animals. There are no such data available for intranasal decongestants. Results of a case-controlled study [53] concerning the use of oral decongestants during the first trimester are compatible with a potentially cardiotoxic effect in utero (ventricular septal defect) (OR 5.1; 95% CI, 2.56–11.27). Pseudoephedrine has been shown to increase the risk for gastroschisis and small intestinal atresia by a factor of 2 to 3 in one study [54], although no increased adverse outcomes compared to controls were reported in 2509 pregnant women exposed to pseudoephedrine [55,56]. Avoidance of decongestants only during the first trimester has been previously recommended [57]. Because extensive studies are lacking, we consider that intranasal decongestants cannot be safely administered to pregnant women, even after the first trimester.

Specific immunotherapy
Allergen-specific immunotherapy (SIT) is the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to ameliorate the symptoms associated with the subsequent exposure to the causative allergen. SIT has a place in selected patients with demonstrable immunoglobulin E (IgE)-mediated diseases who either have a long duration of symptoms or in whom pharmacotherapy is not effective or induces side effects. Guidelines and indications for SIT with inhalant allergens have been published regularly in past years, in particular by the WHO [15,58].

There are no teratogenicity data available in animals. Metzger et al. [59] have shown its safety by a study in 115 pregnant women, each receiving specific immunotherapy for allergic rhinitis. Pregnancy is, therefore, not considered to be a contraindication for the continuation of immunotherapy; however, it is not advisable to increase the dosage during pregnancy to avoid any possibility of an anaphylactic accident. It is also not advisable to begin specific immunotherapy for allergic rhinitis during pregnancy [15,58].

Treatment Strategy for Allergic Rhinitis
Development of guidelines for allergic rhinitis
Evidence-based guidelines for the treatment of allergic rhinitis have been published. In the most recent ARIA—WHO guidelines [15], a new subdivision of allergic rhinitis was proposed: intermittent (for symptoms lasting less than 4 days a week or less than 4 consecutive weeks a year) versus persistent (for symptoms lasting more than 4 days a week and more than 4 consecutive weeks a year). These two terms replace seasonal and perennial, respectively. The severity of allergic rhinitis has been classified as “mild” and “moderate/severe,” depending on the severity of symptoms and quality-of-life outcomes. Depending on the subdivision and severity of allergic rhinitis, a stepwise therapeutic approach has been proposed. The treatment of allergic rhinitis combines allergen avoidance (when possible), pharmacotherapy, and immunotherapy. It is recommended that allergic rhinitis is considered as a risk factor for asthma, especially in patients with persistent allergic rhinitis, and, therefore, to evaluate for asthma by history, chest examination, and, if possible and when necessary, assessment of airflow obstruction before and after bronchodilator. If both allergic rhinitis and asthma are present, a strategy considering efficacy and safety issues should be considered to combine the treatment of both the upper and lower airway disease.

Pharmacologic management of allergic rhinitis
For mild, intermittent allergic rhinitis, the ARIA—WHO recommendations [15] for treatment are: oral or intranasal H1-antihistamines, intranasal decongestants (fewer than 10 days and not more than twice a month), and oral decongestants. For moderate/severe intermittent and mild persistent allergic rhinitis, the options for treatment are: oral or intranasal H1-antihistamines, oral H1-antihistamines and decongestants, intranasal glucocorticosteroids, and chromones. For moderate/ severe persistent allergic rhinitis, it is advisable to use intranasal glucocorticosteroids as a first-line treatment. If the nose is very blocked, a short course (eg, 1 to 2 weeks) of oral glucocorticosteroids may be added, or intranasal decongestants for fewer than 10 days. The patient should be re-assessed after 2 to 4 weeks, and, if the patient does not improve, reasons for failure should be considered. Reasons include inadequate compliance; patient or doctor misunderstanding of the dose and frequency of administration of intranasal glucocorticosteroids.
corticosteroids; prevention of drug delivery due to nasal obstruction (nasal polyps or nasal septal deviation); heavy, persistent allergen exposure; and wrong diagnosis. If none of the above reasons are found, the following options are proposed: 1) double the dose of intranasal glucocorticosteroid if the major symptom is nasal blockage; 2) add H1-antihistamines if the major symptoms are sneezing, itching, or rhinorrhea; 3) add ipratropium bromide if the major symptom is rhinorrhea; and/or 4) add oral H1-antihistamines combined with an oral decongestant. Referral to a specialist may be considered at this point. If the patient improves, a step-down approach should be used, and low-dose intranasal glucocorticosteroids may be required as a maintenance treatment to control symptoms.

