HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

13 January 2010

XOLAIR 150 mg, powder and solvent for solution for injection
Box containing 1 x 150 mg vial + 1 x 2 ml solvent ampoule (CIP: 370 225-7)

XOLAIR 150 mg, solution for injection
Box containing 1 pre-filled syringe (CIP: 392 124-9)

XOLAIR 75 mg, solution for injection
Box containing 1 pre-filled syringe (CIP: 392 122-6)

Applicant: NOVARTIS PHARMA S.A.S.

Omalizumab

ATC code: R03DX05

List I
Medicine requiring initial annual hospital prescription.
Initial prescription and renewal restricted to chest medicine or paediatric specialists.
Exception medicinal product.

Date of Marketing Authorisation: 25 October 2005 (centralised procedure)
Variation of 27 July 2009: extension of indication to children 6 years of age and above

Reason for request: Inclusion on the list of medicines reimbursed by National Insurance and approved for hospital use in the extension of indication to children 6 to 11 years of age.

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Omalizumab

1.2. Indication

"Adults and adolescents (12 years of age and older):
XOLAIR is indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and who have reduced lung function (FEV <80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta-2 agonist.

Children (6 to <12 years of age):
XOLAIR is indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta-2 agonist.

XOLAIR treatment should only be considered for patients with convincing IgE (immunoglobulin E) mediated asthma."

1.3. Dosage

"XOLAIR treatment should be initiated by physicians experienced in the diagnosis and treatment of severe persistent asthma.

The appropriate dose and dosing frequency of XOLAIR is determined by baseline IgE (IU/ml), measured before the start of treatment, and body weight (kg). Prior to administration of the initial dose, patients should have their IgE level determined by any commercial serum total IgE assay for their dose assignment. Based on these measurements 75-375 mg of XOLAIR in 1 to 3 injections may be needed for each administration.

Patients with IgE lower than 76 IU/ml were less likely to experience benefit. Prescribing physicians should ensure that adult and adolescent patients with IgE below 76 IU/ml and paediatric (6 to < 12 years of age) patients with IgE below 200 IU/ml have unequivocal *in vitro* reactivity (RAST) to a perennial allergen before starting therapy.

For the conversion chart and the dose determination charts in adults and adolescents (12 years of age and older), or dose determination charts in children (6 years of age to under 12), refer to the SPC.

Administration:
For subcutaneous administration only. Do not administer by the intravenous or intramuscular route.
The injections are administered subcutaneously in the deltoid region of the arm. Alternatively, the injections can be administered in the thigh if there is any reason precluding administration in the deltoid region.
There is limited experience with self-administration of XOLAIR. Therefore treatment is intended to be administered by a healthcare provider only.

Treatment duration, monitoring and dose adjustments:
Discontinuation of XOLAIR treatment generally results in a return to elevated free IgE levels and associated symptoms.
Clinical trials have demonstrated that it takes at least 12-16 weeks for XOLAIR treatment to show effectiveness. At 16 weeks after commencing XOLAIR therapy patients should be assessed by their physician for treatment effectiveness before further injections are administered. The decision to continue XOLAIR should be based on whether a marked improvement in overall asthma control is seen.
Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during XOLAIR treatment cannot be used as a guide for dose determination. Dose determination after treatment interruptions lasting less than one year should be based on serum IgE levels obtained at the initial dose determination. Total serum IgE levels may be re-tested for dose determination if treatment with XOLAIR has been interrupted for one year or more.
Doses should be adjusted for significant changes in body weight.

Elderly (65 years of age and older):
There are limited data available on the use of XOLAIR in patients older than 65 years but there is no evidence that elderly patients require a different dosage from younger adult patients.

Children (below 6 years of age):
XOLAIR is not recommended for use in children below age 6 due to insufficient data on safety and efficacy.

Patients with renal or hepatic impairment:
There have been no studies on the effect of impaired renal or hepatic function on the pharmacokinetics of XOLAIR. Because omalizumab clearance at clinical doses is dominated by the reticular endothelial system (RES) it is unlikely to be altered by renal or hepatic impairment. While no particular dose adjustment is recommended for these patients, XOLAIR should be administered with caution."

