3. Treatment

3.1 Objectives

The main goal of asthma management is to achieve and maintain disease control as earlier as possible, to prevent exacerbations and chronic airflow obstruction and to maximally reduce mortality. With a properly designed treatment plan, therapeutic targets (table 3.1) can be achieved in the majority of patients in terms of daily symptom control (current control domain) and prevention of both exacerbations and excessive loss of pulmonary function (future risk domain).

C

To attain these objectives a global and individualized long-term strategy must be followed based on an optimally adjusted pharmacological treatment along with supervision measures, environmental control and asthma education activities[155]. Pharmacotherapy must be adjusted according to the degree of control after considering the most effective therapeutic options, safety and cost of the different alternatives, and the patient's satisfaction with the degree of control achieved. Patients should be periodically evaluated to check if targets are being met. Patients, clinicians and the healthcare system alike should avoid therapeutic inertia and the factors causing it. A number of validated questionnaires are available to objectively assess the level of current asthma control (chapter 2.6).

Table 3.1. Asthma management goals

In the domain of current control of asthma
• To prevent daytime, nighttime and exercise-related symptoms. • Use of short-acting β_2-agonists no more often than twice a week. • Maintain a normal or near-normal pulmonary function. • No restrictions on daily life and physical exercise. • Fulfillment of the expectations of both patients and their families.
In domain of future risk
• To prevent exacerbations and mortality. • To minimize the progressive loss of pulmonary function. • To avoid treatment-related adverse effects.
Avoid therapeutic inertia

3.2 Pharmacological treatment

Asthma treatment should follow an overall plan, established by consensus of the physician and the patient (and eventually by the patient's family), in which the goals, the interventions to achieve them and the criteria for their modification or adaptation according to changing disease circumstances must be made clear. Distinguishing between the 'current control' domain and the 'future risk' domain in the control of the disease is relevant, because it has been documented that these domains may respond differently to treatment[156,157]. For example, some patients may have a good daily control of asthma symptoms and yet experience exacerbations.

C

C

For patients to be consistently well-controlled, their treatment schedule should be adjusted on a continuous basis. This cyclic treatment adjustment means that asthma control should be objectively assessed (chapter 2.6), that the patient is being treated to achieve control and that treatment is periodically revised to maintain asthma control (figure 3.1). That is, if a patient is not well controlled, treatment must be stepped up as needed in order to regain control, always taking into account non-pharmacological measures, treatment adherence and risk factors susceptible to be modified.

D

If asthma has been controlled for at least 3 months, maintenance therapy may be gradually decreased in order to determine minimum treatment needs that are required to maintain control[120].

C

Drugs used to treat asthma are classified as controller or maintenance medications and reliever medication, also called "rescue" medication. **Drugs for controller or maintenance treatment**, which should be administered on a daily basis during prolonged periods of time, include inhaled glucocorticoids (IGC) or systemic glucocorticoids, leukotriene receptor antagonists (LTRA), long-acting β_2-agonist (LABA), tiotropium and anti-IgE monoclonal antibodies (omalizumab). Chromones and sustained-release theophylline have fallen into disuse because of their lower efficacy.

Reliever medication is used on-demand for rapid treatment or prevention of bronchoconstriction, and includes inhaled short-acting β_2-agonist (SABA) (first-choice) (table 3.2) and inhaled anticholinergics (ipratropium bromide).

The six treatment steps (figure 3.2) aimed at achieving asthma control are the following:

