

Duplicate Prescriptions of Inhaled Medications for Obstructive Lung Diseases

Inkompatible Doppelverordnungen von inhalierbaren Medikamenten für obstruktive Lungenerkrankungen

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ABSTRACT

Introduction Inhalative treatments with metered dose aerosols and dry powder inhalers are the backbone of the pharmacotherapy for asthma and COPD. In the last decade many new and generic inhalative bronchodilators were launched at the German market, both monotherapies and fixed dose double bronchodilator (LABA/LAMA, beta adrenergic and antimuscarinic) or LABA and inhaled corticosteroid (ICS) and triple (LABA/LAMA/ICS) combinations. According to two surveys in 2015 among respiratory physicians we expected a high proportion of patients receiving duplicate prescriptions, e.g. a fixed dose new LABA/LAMA combination in addition to an existing ICS/LABA fixed dose combination.

Methodology We searched the database of a large mail order pharmacy (DocMorris) to identify duplicate prescriptions of inhalative drugs for a patient by the same or by two or more different physicians during a 3 months period.

Results Unexpectedly, we found as little as around 1% duplicate prescriptions for the same patient. Duplicate prescriptions involving combination products were found to be much more common than duplicate prescriptions of different mono-products. Irrespective the low percentage number of all prescriptions we saw in just one large mail order pharmacy several thousands of erroneous prescriptions.

Conclusion At least in the setting of this mail order pharmacy duplicate (i.e. contraindicated and potentially dangerous) prescriptions are relatively rare. Prescribers and pharmacists should be aware of the issue of duplicates – especially when prescribing or filling prescriptions with combination products.

ZUSAMMENFASSUNG

Einführung Inhalative Behandlungen mit Dosieraerosolen und Trockenpulverinhalatoren sind das Rückgrat der Pharmakotherapie für Asthma und COPD. In den letzten 10 Jahren wurden viele neue und generische inhalative Bronchodilatoren auf den deutschen Markt eingeführt, sowohl Monotherapien als auch Fixdosis-Kombinationen aus 2 Bronchodilatoren (LABA/LAMA, beta-Adrenergikum und Anticholinergikum) oder LABA und inhalatives Kortikosteroid- (ICS) und Triple-Kombinationen (LABA/LAMA/ICS). Laut 2 Umfragen, die unter Lungenfachärzten im Jahr 2015 durchgeführt wurden, erwarteten wir einen hohen Anteil von Patienten, die doppelte Verschreibungen erhielten, z.B. eine neue LABA/LAMA-Kombination zusätzlich zu einer bestehenden ICS/LABA-Therapie.

Methodik Wir haben die Datenbank einer großen Versandapotheke (DocMorris) durchsucht, um doppelte Verordnungen von Inhalationspräparaten für einen Patienten von demselben Arzt am gleichen Tag oder von 2 oder mehreren verschiedenen Ärzten innerhalb von 3 Monaten zu identifizieren.

Ergebnisse Unerwartet fanden wir nur etwa 1% doppelte Verschreibungen für den gleichen Patienten. Dabei wurden Doppelverordnungen mit Kombinationsprodukten deutlich häufiger beobachtet als solche mit verschiedenen Monoprodukten. Immerhin handelt es sich um mehrere Tausend Rezepte, die wir in einer einzigen großen Apotheke gezählt haben.

Fazit Zumindest in der Datenbasis dieser großen Versandapotheke sind Doppelverordnungen von Inhalativa (d. h. kontraindizierte und potenziell gefährliche Kombinationen) relativ selten. Zur Vermeidung von Medikationsfehlern soll-

ten sich Verordner und Apotheker dieser Problematik bewusst sein, insbesondere bei der Verordnung bzw. Prüfung und Belieferung von Kombinationsprodukten.

Introduction

Duplicate prescriptions are a general, yet little considered problem, not limited to geographic regions, healthcare systems, electronic or manual prescribing, outpatient or inpatient care. We found with the search term duplicate prescription some 140 publications but just one paper according to the respiratory care [1] while most papers elucidate more frequently prescribed drugs, e. g. for hypertension, diabetes or hypercholesterolemia [2–6].

The problem prescribing multiple bronchodilators from the same class was only addressed in the article by Kern et al. [1].