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2009)

R	Respiratory system
R03	Drugs for obstructive airway diseases
R03D	Other systemic drugs for obstructive airway diseases
R03DX	Other systemic drugs for obstructive airway diseases
R03DX05	Omalizumab

2.2. Medicines in the same therapeutic category

2.2.1. Strictly comparable medicines

XOLAIR is the only representative of its therapeutic category.

2.2.2. Medicines that are not strictly comparable

None.

2.3. Medicines with a similar therapeutic aim

These are other products used in the treatment of severe persistent asthma: inhaled corticosteroids, long-acting bronchodilators, sustained-release theophylline, oral and systemic corticosteroids.

3 ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

Study versus placebo in children between 6 and 11 years of age (study IA05):
Double-blind randomised (in a ratio of 2:1) study which compared the efficacy and safety of omalizumab versus placebo for a period of 1 year in children between 6 and 11 years of age with moderate-to-severe persistent allergic asthma which was poorly controlled despite treatment with a dose of ≥ 200 µg fluticasone or equivalent per day, with or without other continuous treatments.

A subgroup analysis was performed on the population of children who had severe persistent asthma which was treated with high-dose inhaled corticosteroids (≥ 500 µg fluticasone or equivalent per day) plus a long-acting beta-2 agonist (population covered by the Marketing Authorisation).

Study design:
The patients received omalizumab or a placebo for 24 weeks during which the inhaled corticosteroid dose remained stable, then for 28 weeks during which the inhaled corticosteroid dose could be adjusted according to the NHLBI recommendations for reducing corticosteroid therapy. After 52 weeks of treatment, the patients were followed up for 16 weeks for the evaluation of safety.

Characteristics of the patients:
- Children between 6 and 11 years of age
- Weight between 20 and 150 kg
- Total serum IgE levels between 30 and 1,300 IU/ml
- Allergic asthma for at least 1 year with a positive skin test to at least one perennial allergen
- FEV reversibility ≥ 12% of the baseline value after salbutamol inhalation
- Poorly controlled asthma:
    - asthma symptoms during the 4 weeks prior to inclusion despite inhaled corticosteroid therapy at a dose of ≥ 200 µg fluticasone or equivalent per day and a history of exacerbations (at least 2 separate exacerbations requiring systemic corticosteroid therapy and/or doubling of the dose of inhaled corticosteroids for at least 3 days in the course of the previous year)
    - or 3 separate exacerbations in the course of the previous 2 years, including one in the course of the first year
    - or a severe exacerbation with FEV or PEF < 60% of the theoretical value or of the best personal value and which resulted in admission to hospital or a stay in an emergency department

Treatment:
The patients treated with omalizumab received a dose of between 75 and 375 mg every 2-4 weeks in accordance with the predefined dose determination charts.

Primary efficacy endpoint: Clinically significant asthma exacerbation rate during the first 24 weeks of treatment.
A clinically significant asthma exacerbation was defined as a worsening of asthma symptoms as judged clinically by the investigator, requiring treatment with rescue systemic (oral or intravenous) corticosteroids for at least 3 days and/or doubling of the baseline inhaled corticosteroid dose for at least 3 days.

Secondary endpoints:
- Night-time asthma symptom score after 24 weeks of treatment
- Clinically significant asthma exacerbation rate after 52 weeks of treatment
- Consumption of rescue bronchodilator treatments during the 24 weeks of treatment
- Quality of life after 24 weeks of treatment: “Pediatric Asthma Quality of Life Questionnaire”

The analysis of the secondary endpoints took into account the increase in the significance level: the significance threshold was reached for a p value of ≤ 0.025.

Results:

- **Patient characteristics**

A total of 628 patients (ITT population) was included in the study (421 in the omalizumab group and 207 in the placebo group), 246 of whom had severe persistent asthma (population covered by the Marketing Authorisation) (166 in the omalizumab group and 80 in the placebo group).

The results were analysed in the modified intention-to-treat population (modified ITT, n = 576, 235 of whom corresponded to the population covered by the Marketing Authorisation) after exclusion of patients from 2 centres which did not comply with Good Clinical Practice, i.e. 384 patients under omalizumab (including 159 who corresponded to the population covered by the Marketing Authorisation) and 192 under placebo (including 76 who corresponded to the population covered by the Marketing Authorisation).