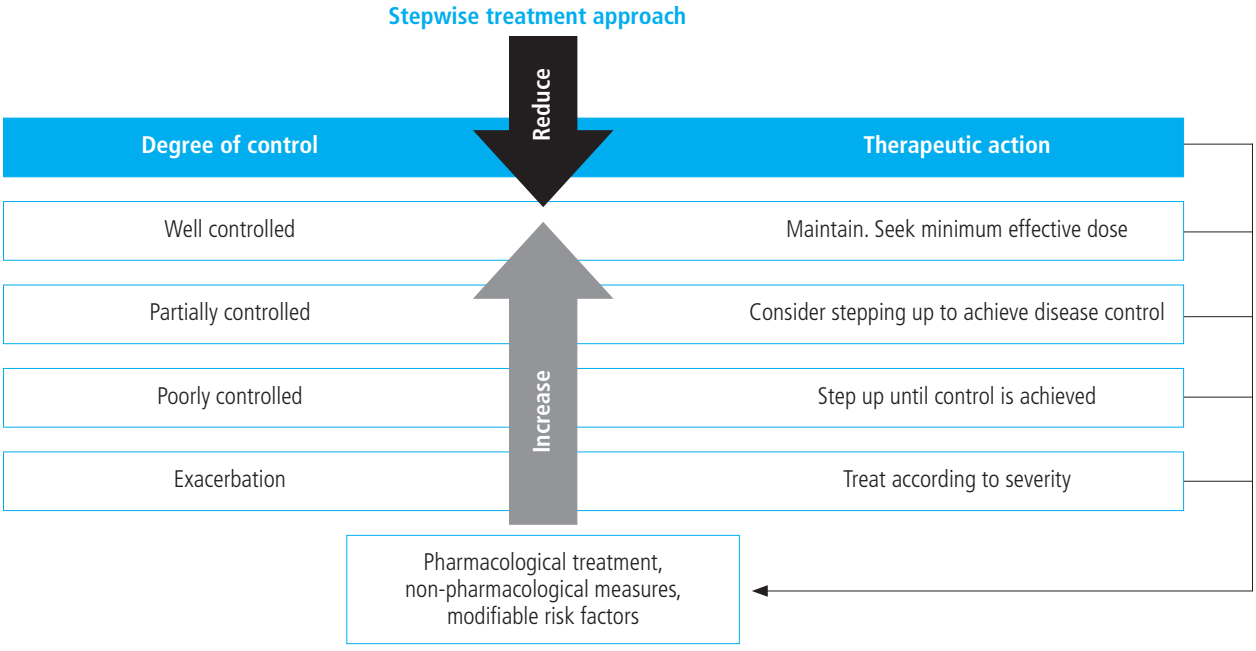


Figure 3.1. Cyclic treatment adjustment according to periodic assessment of disease control.

Table 3.2. Characteristics of inhaled β2-adrenergic agonists

Drug	Amount per puff (µg)		Time of effect (min)		
	Pressurized inhaler	Dry powder	Onset	Maximum	Duration
Short-acting					
Salbutamol	100	100	3-5	60-90	180-360
Turbutaline	-	500	3-5	60-90	180-360
Long-acting					
Formoterol	12	4.5 – 9 - 12	3-5	60-90	660-720
Salmeterol	25	50	20-45	120-240	660-720
Vilanterol	-	22	3-5	-	1440

3.2.1 Steps

Step 1

The first step includes the prescription of inhaled SABA (salbutamol or terbutaline) exclusively on-demand basis. This treatment is reserved for well-controlled patients with occasional, mild daytime symptoms (up to twice a week and for a short time), but no nighttime symptoms. The patient remains asymptomatic and with normal pulmonary function between episodes, with no exacerbations in the previous year and no risk factors for exacerbations (table 2.11)[6]. B

For the vast majority of patients the treatment indicated for rapid symptom relief is an inhaled SABA[158]. A

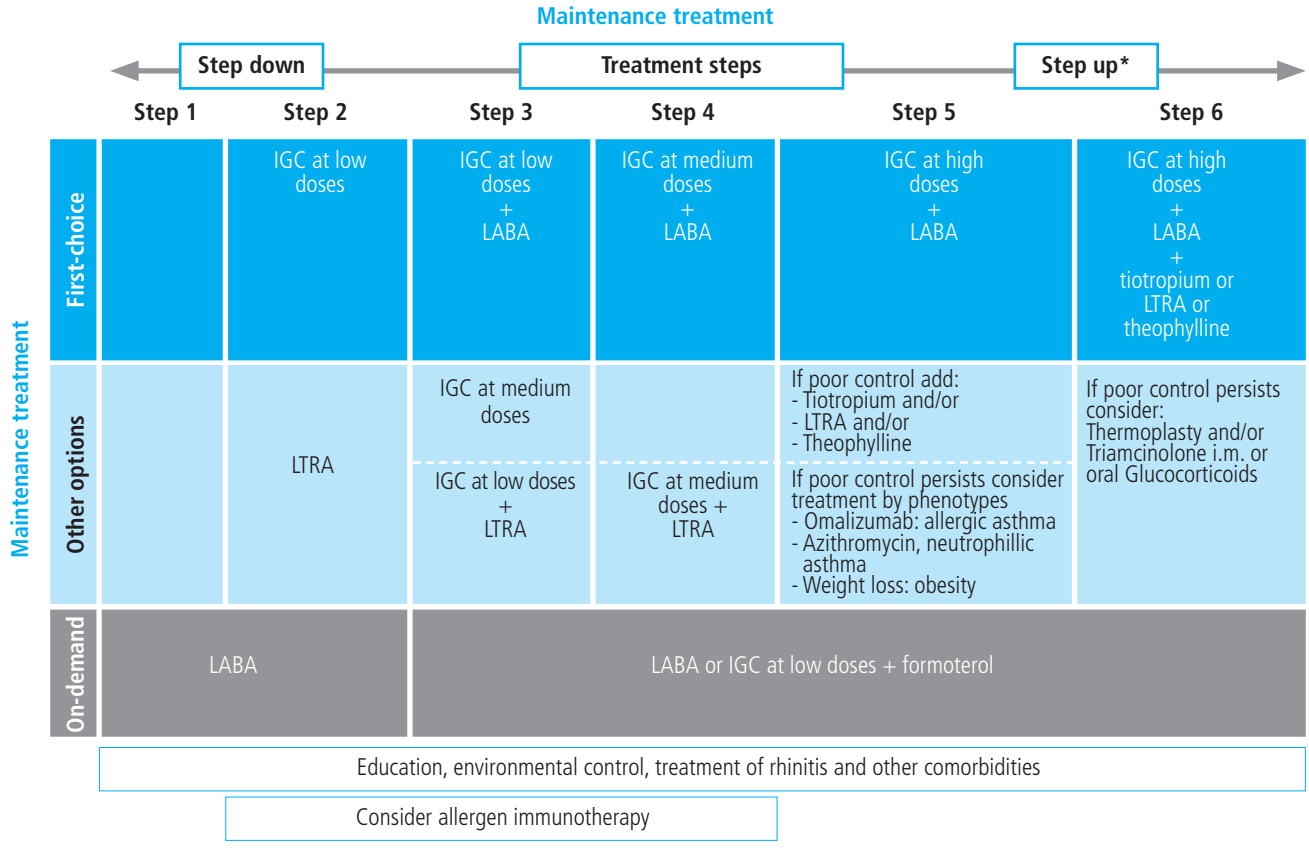
The use of an inhaled SABA on-demand for symptom more than twice a week for the treatment of symptoms (excluding its preventive use before exercise), or having had exacerbations in the previous year, or a FEV_1 value < 80 % suggests an inadequate asthma control and prompts the initiation of maintenance therapy[158-160]. B