It is some 40 years that in Germany the first fixed combination of two inhalative drugs was launched on the market (the SABA/SAMA fixed dose inhaler Berodual®), and almost twenty years ago the first ICS/LABA fixed combination was introduced. Marketing both, the same drugs as monotherapy as well as an ingredient in a fixed dose combination inhaler already paved the way for duplicate prescriptions shortly after the millennium. Until 2012 only a few numbers of new inhalative drugs were launched (i. e. single LABA's and LAMA's).

In contrast, during the last few years many new inhalative fixed dose combination brands emerged on the German market. In addition, after the patent of many brands (e. g. Budesonide/Formoterol, Fluticasonpropionate/Salmeterol, Tiotropium) expired, several new generics were introduced. Moreover, the constituents of the new fixed dose combinations are not easily recognizable by color codes, as was in the past the blue inhaler for short acting beta2 agonists, reddish for inhaled corticosteroids or green for anticholinergics.

Most patients with airway disease are treated in primary care, but each primary care physician treats only a few such patients. In Germany, Asthma and COPD patients are frequently treated by both the family physician and the respiratory specialist without good functioning platforms to prevent duplicate prescriptions. Also, patients can consult more than a single general or respiratory physician.

Hence, the German Airway League published and updated working tables with color codes and symbols showing the mode of action and the approved frequency of daily inhalations to be used by prescribing physicians (see ► Fig. 1).

Data from the DocMorris database (on file) show, that duplicate prescriptions of different statins like Atorvastatin and Simvastatin are lower than 1%. We hypothesized that in contrast to well established cholesterol-lowering-therapy many duplicate prescriptions of inhalative drugs will occur, e. g. LABA/LAMA together with ICS/LABA or triple therapy, LABA/LAMA with single LAMA or LABA etc.

In 2015 the German Airway league did a survey among 185 respiratory physicians in secondary outpatient care via ques-

tionnaire to assess duplicate prescriptions detected in patients referred to specialist care. 69.73% or 129 physicians stated having seen duplicate prescriptions at all; roughly 60% of these in less than 5% of their patients, some 29% in 5–10% of their patients and some 9% in 10–20%. (Data on file)

The Federal Association of Respiratory Physicians performed a similar survey. 152 respiratory physicians participated. 50% saw duplicate prescriptions in less than 5% of their patients (26.3% in 5–10%, 4.6% in 10–20% and 0.7% in more than 20%) (see ► Table 1).

Methodology

The German Airway's League cooperates with pharmacies to promote patient education on inhaled therapy and inhalation technique.

DocMorris, a mail order pharmacy, that patients can choose to fill their prescriptions with, is one of the cooperation partners. It maintains a large digital database containing prescriptions of inhaled medication. We searched this digital database for duplicate prescriptions of inhalative bronchodilator drugs fully respecting personal data protection law. Hence, ethics commission approval was not deemed to be necessary.

The retrospective survey was done between January 1st and October 31st, 2018. DocMorris fills prescriptions reimbursed by the German statutory health care system (GKV, gesetzliche Krankenversicherung). We looked for duplicate prescriptions of bronchodilator drugs in the context of the GKV patients.

In detail, we differentiated between duplicate prescriptions of long acting bronchodilator inhalatives on the one hand and short acting ones on the other. We only considered prescriptions by respiratory specialists and primary care physicians (i. e. GP's and internists working for family care).

We considered duplicate prescriptions from two different perspectives:

- Same physician's perspective: duplicate prescriptions for the same patient by the same physician at the same day or
- Different physician's perspective: duplicate prescriptions for the same patient by different physicians within 14 weeks, where the older prescription is a large package.

In case of the different physician's perspective only large packages (usually a supply for 90 daily doses) were considered in order to exclude consecutive prescriptions of several 30 daily doses of different bronchodilators (supposedly representing rather a change in medication than a true duplicate prescription). Thus, our definition of duplicates was very conservative, since many patients have a lower than maximum adherence and some patients might have been prescribed lower than average doses, e. g. MART (maintenance and reliever treatment)

Metered Dose Inhalers, Dry powder inhalers and soft mist inhaler for Asthma and COPD