The average age of the patients was 8.6 (median: 9), with an average weight of 33.8 kg (median: 30.9 kg). Their FEV was 85.4% of the theoretical value with reversibility of 25.4% on average after salbutamol administration. The average total serum IgE level was 479.1 IU/ml (min.: 27.0 IU/ml – max: 1,376.0 IU/ml), 52.4% of the patients had a positive skin test or RAST to a mould (population covered by the Marketing Authorisation), 54.3% of the

patients had at least one seasonal allergy and 24.7% of the patients had at least one food or drug allergy.

Practically all the patients had asthma which was poorly controlled by inhaled corticosteroid therapy. The average number of exacerbations in the course of the previous year was 2.6 in the overall population and 2.8 in the subgroup of patients from the population covered by the Marketing Authorisation. The percentage of patients treated with a long-acting bronchodilator in addition to inhaled corticosteroid therapy (population covered by the Marketing Authorisation) was 70.5% in the placebo group and 65.8% in the omalizumab group. The average consumption of short-acting beta-2 agonists was 2.7 puffs per day in the overall population. In the course of the 28 weeks preceding the study, 75.8% of the patients had a symptom score of ≥ 1 for at least 20 days, 65.0% had an average score of ≥ 1.5 over 28 days and 76.6% of the patients had night-time awakenings requiring rescue treatment more than once a week.

The patients who completed the study represented 83.9% of the total study population (83.6% of the patients treated with omalizumab and 84.5% of the patients under placebo).

The reasons for discontinuation of treatment were similar in the two treatment groups and other than an inadequate therapeutic effect (0.2% under omalizumab and 1.0% under placebo) or an adverse event (0.5% under omalizumab and placebo) in the majority of cases.

- **Result for the primary efficacy endpoint (modified ITT population)**

During the period of 0 to 24 weeks of treatment, in the total analysable population (n = 576), the average number of clinically significant asthma exacerbations was lower with omalizumab (0.45) than with placebo (0.64), with a relative risk of 0.693 ($CI_{95\%}$ = [0.533; 0.903]; p = 0.007).

A similar result was observed in the children corresponding to the population covered by the Marketing Authorisation (n = 235): 0.42 exacerbations with omalizumab compared with 0.63 with the placebo (RR = 0.662; $CI_{95\%}$ = [0.441; 0.995], p = 0.047).

- **Results for the secondary endpoints (modified ITT population)**

During the period of 0 to 52 weeks of treatment, in the total analysable population (n = 576), the average number of clinically significant asthma exacerbations remained lower with omalizumab (0.78) than with placebo (1.36), with a relative risk of 0.573 ($CI_{95\%}$ = [0.453; 0.725]; p < 0.001).

A similar result was observed in the children corresponding to the population covered by the Marketing Authorisation (n = 235): 0.73 exacerbations with omalizumab compared with 1.44 with placebo (RR = 0.504; $CI_{95\%}$ = [0.350; 0.725]; p < 0.001).

After 24 weeks of treatment, in the total analysable population and in the subgroup of children corresponding to the population covered by the Marketing Authorisation, no statistically significant difference was observed in:

- the night-time symptom score
- the quality of life

After 24 weeks of treatment, a statistically significant reduction in rescue bronchodilator consumption was observed with omalizumab compared with placebo in the total analysable study population (n = 576), but not in the subgroup of children corresponding to the population covered by the Marketing Authorisation (n = 235) (see Table 1).

Table 1: Variation in rescue bronchodilator consumption at 24 weeks (measurement during the 4 last weeks of the period)

	Total population		**Severe asthma subpopulation**	
Rescue bronchodilators	**Omalizumab** N = 384	**Placebo** N = 192	**Omalizumab** N = 159	**Placebo** N = 76
Variation in the number of puffs/day	-1.3 (± 2.84)	-1.0 (± 2.50)	-1.3 (± 2.80)	-0.7 (± 3 .22)
p	0.047		0.157	

3.2. Tolerance

The safety of omalizumab in children between 6 and 12 years of age was evaluated mainly on the basis of the results of two studies, study IA05 described above and study 010C conducted in children with moderate persistent asthma.

The overall exposure in the two studies was 502.9 patient years for omalizumab and 244.6 patient years for placebo, with an average duration of exposure of 42.0 ± 13.51 weeks for omalizumab and 42.3 ± 13.85 weeks for placebo.