Inhaled SABA administered 10-15 minutes before exercise are the drugs of choice to prevent exercise-induced bronchoconstriction[161]. A

An inhaled anticholinergic is only recommended as a reliever medication in those rare cases of intolerance to SABA agents[6]. D

Step 2

The treatment of choice at this step is an IGC (beclomethasone, budesonide, ciclesonide, fluticasone or mometasone) at low doses administered daily[162-165]. In general, this is the first step for most patients with persistent asthma who have not been previously treated. The usual dose is 200 to 400 µg/day of budesonide or equivalent. The equipotent doses of the most common IGC are shown in table 3.3. A A



*After confirmation of correct treatment adherence and use of inhalers.
IGC: Inhaled glucocorticoid; LABA: Long-acting β2-agonist; LTRA: Leukotriene receptor antagonist; SABA: Short-acting β2-agonist.

Figure 3.2. Steps for maintenance treatment in adult asthma.

Table 3.3. Equipotent doses of inhaled glucocorticoids

	Low dose (µg/day)	Medium dose (µg/day)	High dose (µg/day)
Beclomethasone dipropionate	200-500	501-1000	1001-2000
Extrafine beclomethasone	100-200	201-400	> 400
Budesonide	200-400	401-800	801-1600
Ciclesonide	80-160	161-320	321-1280
Fluticasone furoate	-	92	184
Fluticasone propionate	100-250	251-500	501-1000
Mometasone furoate	100-200	201-400	401-800

A IGCs are the most effective maintenance treatment for persistent asthma for both relieving daily symptoms and reducing the risk of exacerbations[159,165-167]. The possibility of using IGC intermittently is controversial, and the same degree of control of daily symptoms as that obtained with treatment administered on a regular basis is not obtained[168].

A At this level, an alternative treatment includes leukotriene receptor antagonists (LTRA) or anti-leukotrienes (montelukast and zafirlukast)[169,170], although ICGs are more effective for long-term treatment[169]. Patients who are well controlled on IGC at low doses fail to maintain the same level of asthma control with montelukast[171].

A LTRA would be particularly indicated as alternative drugs in patients who are unable or unwilling to receive or are intolerant to IGCs, have difficulty with the inhaler technique, or suffer from concomitant allergic rhinitis[172,173].

B

A For patients who have not received a previous maintenance treatment with IGC, the combination of an IGC at low doses and a LABA as initial therapy improves both symptoms and pulmonary function in comparison with low dose of IGC, but it is more expensive and does not reduce the risk for exacerbations as compared with low dose of IGC[174].

There is no evidence as to whether the addition of an LABA drug provides a significant effect at this level[166].