Anticholinergics	Fixed dose combination Bronchodilators	Beta-Adrenergics	Fixed dose combination anticholinergic/ beta-adrenergic/ICS	Fixed dose combination beta-adrenergic/ICS	(ICS) Inhaled corticosteroids
SAMA (short acting anticholinergics)	SAMA/SABA	SABA (short acting beta-adrenergics)	LAMA/LABA/ICS	LABA/ICS	ICS (Inhaled corticosteroids)
Short acting			Long acting (12 hours)		Beclometason Budesonid Ciclesonid Fluticasonpropionat Mometason
Ipratropium	Ipratropium + Fenoterol	Fenoterol Salbutamol Terbutalin	Glycopyrronium + Formoterol + Beclometason Trimbow®	Formaterol + Beclometason Foster® Inuvair®	
LAMA (long acting anticholinergics)	LAMA/LABA	LABA (long acting beta-adrenergics)		Formoterol + Budesonid Airbufo® Bufori® DuoResp® Pulmelia® Symbicort®	
Long acting (12 hours)			Formoterol + Fluticasonpropionat Flutiform®	Formoterol + Fluticasonpropionat Flutiform®	
Acidinium Bretaris® Eklira®	Acidinium + Formoterol Brimica® Dukalir® Glycopyrronium + Formoterol Bevespi®	Formoterol Foradil® Forair® Formatrix® Oxis® Formoterol ... Salmeterol Salmeterol HEXAL® Serevent®		Salmeterol + Fluticasonpropionat Aerivio® Aerflusal® Atmadisc® Flusarion® Rolenium® Serkep® Serroflo® Viani®	
Long acting (24 hours)					
Glycopyrronium Seebri®	Glycopyrronium + Indacaterol Ultibro® Ulnar®	Indacaterol Onbrez®	Umeclidinium + Vilanterol + Fluticasonfuroat Elebrato® Trelegy®	Vilanterol + Fluticasonfuroat Relvar® Revinty®	
Tiotropium Braltus® Spiriva® Srivasso®	Tiotropium + Olodaterol Spiolto®	Olodaterol Striverdi®			
Umeclidinium Incruse®	Umeclidinium + Vilanterol Anoro®				

► Fig. 1 Color coded table of the German Airway League with different classes of inhalative drugs. Green: Antimuscarinic substances, Blue: Beta Adrenergics, Red: inhalative corticosteroids; combined colors for fixed dose combinations.

regimen (half of the approved daily dose plus prn [pro re nata] use).

For both perspectives we calculated the percentage of duplicate prescriptions within the respective drug classes in relation to the overall number of prescriptions in that class (irrespective of prescriber): one class being long acting bronchodilators (i. e. LAMA- and/or LABA-containing inhalatives) the other one short acting bronchodilators (i. e. SABA-containing inhalatives).

We additionally recorded whether the prescriber was a family physician, a respiratory physician or other.

We restricted our analysis to prescriptions for adult patients (18 years and older) listed in the statutory health insurance (GKV), comprising some 90% of the German population.

Duplicate prescriptions of long acting bronchodilators were defined as:

Prescribed drug 1 and prescribed drug 2 both containing LABA (possibly as part of a combination product) but different product group numbers ("Warengruppenschlüssel"), or/and: Prescribed drug 1 and prescribed drug 2 both containing LAMA (possibly as part of a combination product) but different product group numbers ("Warengruppenschlüssel").

► **Table 1** Two independent surveys on duplicate prescriptions.

Percentage of patients	Percentage of respiratory physicians reporting duplicate prescriptions	
	German Airway League (n = 185)	Federal Association of Respiratory Physicians (n = 152)
<5%	59.7	50
5–10%	28.7	26.3
10–20%	9.3	4.6
>20%	0.8	0.7

(data on file)

To identify physicians, their lifelong doctor identifier number (“lebenslange Arztnummer LANR”) was used. If not given, the doctor’s office number (“Betriebsstättennummer BSNR”) was used instead, for example for clinics like medical care center, hospital, emergency unit. The last two digits of the LANR specify the physician’s specialist field (“Facharzttrichtung”). When no LANR was available we chose the label “other specialist”.

For family physicians (FP) (“Hausarzt”) the last two digits are

01: “Allgemeinmediziner (Hausarzt)”

02: “Arzt/Praktischer Arzt (Hausarzt)”

03: “Internist (Hausarzt)”

For respiratory physicians (RP) the last two digits are 30 (“Pneumologie”).

Prescribed drug: pharmacy product identifier number (“Pharmazentralnummer PZN”). Product group number (“Warengruppenschlüssel”), starting with an A and followed by the ATC code (according to WHO). Package size: standardized size (“Normgröße”) and pack size (“Packungsgröße”).