Globally, the safety profile of omalizumab was similar to that of the placebo. The most common adverse events were respiratory tract infections (rhinopharyngitis, upper respiratory tract infections and sinusitis), headaches and fever (see Table 2). These effects were generally of mild-to-moderate severity.
Adverse effects at the injection site (redness, pain, swelling, itching) following the first injection concerned 6.1% of the patients treated with omalizumab and 7.0% of the patients under placebo.
The most frequently reported severe adverse effects were headaches (1.3% with omalizumab and 0.3% with placebo), pneumonia (0.3% compared with 1.3%) and sinusitis (0.5% compared with 1.3%).

Table 2: Most frequent adverse events

Common adverse effects (% of patients)	**Omalizumab** N = 624	**Placebo** N = 302
Rhinopharyngitis	23.6	23.2
Upper respiratory tract infections	21.3	25.8
Sinusitis	16.2	18.9
Headache	20.7	19.5
Fever	15.1	11.3

Adverse effects which were potentially related to the treatment were observed in 6.6% of the patients under omalizumab and 5.0% of the patients under placebo. These were headaches (1.3% compared with 1.7%), dizziness (0.2% compared with 0.3%), abdominal pain (0.2% compared with 0%), redness (1% compared with 0.7%) and urticaria (1.0% compared with 0.3%).

Four patients (3 treated with omalizumab compared with 1 treated with placebo) withdrew from the study because of adverse effects.

No deaths or tumours were reported during the paediatric clinical development process. Severe adverse effects were observed in 3.4% of the patients treated with omalizumab and 6.6% of the patients treated with placebo. These effects were not linked to the treatment, however.

A reduction in the platelet count within the normal range was observed in 5 patients (0.6%) treated with omalizumab and 1 patient (0.3%) under placebo.

The European risk management plan concerning children between 6 and 11 years of age makes provision notably for the study of the anaphylactic, carcinogenic and haematological (thrombocytopenia) risk and the risk of incorrect (off-label) use.

3.3. Conclusion

The efficacy of omalizumab was evaluated versus placebo, over a period of 1 year, in a double-blind randomised (in a ratio 2 :1) study in 628 children between 6 and 11 years of age with persistent allergic asthma of a moderate (off-label) to severe nature which was poorly controlled despite treatment with fluticasone or equivalent at a dose of ≥ 200 µg per day, with or without (off-label) other continuous treatments. The analysis was performed in a modified intention-to-treat population (n = 576).

Omalizumab (n = 384) proved superior to placebo (n = 192) in terms of the average number of clinically significant asthma exacerbations (worsening of the asthma requiring doubling of the inhaled corticosteroid dose or systemic corticosteroid therapy) measured after 24 weeks for the primary efficacy endpoint: 0.45 compared with 0.64 exacerbations with a relative risk of 0.693 ($CI_{95\%}$ = [0.533; 0.903]; p = 0.007), or 1 exacerbation avoided every 2.7 years.

A similar result was observed in the subgroup of patients who had severe persistent asthma treated with high-dose inhaled corticosteroids combined with a long-acting beta-2 agonist (population covered by the Marketing Authorisation, n = 235): 0.42 exacerbations with omalizumab (n = 159) compared with 0.63 with placebo (n = 76), with a relative risk of 0.662 ($CI_{95\%}$ = [0.441; 0.995], p = 0.047), or one exacerbation avoided every 2.4 years. The size of the effect can be categorised as mild-to-moderate. The validity of this result is open to question because of subgroup analysis.

After 52 weeks of treatment, the difference between omalizumab and placebo in terms of the occurrence of clinically significant exacerbations was maintained both in the overall analysable population and the subgroup of patients corresponding to the indication covered by the Marketing Authorisation.

However, omalizumab did not reduce rescue bronchodilator consumption in the subgroup of children with severe persistent asthma. No statistically significant difference was observed either in terms of the night-time symptoms or quality of life.

The effect on corticosteroid consumption was not studied and omalizumab was not compared with oral corticosteroid therapy.

