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Review

Asthma and COPD: Interchangeable use of inhalers. A document of Italian Society of Allergy, Asthma and Clinical Immmunology (SIAAIC) & Italian Society of Respiratory Medicine (SIMeR)

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ABSTRACT

Prescription cost-containment measures are increasing in many European countries and, as more inhaler devices become available, there may be pressure to switch patients from reference inhaled medication to cheaper generic inhaled drugs. Indeed, in some countries, such a substitution is mandated by current regulations, and patients who do not accept the substitution have to pay the difference in cost. Generic inhaled drugs are therapeutically equivalent to original branded options but may differ in their formulation and inhalation device. This new situation raises questions about the potential impact of switching from branded to generic inhaled medications in patients with asthma or chronic obstructive pulmonary disease (COPD), with or without their consent, in countries where this is permitted. Acquisition cost savings from a substitution could be offset by costs related to deterioration in asthma control or worsening in COPD outcomes if the patient is unable or unwilling to use the inhaler device properly. Non-adherence to therapy and incorrect inhaler usage are recognised as major factors in uncontrolled asthma and worsening of COPD outcomes. Switching patients to a different inhaler device may exacerbate these problems, particularly in patients who disagree to switch. Where switching is permitted or mandatory, it is crucial that the reason for switching has been properly explained to the patient and adequate instruction for operating correctly the inhaler have clearly been provided.

Contents

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1. Introduction

A 3-years observational cohort study showed that persistence with the initial branded treatment in COPD is low, with a substantial proportion of patients changing therapy (switch or add-on therapy). Whether these changes in dispensing patterns are physician-instigated or patient-driven is not clear, neither are fully understood the factors driving the changes but, among them, device acceptability must be considered [1].

Several European countries are experiencing an explosion of new drugs and inhaler devices, either pressurized metered dose inhalers (pMDIs) or dry powder inhalers devices (DPIs), being licensed for patients with asthma or chronic obstructive pulmonary disease (COPD). Some pharma companies have invested much money in research and development of unique new inhaler device platforms for delivering different inhaled drugs. Examples of these new delivery system platforms are the Respimat® soft mist inhaler which is the inhaler of choice for administration of the long-acting antimuscarinic (LAMA) drug Tiotropium and the long-acting beta adrenergic bronchodilator (LABA) drug Olodaterol; the Ellipta® DPI for administration of the LAMA drug Umeclidinium, the LABA drug Vilanterol, and the corticosteroid Fluticasone Furoate; the Genuair® DPI for administration of LAMA drug Aclidinium and LABA drug Formoterol, the Breezhaler® DPI for administration of the LABA drug Indacaterol and the LABA drug Glycopirronium; the Nexthaler® DPI for administration of the fixed combination of the corticosteroid Beclomethasone Dipropionate with the LABA Formoterol; the Spiromax® DPI for the administration of the fixed combination of the LABA drug Formoterol with the corticosteroid Busonide, and the fixed combination of the LABA drug Salmeterol with the corticosteroid Fluticasone Propionate. In addition to these branded inhaled medications, the expiration of the patent protection covering the established inhaled bronchodilators, corticosteroids, and their fixed combinations has contributed to the development of several "generic" inhaled drugs that are bioequivalent [2] to the original reference listed inhaled medications. Generic inhaled medications have the same chemical structure as branded medications but they are not necessarily delivered by the same devices as the original branded options, being the original devices often protected by ongoing patents. Rather generics are delivered by relatively low cost inhalation devices that can vary markedly in design, drug delivery and method of operation than devices of the original branded drugs. The substantial differences that exist in the design of inhaler products makes very difficult to develop generic versions of inhaler products that are interchangeable and substitutable with the originator products. We will face in the next years with newly engineered devices, with the availability of more drugs delivered by the same device but also with the pressure of prescribing cost-containment measures. The last are increasing in many countries and, as more inhalers become available, it is feasible that extending the use of generics is considered an important element to achieve substantial savings theoretically at no detrimental to patient care. Thus, switching patients from reference inhaled drugs to lower-cost "generic" inhaled ones may represent an opportunity for reducing cost of drug treatments in asthma and COPD [3,4].

The present document has been prepared by a working group of Italian Society of Respiratory Medicine (SIMeR) and Italian Society of Allergy, Asthma and Clinical Immunology (SIAACI) with the aim to review the current regulations on generic substitution of marketed reference inhaled medications in Europe. We also question if switching patients from reference to generic inhaled drugs may have potential deleterious effects on asthma control and COPD outcomes. Description of current regulatory requirements associated with the development and submission of dossiers for inhaled medications is outside the scope of this article; excellent descriptions of this aspect can be found in the literature [see e.g. [5–7] also for further references].

2. Regulatory framework for orally inhaled medications

When developing a new therapeutically active moiety, the applicant has to provide evidence for the safety, efficacy and quality of the new therapeutically active moiety, as well as the drug product containing the therapeutically active moiety. In case the therapeutically active moiety is known and marketed drug product

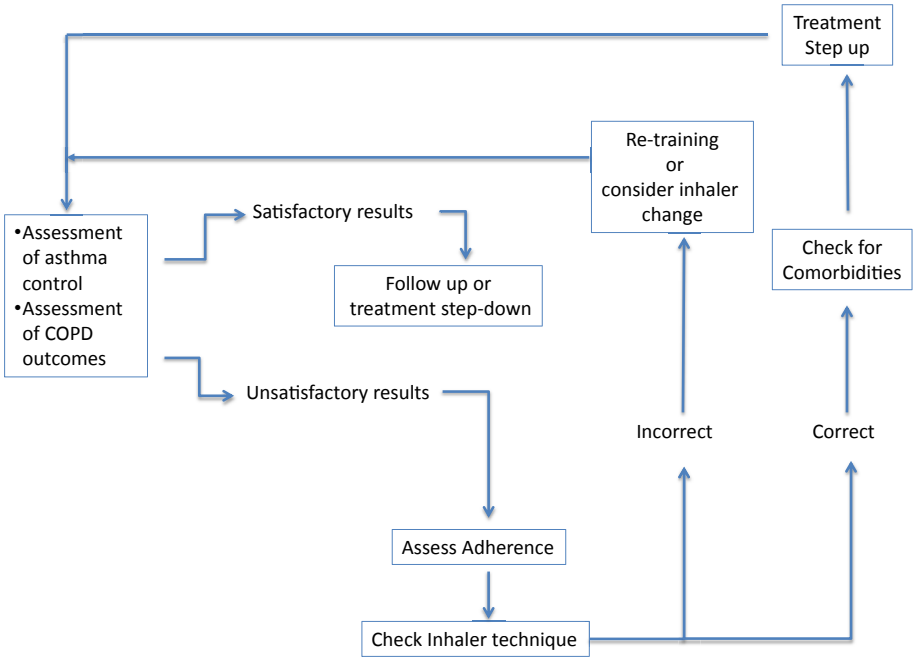

Fig. 1. Treatment algorithm in obstructive lung diseases.