For the 90 days’ supply, package size N3 was taken for SABA containing drugs. For LABA and LAMA containing inhalatives due to lack of standardized sizes in some cases, the following pack sizes were taken: 180 St, 3 St, 3×1 St, 3×30 St, 3×4.0 ml; 3×4 ml, 3×60 St, 90 St (see ► **Table 2** and ► **Table 3**).

In particular, if one drug contained only LABA and another one only LAMA, this was not considered to be a duplicate prescription.

An example: Following four inhalatives were prescribed by one physician for a patient at the same day: ► **Fig. 2**.

By our definition of duplicate prescriptions this generated a count of four individual duplicates, one of them (Spiriva and Anoro) caused by duplicate LAMA components, and three (Symbicort and FormoLich, FormoLich and Anoro and Anoro and Symbicort) by duplicate LABA components as shown in ► **Table 4**.

In contrast, drug pairings Spiriva (LAMA only) plus Symbicort (ICS/LABA) and Spiriva plus FormoLich (LABA only) did not generate a duplicate.

Duplicate prescriptions of short acting inhalative bronchodilators were defined as:

Prescribed drug 1 and prescribed drug 2 both containing SABA but different product group numbers (“Warengruppenschlüssel”). (For details see ► **Table 5**)

Out of scope were duplicate prescriptions of inhalative bronchodilators containing the exact same composition of ingredients but differing only in brand name (called also co-marketing).

Results (long acting bronchodilators)

Overall, in the 10-month review period there were 99 145 prescriptions containing long acting bronchodilators such as LABA Mono, LAMA Mono, LABA/LAMA-combinations, LABA/ICS-combinations, LAMA/LABA/ICS-combinations. 62 035 (62.57%) of them were prescribed by family doctors, 31 183 (31.45%) by respiratory physicians and 5927 (5.98%) through other specialists or clinics.

Same day duplicate prescriptions for long acting bronchodilators by one physician for the same patient were seen 765 times, corresponding to 0.77% of overall long acting prescriptions (534 by family physicians, i. e. 0.86% of the family physician prescriptions, 178 by respiratory specialists i. e. 0.57% of the respiratory physician prescriptions, 53 by others, i. e. 0.89% of the other specialists’ prescriptions).

Restricting to large package sizes (according to the 90 days’ supply) we had an overall of 61 394 prescriptions with 35 693 (58.14%) by family doctors, 22 103 (36.02%) by respiratory specialists and 3598 (5.86%) by other specialists or clinics.

We saw 724 duplicate prescriptions by different physicians for the same patient within 14 weeks with the older prescription being a large package size (equaling 1.18% of overall long acting prescriptions with large package size).

- 416 times (57.46% of 724) the duplicate was caused by prescriptions by a family physician for one of the drugs and a respiratory physician for the other one
- 24 times (3.32% of 724) it was brought up by two different respiratory physicians
- 50 times (6.91% of 724) by two different family physicians and
- 234 times (32.32% of 724) by others including hospital outpatient or emergency departments.

► **Table 2** Ingredients and product group numbers of LABA containing inhalatives.

LABA Mono		LABA + LAMA Combi (double)		LABA + LAMA Combi (triple)		LABA Combi (double)	
LABA (ingredients and product group numbers)		LABA + LABA (ingredients and product group numbers)		LABA + LABA + ICS (ingredients and product group numbers)		LABA + ICS (ingredients and product group numbers)	
Formoterol	AR03AC13	Indacaterol	AR03AC18	Formoterol	AR03AK07	Formoterol + Vilanterol + Fluticasone furoate	AR03AK10
		Olodaterol	AR03AC19	Glycopyrronium + Formoterol + Beclomethason	AR03AL09	Formoterol + Fluticasone propionat	AR03AK06
		Salmeterol	AR03AC12	Umeclidinium + Vilanterol	AR03AL03	Formoterol + Beclomethason	AR03AK11
				Glycopyrronium + Vilanterol + Fluticasone furoate	AR03AL08	Formoterol + Budesonid	
				Umeclidinium + Vilanterol	AR03AL06	Formoterol + Fluticasone propionat	
				Olodaterol + Tiotropium	AR03AL04		
				Glycopyrronium + Indacaterol	AR03AL05		
				Acidinium + Formoterol	AR03AL04		

Spiriva 18 µg CC Pharma 90 Kaps. Nachf. N3

CC-Pharma 05468050 mo:1

Symbiocort® Turbohaler® 320/9 µg/Dosis 60 ED N1

03109200 mo:1, ab:1

FormoLich® 3×60 Hartkaps. z. Inhalat+3 Inhalat N3

04100158 mo:2

ANORO® 55 µg/22 µg 3 Inh. m. je 30 ED Plv. z. Inh.