In this age range, the most frequent adverse effects linked to the treatment were headaches, fever, abdominal pain, urticaria and reactions at the injection site. These effects were of mild-to-moderate severity in the majority of cases. No cases of tumour were observed. No unexpected adverse effects were reported. The risks of anaphylaxis and long-term carcinogenicity, the haematological risk (thrombocytopenia) and the risk of incorrect (off-label) use must be evaluated within the scope of the European risk management plan.

4 TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

In the extension of indication to children between 6 and 11 years of age:

Asthma of atopic origin is common. Poorly controlled severe persistent asthma exposes patients to the risk of severe exacerbations leading to admissions to hospital or treatment in an intensive care unit and may be life-threatening.

This medicinal product is intended as a prophylactic treatment.

Public health benefit:

In terms of public health, the burden represented by asthma is high. The subpopulation constituted by children between 6 and 11 years of age capable of benefiting from XOLAIR (children with poorly controlled severe, persistent allergic asthma) represents a low burden.

A therapeutic need exists but the data available are not sufficient to assert that the medicinal product XOLAIR can meet this need.
In the light of the data from the clinical study (significant results only for the clinically significant exacerbation rate at 24 and 52 weeks and no difference for all the other secondary endpoints), a low impact is expected in terms of morbidity and mortality. This medicinal product is not expected to have any impact on quality of life or on the healthcare system.

In addition, the transferability of the results of this single study is not completely guaranteed owing to the risk of withdrawal from treatment because of the time to onset of action (16 weeks) and to doubts regarding the maintenance of this subcutaneous treatment in the long term.

Consequently, it is not expected that the medicinal product XOLAIR will benefit public health.

The efficacy / adverse effects ratio for this medicinal product is moderate.

This medicinal product is reserved for patients with severe persistent allergic asthma (measurement of IgE levels required) which is poorly controlled by the usual treatments: high-dose inhaled corticosteroids combined with a long-acting $beta_2$ agonist and sustained-release theophylline if necessary.

No alternative exists within the same therapeutic category. In these patients, corticosteroid therapy is the only treatment alternative.

The actual benefit of XOLAIR 150 mg is substantial.

4.2. Improvement in actual benefit (IAB)

In view of:

- the serious nature of severe persistent asthma which is inadequately controlled by high-dose corticosteroid therapy combined with a long-acting $beta_2$ agonist
- the frequency of asthma of allergic origin in children
- the safety problems associated with long-term treatment with oral corticosteroid therapy, the only alternative for this stage of severity
- the inadequacy of the efficacy data for omalizumab in the patient population corresponding to the indication covered by the Marketing Authorisation

XOLAIR provides a minor improvement in actual benefit (IAB IV) in the standard management of children between 6 and 11 years of age with severe persistent asthma of allergic origin poorly controlled by high-dose inhaled corticosteroid therapy combined with a long-acting beta$_2$ agonist.

4.3. Therapeutic use

4.3.1. Therapeutic strategy

In children (> 6 years of age) as in adults, the usual treatment for severe persistent asthma comprises a high-dose inhaled corticosteroid combined with continuous bronchodilator treatment with a long-acting inhaled beta-2 agonist.
Where the asthma is poorly controlled despite high-dose inhaled corticosteroid therapy combined with a long-acting inhaled beta-2 agonist, sustained-release theophylline may be added and, as a last resort, additional short course or continuous treatment with oral corticosteroid therapy. Regular attempts must then be made to reduce the level of this therapy or to stop it completely.

4.3.2 Therapeutic use of the medicinal product

Omalizumab, an anti-IgE monoclonal antibody, is the first representative of a new therapeutic category which fits into the therapeutic strategy as an additional treatment in patients with severe persistent asthma when it is of allergic origin and poorly controlled with high-dose inhaled corticosteroid therapy combined with a long-acting inhaled beta-2 agonist and sustained-release theophylline if necessary.

Omalizumab is restricted to use in adult patients and children aged 6 and above.

In children between 6 and 11 years of age, poor control of asthma by high-dose inhaled corticosteroid therapy is defined by (SPC):

- frequent daytime symptoms or night-time awakenings and
- severe, multiple and documented exacerbations of the asthma

Omalizumab is an alternative to oral corticosteroid therapy. However, its efficacy compared with oral corticosteroids and its benefit in terms of reducing the use of inhaled or oral corticosteroids remain to be demonstrated.