B Sustained-release theophyllines are not recommended for use at this step since they have been shown to be modestly effective as both bronchodilators and anti-inflammatory drugs[175,176], and may cause milt to serious adverse events.

A Chromones (disodium cromoglycate and nedocromil sodium) show low efficacy, although they have a good tolerability[177].

Step 3

A First-line treatment at this step is a combined inhaled treatment with IGC at low doses and a LABA (salmeterol or formoterol or vilanterol)[126,178-182], as they can be administered in a single device (preferred option)[183], or in separate inhalers. By using this combination a more pronounced reduction of symptoms, improvement of pulmonary function, and reduction of exacerbations and use of reliever medications is obtained as compared to increasing the dose of IGC. However, an appropriate individualized risk/benefit assessment for both strategies is required. Combinations available in the Spanish market are fluticasone propionate plus salmeterol, budesonide plus formoterol, beclomethasone plus formoterol, fluticasone propionate plus formoterol, and fluticasone furoate plus vilanterol. LABAs must never be used as monotherapy.

Formoterol is a rapid-onset LABA. For this reason, if *budesonide/formoterol or beclomethasone/formoterol* combinations are chosen, they can be used as both maintenance and reliever therapy (MART strategy). This strategy leads to reduced exacerbations and a better asthma control, despite requiring a lesser amount of IGC[184-191].

A A further option at this step includes increasing IGC doses up to medium doses, but this approach is less effective than adding a LABA[192-194]. Alternatively, IGC at low doses associated with a LTRA may be used. This option has been found to be superior to IGS monotherapy and although it is not as effective as the IGS and LABA combination, has an excellent safety profile[195-198].

Step 4

B The first-line treatment at this step is the combination of an IGC at medium doses with a LABA[126,179,199].

A For patients who had at least one exacerbation in the previous year, the combination of an IGC at low doses (budesonide or beclomethasone) and formoterol in a fixed schedule using the MART approach is more effective in reducing exacerbations than the same dose of an IGC and LABA, or higher doses of IGC[200].

B Alternatively, a combination of an IGC at medium doses with a LTRA can be used, although the addition of LABAs to the IGC is more effective in preventing exacerbations, control of daily symptoms and improving pulmonary function[196].

Step 5

B This step consists of up-titrating IGC dosage and using it in combination with a LABA[126,179,199]. IGC at medium and high doses are usually administered twice daily, although a greater therapeutic efficacy can be achieved with budesonide by increasing the dosing frequency up to 4 times a day[201].

C Other drugs can be added for maintenance therapy; a subgroup of patients improves with the addition of LTRA[202,203] or sustained-release theophylline[204].

B In patients not well controlled with the combination of an IGC at low doses and a LABA, who show post-bronchodilator $FEV_1/FVC \leq 70$ %, the addition of tiotropium as maintenance therapy improves pulmonary function and reduces exacerbations[205,206].

A In case of allergic asthma that is poorly controlled with high doses of IGC and LABA, the anti-IgE monoclonal antibody (omalizumab) by the subcutaneous route can be added. Omalizumab improves daily symptoms and exacerbations[207-210], increasing the overall control of asthma. See chapter 8 for further details.

D Macrolide antibiotics, particularly azithromycin at low doses for several months, may play a role as an add-on medication in patients with severe non-eosinophilic asthma and frequent exacerbations[211,212]. See chapter 8.

Step 6

D For asthma patients who remain uncontrolled despite being treated with high doses of IGC in combination with a LABA, with or without another maintenance drugs (LTRA, tiotropium, theophylline, omalizumab) and who also experience both a limitation of their daily activities and frequent exacerbations, the addition of oral glucocorticoids should be considered (always used at the lowest effective dose and for the minimum period of time possible)[213,214], even though they are also associated with adverse effects (occasionally serious).

Other possible treatments at step 6 include systemic glucocorticoids and endobronchial thermoplasty as well as other available options or in advanced stage of development for a directed treatment approach according to the phenotype of severe asthma that are described in chapter 8.

3.2.2 Inhalers and nebulizers

C Inhaled therapy is the preferred administration route for the treatment of asthma as it acts directly on the lungs, delivers a greater amount of drug into the airways, elicits a rapid response and is associated with few or no systemic effects. On the other hand, certain skills are needed for a correct inhalation technique[215-218]. Currently available inhalation devices include: the conventional pressurized inhaler, which can be used with or without a spacer, the Modulite® system, Respimat® soft mist inhaler (SMI), the dry powder inhalers (DPI) (Accuhaler®, Aerolizer®, Breezhaler®, Easyhaler®, Ellipta®, Genuair®, Handihaler®, Nexthaler®, Spiromax®, Turbuhaler® and Twisthaler®) and the nebulizers (*jet*, ultrasonic or vibrating mesh). Each of them has their own technical characteristics that should be considered when prescribed (table 3.4)[218].