Conclusions
The management of allergic rhinitis in pregnant women should follow the same guidelines as for other patients. A firm diagnosis is needed as well as an assessment of the severity of the rhinitis. Although allergen avoidance is the best first-line approach, especially during pregnancy, it is not possible to avoid outdoor allergens. The real challenge is to create a low allergen environment in patients’ homes [60]. Nasal saline drops or spray can help to clear the nose, in particular before eating and sleeping [61] and may be of interest in pregnancy. When the disease is severe enough, and allergen avoidance has failed to control symptoms, drugs are necessary. Although the choice of agents should partly be based on the evidence of fetal safety, the issue of maternal health also needs to be considered to provide optimal management. This is particularly the case when a systemic glucocorticosteroid is needed, which should very seldom be the case for allergic rhinitis (without association with asthma).

At least one drug of each major class used to control symptoms can be given safely [4,5,15,19,40,57] in moderate to severe allergic rhinitis (Table 2). Intranasal chromones, considering their excellent safety profile, would be considered as first-line therapy, especially during the first trimester [3,35]. If chromones are ineffective, second-generation antihistamines (L-cetirizine and D-loratadine) are given [3,35], especially for sneezing, itching, and rhinorrhea relief. If nasal obstruction is the major symptom, intranasal glucocorticosteroids, especially budesonide (pregnancy risk category B) and beclomethasone (category C), can be considered [3,35,41•,62].

Table 2. Possible treatment for allergic rhinitis during pregnancy, first trimester included

<table>
<thead>
<tr>
<th>Anti-inflammatory drugs</th>
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<tr>
<td>Cromoglycate</td>
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<td>Beclomethasone</td>
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<tr>
<td>Budesonide</td>
<td></td>
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<tr>
<td>Prednisone or prednisolone (only if clearly needed)</td>
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<tr>
<td>Anti-allergic measures</td>
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<tr>
<td>Allergen avoidance</td>
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<tr>
<td>Cetirizine</td>
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<tr>
<td>Loratadine</td>
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<tr>
<td>Specific immunotherapy</td>
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</table>

References and Recommended Reading
Papers of particular interest, published recently, have been highlighted as:
- Of importance
-• Of major importance


In this cross-sectional study involving more than 1000 pregnant women, a high intake of soy and isoflavones was associated with a reduced prevalence of allergic rhinitis. This may give some insight for dietary prevention of allergic rhinitis during pregnancy.