10045156

► **Fig. 2** Original prescription for a patient.

► **Table 6** and ► **Fig. 3** and ► **Fig. 4** show that duplicate prescriptions of mono-products with combination-products as well as two different combination products (roundabout 50% each) was a lot more common than duplicates of different mono-products, no matter whether from the same day same physicians' or from the different physicians within 14 weeks period perspective.

Results (short acting bronchodilators)

On the SABA side there were 43 503 overall prescriptions such as SABA Mono, SABA/SAMA-combinations and SABA/sodium cromoglycate combinations. 27 888 (64.11%) of them were prescribed by family doctors, 12 827 (29.49%) by respiratory specialists and 2788 (6.41%) by other specialists or hospital outpatient and emergency departments. The 90 days' supply perspective shows 16 427 prescriptions, of these 11 611 (70.68%) by family doctors, 3839 (23.37%) by respiratory specialists, 977 (5.95%) by other specialists or clinics.

Same day duplicate prescriptions in SABA by one physician for the same patient were seen 667 times corresponding to 1.47% of overall SABA prescriptions (391 through family physicians, i.e. 1.40% of the family physician prescriptions. 229 by respiratory specialists i.e. 1.79% of the respiratory physician prescriptions, 47 through others, i.e. 1.69% of the other specialists' prescriptions).

We saw 380 duplicate SABA prescriptions within 14 weeks with the respective older one being a large package size. This means 2.31% of the overall large package size SABA prescriptions were duplicate prescriptions. 255 (67.11%) of the SABA duplicates were triggered by family physicians and respiratory specialists, 3 (0.79%) by different respiratory specialists, 53 (13.95%) by different family practitioners and 69 (18.16%) by others.

Looking at the details of the respective drug groups (see ► **Table 7** and ► **Fig. 5** and ► **Fig. 6**, respectively) involved in the SABA duplicate prescriptions, about 75% of them are caused by mono with combination drugs, whereas prescriptions of two different mono-drugs account for about 20%. This is true for both the one physician, same day and the different physicians within 14 weeks perspective.

► **Table 3** Ingredients and product group numbers of LAMA containing inhalatives.

LAMA Mono				LABA + LAMA Combi (double)				LABA + LAMA Combi (triple)	
LAMA (ingredients and product group numbers)				LAMA + LABA (ingredients and product group numbers)				LAMA + LABA + ICS (ingredients and product group numbers)	
Acclidinium	Gycopyr- ronium	Tiotropium	Umeclidinium	Acclidinium + Formoterol	Glycopyr- ronium + Indacaterol	Olodaterol + Tiotropium	Umeclidini- um + Vilan- terol	Glycopyr- ronium + For- moterol + Be- clomethason	Umeclidini- um + Vilan- terol + Fluti- casonfuroat
AR03BB05	AR03BB06	AR03BB04	AR03BB07	AR03AL05	AR03AL04	AR03AL06	AR03AL03	AR03AL09	AR03AL08

► **Table 4** Count of duplicates of different inhalatives in the “same physicians” perspective.

Name of the drug	Ingredients	Product group number	LABA	LAMA	Name of the drug	Ingredients	Product group number	LABA	LAMA
SPIRIVA 18 µg Kapseln m. Inhalationsplv. Nachfüll	Tiotropium	AR03BB04	no	yes	ANORO 55 µg/ 22 µg 30 ED Plv. z. Inhalation	Vilanterol and Umeclidinium	AR03AL03	yes	yes
SYMBICORT Turbohaler 320/9 µg/Dosis 60 ED	Formoterol and Budesonid	AR03AK07	yes	no	FORMOLICH 12 Mikro-gramm Hart-kaps. m. Plv. z. Inhal.	Formoterol	AR03AC13	yes	no
FORMOLICH 12 Mikro-gramm Hart-kaps. m. Plv. z. Inhal.	Formoterol	AR03AC13	yes	no	ANORO 55 µg/ 22 µg 30 ED Plv. z. Inhalation	Umeclidinium and Vilanterol	AR03AL03	yes	yes
ANORO 55 µg/ 22 µg 30 ED Plv. z. Inhalation	Vilanterol and Umeclidinium	AR03AL03	yes	yes	SYMBICORT Turbohaler 320/9 µg/Dosis 60 ED	Formoterol and Budesonid	AR03AK07	yes	no