C The main disadvantage of this route is the difficulty of the inhalation technique of the various devices, particularly the pressurized inhalers, for the need of a correct coordination between inhalation and actuation of the device[219,220]. The use

Table 3.4. Deposits and mass median aerodynamic diameter (MMAD) of aerosols generated by various devices[189]

	Lung deposition (%)		Oropharyngeal deposition (%)		DMMA (µm)
	in vivo	in vitro	in vivo	in vitro	
pMDI					
Conventional pMDI	7.8-34	-	53.9-82.2	-	1.4-8
Conventional pMDI with spacer	11.2-68.3	-	31.2	40	2-3.2
Breath-actuated pMDI	50-60	-	30	-	-
Modulite®	31-34	-	33-58	-	1-2
Alvesco®	50-52	-	32.9	-	-
Respimat®	40-53	-	19.3-39	-	-
DPI (by alphabetical order)					
Accuhaler®	7.6-18	15-30	-	-	3.5
Aerolizer®	13-20	21.7-28	73	-	1.9-7.9
Breezhaler®	36	39	-	45	2.8
Easyhaler®	18.5-31	29	-	-	-
Genuair®	30.1	-	54.7	-	-
Handihaler®	17.8	17.3-22	-	71	3.9
Ingelheim Inhaler®	16	-	59	-	-
Nexthaler®	56	-	43	-	1.4-1.5
Spinhaler®	11.5	-	30.9	-	-
Turbuhaler®	14.2-38	28	53-71.6	57.3-69.3	1.7-5.4
Twisthaler®	36-37	-	-	-	2-2.2

pMDI: pressurized metered-dose inhaler; DPI: dry powder inhaler.
The comparison of values among devices should be considered with caution because of differences in the methods and drugs used for estimating the corresponding values, as well as differences in human studies, which were performed in diverse clinical settings (healthy and ill subjects with different diseases and degrees of severity), inspiratory flows and ages.

C

of spacers circumvents coordination issues, improves the distribution and the amount of drug reaching the bronchial tree, reduces the deposition of drug particles in the oropharynx, decreases cough and the possibility of oral candidiasis (that may be associated with the use of IGC), decreases systemic bioavailability and, hence, the risk of systemic effects[221-223]. The inhalation technique is easier with dry powder inhalers, although lung deposition depends on the inspiratory flow, which has to be relatively high (from ≥ 30 l/min)[224] and the device resistance[218], although it should be stressed the need to perform a forceful inspiratory maneuver[219,220]. A crucial aspect in the use of inhaled drugs is that the patient should be properly trained in the use of inhaler devices[225,226]. To this purpose, once the device has been chosen based on the patient's preference, the characteristics of the inhaler and appropriate technique of use must be explained and taught to the patient. Patients will then be asked to show how they perform the maneuvers (with a placebo device) and the possible errors must be corrected. They will also be provided with written detailed instructions on the use of the device. The correctness of the inhalation technique should be checked in all subsequent visits[217-219].

Nebulizers are not the first-choice devices for routine maintenance treatment, and should only be used in special situations[224].

3.3 Other treatments

3.3.1 Environmental control

Smokers with asthma have more severe symptoms, a poorer response to glucocorticoid treatment, even in patients with mild asthma[227], and an accelerated loss of pulmonary function[141,228], so that a step-up in treatment is often required[229]. The proportion of asthmatic smokers is high and similar to that in the general population. Furthermore, since longitudinal studies have found a relationship between tobacco use and asthma in both adults and adolescents[230], the main objective in environmental control is getting the patient to stop smoking. To this end, smokers should receive full information of the most appropriate quit smoking methods[231]. Exposure to both environmental contaminants and passive smoking aggravates the course of asthma and is a risk factor for asthma development in childhood[232]. Administrative regulations banning smoking in public spaces are having a highly positive impact[233,234].

C

Some asthma patients, particularly those with sinonasal polyposis, may experience exacerbations when administered acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAID). Many of these reactions are serious or even fatal[235], so that it is necessary that patients are correctly diagnosed based on evident data in the medical history (several

C

C reactions to different NSAID) or by means of an oral challenge test which, in severe cases, can be replaced with bronchial or nasal inhalation challenge testing[236,237]. This issue is more comprehensively explained in chapter 9.4 (acetylsalicylic acid-exacerbated disease, former intolerance to NSAIDs). These patients, however, among their environmental measures, will avoid the use of analgesic or anti-inflammatory treatments with drugs of the NSAID therapeutic class.