Treatment must be instigated after verification of or attempts to improve compliance with the initial treatment.

The allergic origin of the asthma must be established on the basis of a positive skin test or RAST to a perennial allergen. The patient's IgE level must be determined before the instigation of treatment using one of the available methods for determining total serum IgE levels in order to define the dose to be administered. Only patients with total serum IgE levels between 30 and 1,300 IU/ml in children between 6 and 11 years of age with a weight for which the dosage has been established (see SPC) may be placed on treatment with omalizumab.

The efficacy of treatment must be evaluated after 16 weeks before being continued.

4.4. Target population

According to the IRDES[1] survey (2008), the prevalence of asthma is 10% among boys aged 5-10 and 6% among girls aged 5-10. If these prevalence rates are applied to the French population of girls and boys aged 6-11 (INED data 2008), the population of asthmatic children between 6 and 11 years of age can be estimated at 380,000.

[1] Afrite A, Allonier C, Com-Ruelle L, Le Guen N. L'asthme en France en 2006: prévalence et contrôle des symptômes. IRDES questions d'Economie de la Santé. 2008; 138: 1-8.

According to this same survey, 60% of asthmatic patients have inadequately controlled asthma (according to the GINA criteria). According to the (stricter) criteria of the ANAES and Afssaps[2] recommendations (2004), 83% of patients can be classified as having inadequately controlled asthma. In the Er'Asthme[3,4] (2003) study in 1,410 children between 6 and 14 years of age taking into account the Canadian criteria which are similar to the HAS criteria, asthma control was inadequate in 73% of children. Consequently, it can be estimated that 60-83% of children between 6 and 11 years of age have inadequately controlled asthma. Moreover, in the IRDES survey, 12% of the patients with inadequate asthma control were receiving treatment steps 4 and 5 according to the GINA guidelines (i.e. severe persistent asthma in most cases). If equal distribution is hypothesised between patients treated with step 4 (medium- or high-dose inhaled corticosteroid + long-acting beta-2 agonist) and step 5 (addition of oral corticosteroid therapy at the lowest dose), it may be considered that 6% of the patients had asthma which was inadequately controlled by treatment step 4. If equal distribution is also hypothesised among the patients treated with step 4 between those with a medium- and high-dose inhaled corticosteroid, it may also be considered that 3% of the patients had asthma which was inadequately controlled by a high-dose inhaled corticosteroid combined with a long-acting beta-2 agonist.

Consequently, the population of children aged 6-11 with severe persistent asthma which is inadequately controlled by high-dose inhaled corticosteroid therapy can be estimated at between 7,000 and 10,000 children.

Around 80% of asthma cases are of allergic origin (Programme of actions, prevention and management of asthma, 2002-2005, Ministry of Solidarity, Health and the Family), i.e. a population of 5,600 and 8,000 children with severe persistent asthma of allergic origin inadequately controlled by high-dose inhaled corticosteroids and a long-acting beta agonist.

However, the proportion of children weighing between 20 and 150 kg and with total serum IgE levels between 30 and 1,300 IU/ml for whom a dosage has been established is not known. According to expert opinion, this population should be around 1,000 patients.

4.5. Transparency committee recommendations

The Transparency Committee recommends inclusion on the list of medicines reimbursed by National Insurance and on the list of medicines approved use by hospitals and various public services in the new indication and at the dosages in the Marketing Authorisation.

The committee wishes to be copied in on the results of the planned observational studies, notably those which come under the risk management plan, on long-term safety in particular.

Packaging: Appropriate for the prescription conditions.

Reimbursement rate: 65%

[2] Recommandations pour le suivi médical des patients asthmatiques adultes et adolescents. ANAES-Afssaps (2004) : www.has-sante.fr.

[3] Godard P, De Blic J, Huas D, Boucot I, Pribil C. ER'ASTHME: évaluation du contrôle de l'asthme chez 410 enfants âgés de 6 à 14 ans en médecine générale. Revue des Maladies Respiratoires, 2006; 23(HS1): 8

[4] De Blic J, Boucot I. Pribil C, Huas D, Godard P. Niveau de contrôle de l'asthme chez l'enfant en médecine générale en France : résultats de l'étude ER'ASTHME. Archives de Pédiatrie, 2007;14(9):1069-75