Discussion

Despite lack of control of prescriptions on a patient level in the German healthcare system and the possibility of mistakes due to a vast number of old and new single and combination brands on the market the proportion of duplicate prescriptions in the database was only some 1%. Duplicate prescriptions involving combination products were found to be much more common than duplicate prescriptions of different mono-products (see ► **Fig. 3–6**). This finding might be owed to the fact that during the last few years many new inhalative fixed dose combination brands emerged on the German market as well as several new generics were introduced.

In 2015 both the German Airway League and the Federal Association of Respiratory Physicians performed a survey among respiratory physicians who roughly estimated frequency of duplicate prescriptions in patients referred by family physicians (FPs): In both surveys 50–60% of the RP's reported duplicate

prescriptions by family physicians in less than 5%, by another 26–29% up to 10% of the cases. However, this was just an estimation, not a retrospective analysis. Yet in 2015, the FP's might have been less familiar with the newly launched brands than in 2018 at the time of our data analysis. Nonetheless, according to the authors present clinical experience we also expected a much higher duplicate prescription rate.

We decided to focus the research on the patient's perspective regardless of whether the prescriber was the FP, the respiratory physician (RP) or prescriptions came from both. The database shows, that prescriptions by other specialists i. e. emergency care, ENT, allergologists (dermatologists), gynecologists (for pregnant women) are infrequent, comprising only about 6% of all prescriptions. The German statutory health care system discourages prescriptions for respiratory diseases by other than family physicians and respiratory specialists. Therefore, we restricted the detailed analysis to those two groups. Remaining prescriptions are summarized under “other physicians”.

► **Table 5** Ingredients and product group numbers of SABA containing inhalatives.

SABA Mono			SABA Combi (double)	
SABA (ingredients and product group numbers)			SAMA + SABA (ingredients and product group numbers)	SABA + Cromoglicinic acid (ingredients and product group numbers)
Fenoterol	Salbutamol	Terbutalin	Ipratropium + Fenoterol	Reproterol + Cromoglicinsäure
AR03AC04	AR03AC02	AR03AC03	AR03AL01	AR03AK05

► **Table 6** Results of the overall and duplicate prescriptions of long acting bronchodilators (LABA and/or LAMA containing drugs)

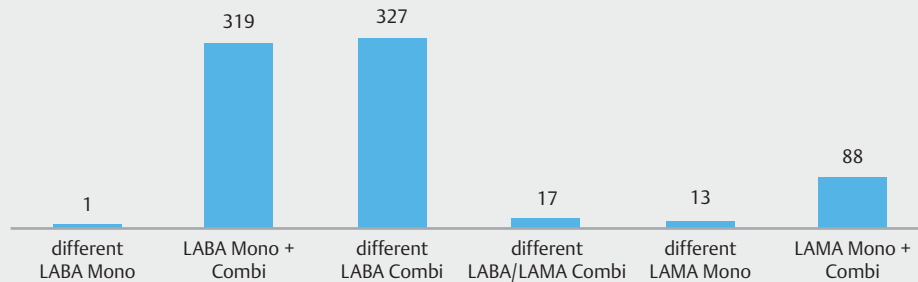
Survey period January 1 st 2018–October 31 st 2018	Number of prescriptions	Percentage duplicate prescriptions of overall prescriptions	Number of prescriptions by FP, RP, OP	Percentage of overall prescriptions by FP, RP, OP	Number of duplicate prescriptions of the respective drug groups
Overall prescriptions long acting bronchodilators					
A.) all package sizes	99 145		A.)	A.)	
			FP 62 035	FP 62.57	
			RP 31 183	RP 31.45	
			OP 5929	OP 5.98	
B.) Large package sizes	61 394		B.)	B.)	
			FP 35 693	FP 58.14	
			RP 22 103	RP 36.02	
			OP 3598	OP 5.86	
Duplicate long-acting bronchodilator prescriptions Same physician	765	0.77	FP 534	FP 0.86	Different LABA Mono: 1
			RP 178	RP 0.57	LABA Mono + LABA Combi: 319
			OP 53	OP 0.89	Different LABA Combi: 327
					Different LABA/LAMA Combi: 17
					Different LAMA Mono: 13
					LAMA Mono + LAMA Combi: 88
Duplicate long-acting bronchodilator prescriptions Different physicians	724	1.18	FP + RP 416	FP + RP 57.46	Different LABA Mono: 0
			RP + RP 24	RP + RP 3.32	LABA Mono + LAMA Combi: 177
			FP + FP 50	FP + FP 6.91	Different LABA Combi: 272
			other constellation 234	other constellation 32.32	Different LABA/LAMA Combi: 76
					Different LAMA Mono: 12
					LAMA Mono + LAMA Combi: 187