C Specific recommendations for patients with allergic asthma must be made once individual sensitization to different allergens has been confirmed. The most effective measures are those enabling a dramatic decrease of exposure levels, such as those applicable to many patients with occupational asthma (job change) or asthma due to animal dander (removal of animals from the patient's home) or cockroach allergy (wise use of pest-control substances)[238-242].

C Isolated individual interventions, such as the use of mattress covers or acaricides are not effective, not even in reducing exposure levels[243-245]. On the other hand, the implementation of combined specific measures has been associated with a significant reduction in the level of allergen exposure and, in consequence, of benefits in clinical efficacy[246-248].

B Two systematic reviews with meta-analyses concluded that isolated control measures against mites are poorly effective in patient with rhinitis[238] and ineffective in asthma[245]. However, a further systematic review on the effect of combined interventions showed favorable results[249].

3.3.2 Allergen immunotherapy

A Subcutaneous immunotherapy with allergen vaccines is an effective treatment in well-controlled allergic asthma on steps 2 to 4, provided that a clinically relevant IgE-mediated sensitization against common aeroallergens has been demonstrated and well characterized and standardized allergen extracts are used[250,251], avoiding complex mixtures[252]. Immunotherapy should not be prescribed to patients with severe or poorly controlled asthma, as it is ineffective and entails a high risk of serious, even fatal, adverse reactions[253,254].

B For this reason, subcutaneous immunotherapy should only be prescribed by specialist physicians with experience in desensitization and administered in centers equipped with the basic resources for the immediate treatment of a possible severe reaction.

B The search for safer and more convenient options has led to investigate the efficacy of **sublingual immunotherapy**. Two systematic reviews concluded that this treatment approach can significantly attenuate bronchial clinical manifestations in children and adolescents with allergic asthma[255,256], as well as in adults[257]. Most clinical trials showing clinical efficacy were performed with well-characterized extracts at much higher doses than those usually prescribed for subcutaneous immunotherapy. The tolerance profile of sublingual immunotherapy is optimal and fatal reactions have not been reported[257].

B No comparative studies on the cost-effectiveness of immunotherapy versus conventional pharmacotherapy are yet available, and they are not likely to be performed since their complex design makes them unfeasible. However, immunotherapy is not only useful in controlling disease manifestations, but it also offers additional advantages over pharmacotherapy, such as the maintenance of clinical benefits for several years after treatment discontinuation[258,259], a halt in the progression from pollen-related allergic rhinoconjunctivitis to asthma[259], or the occurrence of new sensitizations in monosensitive patients[260]. Finally, immunotherapy has been found to be cost-effective in comparison with pharmacotherapy alone in patients with the coexistence of allergic rhinoconjunctivitis and asthma[261,262].

B

3.3.3 Influenza and pneumococcal vaccinations

A Influenza[263,264] and pneumococcal vaccines[265] have not been shown to be effective in preventing asthma exacerbations.

A However, since it is a cost-effective approach, and due to the high risk of complications in patients with chronic diseases[266,267], annual influenza vaccination should be considered in patients with moderate and severe asthma, both in adults and children.

3.4 Education

3.4.1 Objectives

A Education of asthma patients reduces the risk of exacerbations, improves quality of life and decreases healthcare costs[126,268], thus becoming an essential and indispensable part of the overall management of asthma[125,269-274]. The main goal of education is to provide patients with the knowledge and skills they need to improve self-care and treatment compliance. This results in a better adherence to treatment and, in consequence, in an optimal disease control and a greater personal autonomy.

3.4.2 Knowledge and skills

From a practical point of view[275], education should consider two major aspects: transmission of knowledge and acquisition of skills (table 3.5).

Table 3.5. Information and basic skills that should be learned by a patient with asthma

1. To know that asthma is a chronic disease requiring continuous treatment even if symptoms are absent.
2. To know the differences between inflammation and bronchoconstriction.
3. To be able to differentiate between inflammation "controller" drugs and obstruction "reliever" drugs.
4. To recognize the symptoms of the disease.
5. To use inhalers correctly.
6. To identify and triggers and to avoid triggering factors as much as possible.
7. To monitor symptoms and peak expiratory flow (PEF).
8. To recognize the signs and symptoms of asthma worsening (loss of control).
9. To act in case of asthma worsening in order to prevent an attack or exacerbation.

The information that patients should receive about asthma will strongly depend on their needs, previous knowledge, beliefs, age, asthma severity and necessary commitment to self-control and treatment.

B These interventions should consider[276]: symptom self-management or PEF monitoring, written action plans and regular assessments of asthma control, asthma treatment and abilities of the healthcare personnel.