13. Brooks K, Samms-Vaughan M, Karmaus W: Are oral con- 
apractic uses and pregnancy complications risk factors for 
atopic disorders among offspring? Pediatr Allergy Immunol 
physiological changes during pregnancy. Clin Otolaryngol 
Members: Allergic rhinitis and its impact on asthma. ARIA. 
In collaboration with the World Health Organization. 
16. Kusanagi T: Occurrence of cleft palate, palatal slit, and 
and fetal death in mice treated with a glucocorticoid: an 
defects after maternal exposure to corticosteroids: 
prospective cohort study and meta-analysis of epide- 
18. Reinisch JM, Simon NG, Karow WG, Gandelman R: 
Normal pregnancy outcomes by pregnant asthmatic women does not reduce intrauter- 
are of great interest.
Reproductive Toxicology (DART) database, 
in a population-based study including 2,968 pregnant 
mothers were exposed to orally inhaled budesonide.
20. Schatz M, Patterson A: Beclomethasone dipropio- 
21. Snyder RD, Snyder D: Corticosteroids for asthma during 
22. Ellegard EK, Hellgren M, Karlsson NG: Fluticasone 
propionate aqueous nasal spray in pregnancy rhinitis. 
23. Cave A, Arlett P, Lee E: Inhaled and nasal corticosteroids: 
factors affecting the risks of systemic adverse effects. 
24. Greenberger PA, Patterson R: Beclomethasone dipropio- 
25. Briggs GC, Freeman RK, Yaffe SJ: Drugs in Pregnancy and 
Lactation—a Reference Guide to Fetal and Neonatal Risk, 
by pregnant asthmatic women does not reduce intrauter- 
Most of the asthmatics suffer from rhinitis as well. Therefore, 
safety studies on inhaled steroids in pregnant asthmatic women 
are of great interest.
27. Stenius-Aarila BS, Hedman J, Teramo KA: Acute asthma 
28. Kallen B, Rydstroem H, Aberg A: Congenital malfor- 
mations after the use of inhaled budesonide in early 
29. Kallen BA, Otterblad Olausson P: Maternal drug use 
in early pregnancy and infant cardiovascular defect. 
30. Norjavaara E, de Verdier MG: Normal pregnancy outcomes 
in a population-based study including 2,968 pregnant 
women exposed to budesonide. J Allergy Clin Immunol 
after exposure to orally inhaled or intranasal 
In this systematic search of the literature indexed on Medline or 
the Developmental and Reproductive Toxicology (DART) database, 
the authors found no clinically or statistically significant effects 
on fetal outcomes among more than 6600 infants whose mothers 
were exposed to orally inhaled budesonide during pregnancy.
35. Gengo FM, Manning C: A review of the effects of 
antihistamines on mental processes related to 
automobile driving. J Allergy Clin Immunol 1990, 
86:1034–1039.
36. Walker BE, Patterson A: Induction of cleft palate in mice by 
37. King CT, Howell J: Teratogenic effect of buclizine 
and hydroxyzine in the rat and chlorcyclizine in the 
38. Saxen I: Cleft palate and maternal diphenhydramine 
allergic diseases during pregnancy. J Investig Allergol 
41. Gilbert C, Mazzotta P, Loeblstein R, Koren G: Fetal safety of 
drugs used in the treatment of allergic rhinitis: a clinical 
This review lists the many safe treatment options for clinicians 
treating allergic rhinitis during pregnancy.
study of hydroxyzine and cetirizine in pregnancy. 
44. Källén B: Drugs in pregnancy: the dilemma of labeling. 
45. Nelson HS: Advances in upper airway diseases and 
allergen immunotherapy. J Allergy Clin Immunol 2004, 
113:635–642.
Pregnancy outcome after gestational exposure to 
loratadine or antihistamines: a prospective con- 
trolled cohort study. J Allergy Clin Immunol 2003, 
111:1239–1243.
47. Moretti ME, Caprara D, Coutinho CJ, et al.: Fetal safety 
of loratadine use in the first trimester of pregnancy: a 
multicenter study. J Allergy Clin Immunol 2003, 
111:479–483.
characteristics and pharmacokinetics of intranasal 
ipratropium bromide. J Allergy Clin Immunol 1995, 
95:1111–1116.
49. Malm L: Pharmacological background to decongest- 
ing and anti-inflammatory treatment of rhinitis and 
50. Johnson DA, Hricik JG: The pharmacology of alpha- 
adrenergic decongestants. Pharmacotherapy 1993, 
nasal spray (Nezeril) once daily at night induces rebound 
welling and nasal hyperreactivity. Acta Otolaryngol 1995, 
115:71–75.