B Interventions not based on written action plans are less effective[276,277]. Actions that are exclusively informative are ineffective[273,276,277].

Patients will be trained in the following skills: self-administration of prescribed medication, particularly the inhaler device technique[217-220,278], recognition of exacerbations in order to act without delay and avoidance of allergenic triggers[279,280].

3.4.3 Action plan

B The education program should consider setting up an action plan, which consists of a set of individualized written instructions in which asthma severity, disease control and the usually prescribed treatment are taken into account. The education program is mainly intended for the early detection of asthma worsening and the rapid adoption of measures to achieve quick remission. Depending on the patient's and the physician's preferences, the level of control on which the action plan should be based can be assessed in terms of severity and frequency of asthma symptoms, as well as through daily home recording of PEF[281-283]. This plan should include two basic components[284-286]: usual treatment in situation of clinical stability and actions to be implemented in case of asthma worsening (table 3.6). This action plan will

Table 3.6. Asthma action plan

USUAL TREATMENT		
1.- Take daily _____		
2.- Before exercise, take _____		
II. WHEN SHOULD YOUR TREATEMENT BE INCREASED?		
1. Assessment of your degree of asthma control		
Do your asthma symptoms occur more often than twice a day?	No	Yes
Is your activity or physical exercise limited by asthma?	No	Yes
Do you wake up at night because of asthma?	No	Yes
Do you need to take your bronchodilator more often than twice a day?	No	Yes
If you use a peak flow meter (PEF), are PEF values lower than _____?	No	Yes
If your answer has been Yes to three or more questions, then your asthma is not well controlled and your usual treatment needs to be increased		
2. How to increase treatment		
Increase your treatment as follows and assess your improvement daily:		
_____ (write down the increase of your new treatment)		
Maintain this treatment for _____days (specify the number).		
3. When should I call the doctor/hospital for help?		
Call your doctor/hospital _____ (provide phone numbers)		
If your asthma does not improve in _____ days (specify number)		
_____ (space for complementary instructions)		
4. EMERGENCY: severe loss of asthma control		
If you have severe attacks of breathlessness or you can only speak short phrases.		
If you have intense and severe asthma attacks.		
If you have to use your rescue or reliever bronchodilator every 4 hours without any improvement being noted.		
1. Take 2 to 4 puffs _____ (rescue bronchodilator)		
2. Take ___ mg of _____ (oral glucocorticoid)		
3. Ask for medical assistance: go to _____: Address _____		
Call phone number _____		
4. Keep on using your _____ (rescue bronchodilator) until you get medical assistance		

B be reviewed at every visit, either scheduled or unscheduled, as well as on hospital admissions or at visits to the emergency department.

3.4.4 Treatment adherence

B Patient adherence to treatment is a critical factor for achieving and maintaining disease control. It is estimated that adherence is lower than 50% in asthma patients[287,288]. Low adherence is associated with increased morbimortality, as well as with a greater use of healthcare resources[289,290].

D Three types of patients with low adherence or non-adherence have been described: erratic (due to forgetfulness to take medication), deliberated (or intentionally non-adherence where the patient decides not to take medications) and involuntary or unwitting (due to failure in understanding the disease or and its treatment)[291,292].

C Determining the degree of the patient's adherence to treatment is essential, and because adherence is usually overestimated by anamnesis, other methods should be used. In clinical practice, the use of data obtained after pharmacy dispensing of medication (normally recorded on electronic databases) and/or by means of standardized self-administered questionnaires is recommended[6]. The following questionnaires are available in Spanish: the generic Morisky-Green Test[293,294]; a further generic instrument adapted for evaluation of adherence to IGCs, i.e, The Medication Adherence Report Scale for Asthma (MARS-A)[295]; and an inhaler-specific tool, the Test of Adherence to Inhalers (TAI)[296], which also enables to assess the pattern of non-adherence (erratic, deliberated or unwitting).

D The education program should include the assessment of the level of adherence and promote the appropriate corrective measures in case of low adherence, adapting them to the pattern of non-adherence.

3.4.5 Other aspects to be considered

D For education to be effective, a confidence relationship between the healthcare team and the patients should be established, so that patients can raise their doubts, concerns and fears. The healthcare provider should use a simple and understandable language towards both the patients and their relatives, ensure that all concepts have been understood and encourage the patients to put forward their doubts and queries. Also, written personalized goals shared by patients and physicians must be established.

C An appropriate concordance between opinions and expectations of patients and physicians is one of the main factors contributing to asthma control[297].

D Patients and their families should be encouraged to raise doubts and queries regarding the information received or emerging from the medical interview, and sufficient time should be allocated so that they can be sorted out at the next visit[125].

C Although new technologies (telemedicine) might be useful to enhance asthma control, clear-cut evidence supporting their efficacy is not yet available[298].

D Since education is a continuous process and not an isolated event, each visit should give the opportunity to review, strengthen and increase patients' knowledge and skills; hence, education should be agreed on and accepted by the whole team[271].

B Table 3.7 describes the educational tasks that should be undertaken at each visit. Once properly trained, the nursing and pharmacy staff should actively participate in the organization and management of education programs. The benefits provided by these professionals' performance is similar to those obtained from the medical personnel[299-302].

C Educational workshops represent a useful add-on tool to personalized care, being of particular interest when implemented close to the periods when patients are more symptomatic[303].

Table 3.7. Educational tasks to be implemented at each visit

	Communication	Information	Instruction
Initial visit	Assess expectations Agree on common targets Discuss adherence issues	Basic concepts on asthma and its treatment	Inhalation technique Self-monitoring
Control visits	Evaluate achievements concerning expectations and objectives Discuss adherence issues	Reinforce information provided at the initial visit. Inform about environmental avoidance measures	Reinforce inhalation technique How to avoid triggers Interpretation of records Self-management plan
Reviews	Evaluate achievements concerning expectations and objectives Discuss adherence to treatment and environmental avoidance measures	Reinforce the whole information	Review and reinforce inhalation technique Review and reinforce self-monitoring and the self-management plan

RECOMMENDATIONS

3.1.	For patients with asthma symptoms, regardless of the treatment step, the use of a short-acting β_2-agonist (SABA) on-demand for *quick symptom relief* is recommended.	R1
3.2.	SABAs are the drugs of choice to prevent exercise-induced bronchoconstriction when administered 10 to 15 min before the exercise.	R1
3.3.	On-demand inhaled SABAs are recommended for the treatment of intermittent asthma (*step 1*).	R1
3.4.	First-choice treatment for mild persistent asthma (*step 2*) consists of an inhaled glucocorticoid (IGC) at low doses administered daily. Leukotriene receptor antagonists can be considered as an alternative treatment.	R1
3.5.	For first-line management of moderate persistent asthma, a combination of an IGC at low doses (*step 3*) or medium doses (*step 4*) with a long-acting β_2-agonist (LABA) is recommended.	R1
3.6.	For moderate persistent asthma, an IGC at low doses (*step 3*) or medium doses (*step 4*) associated with a leukotriene receptor antagonist can be considered an alternative therapeutic option.	R1
3.7.	The combination budesonide/formoterol or beclomethasone/formoterol may be used as maintenance treatment and on-demand (relief of symptoms).	R1
3.8.	For severe persistent asthma (*step 5*) the combination of an IGC at high doses and a LABA as first-line therapy is recommended.	R1
3.9.	Among patients with *severe persistent asthma (step 5 or 6)* with uncontrolled disease with the combination of an IGC at high doses and a LABA, and with post-bronchodilator FEV1/FVC $\leq$ 70 %, the addition of tiotropium improves pulmonary function and reduces exacerbations.	R2
3.10.	In patients with *uncontrolled severe allergic asthma*, the use of omalizumab should be considered.	R1
3.11.	In patients with severe asthma that remains poorly controlled despite using an IGC at high doses combined with a LABA (*step 6*), with or without maintenance medication, it is necessary to consider the addition of oral glucocorticoids.	R2
3.12.	Inhalation is the route of choice in the management of asthma.	R1
3.13.	Patients should be trained in the inhalation technique of inhaler devices, and the correctness of the technique periodically checked.	R1
3.14.	Smoking cessation is recommended in smokers with asthma.	R1
3.15.	In dust mite allergic asthma, isolated environmental control measures are not recommended.	R2
3.16.	Allergen immunotherapy can be offered to patients with allergic asthma that is well-controlled with low or intermediate levels of treatment (steps 2 to 4), provided a clinically relevant IgE-mediated sensitization against common aeroallergens has been demonstrated and well-standardized extracts have been used.	R1
3.17.	Allergen immunotherapy should be prescribed by experienced specialist physicians and administered in centers with available basic resources for the immediate treatment of possible adverse reactions.	R2
3.18.	Patients with asthma should follow a formal asthma education program. Informative actions alone have not been shown to be effective.	R1
3.19.	Patients with asthma should be provided with a written action plan in order to detect early asthma worsening and to be able to implement actions for rapid remission.	R1
3.20.	It is indispensable to determine the level of adherence to treatment in each individual patient, which can be ascertained from the information obtained after pharmacy medication dispensing (usually registered on electronic databases) and/or by the use of standardized self-administered questionnaires (Morisky-Green Test, MARS-A or TAI).	R2