FP: family physician, RP: respiratory physician, OP: physician other than family physician or respiratory specialist

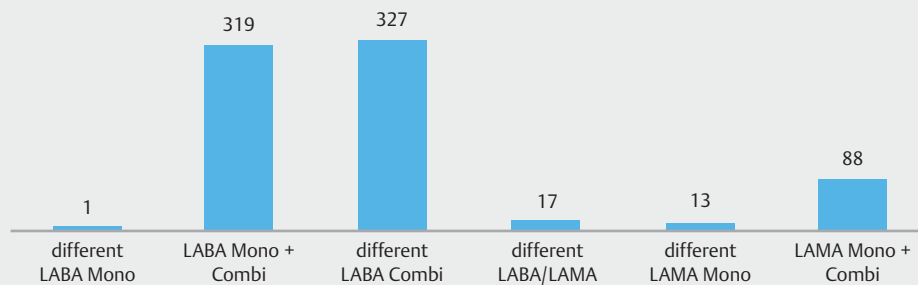
Numbers in the table are either numbers or percentages of prescriptions or of duplicate prescriptions by the respective physicians or numbers of duplicate prescriptions of the respective drug groups as outlined in the heading of the respective column of the table.

For calculation of the respective percentages see explanation in brackets.

Explanation of the column "number of duplicate prescriptions of the respective drug groups": Example from the same physician perspective: there was 1 duplicate prescription by the same physician of two different LABA Mono containing inhalatives, e. g. one containing Formoterol and the other one Salmeterol. 319 duplicates were seen with one of the inhalatives containing a LABA Mono ingredient the other one a LABA Combi (LABA with LAMA and/or ICS). See ► **Table 2** and ► **Table 3** for details.



► **Fig. 3** Same day duplicate prescriptions (long acting bronchodilators).



► **Fig. 4** 14 weeks duplicate prescriptions.

Some 2/3 of all prescriptions arise from FP and 1/3 from RP for both long acting (62.51% vs. 31.45%) and short acting (64.11 vs. 29.49%) bronchodilators which could reflect the proportion of patients with airway diseases cared for.

The average number of prescriptions for long acting bronchodilators was 2.47 per patient; FP's prescribed 2.25 and RP's 2.09 pro patient; remaining prescriptions came from other physicians. The respective numbers for short acting bronchodilators were an average of 1.81 prescriptions per patient; 1.78 by FP and 1.48 by RP. These numbers may indicate that patients referred by FP to RP were already pretreated.

It is surprising that the percentage of RP's same day prescriptions of two different short acting bronchodilators was 1.79% of their total prescriptions versus 1.40% of FP's total. However, SABA prescription and even duplicate prescription can also reflect asthma control. More severe asthma patients in specialty care may ask usually for a higher amount of SABA prescription.

It was expected and it is reassuring, that LABA/LAMA duplicates were 1/3 lower by specialists if compared with FP.

In contrast, it is an unexpected finding that the overall rate of duplicate prescriptions for short acting bronchodilators (1.53 and 2.31% of all, same day and 14 weeks prescriptions, respectively) is higher than the overall duplicate prescription rate for long acting bronchodilators. Short acting substances including combinations were launched decades ago, while

LABA/LAMA combination just around the observation period. Thus, other factors than mistakes and confusion may play an important role. A small number of nebulizer solutions for the use at home and SABA metered dose aerosols as acute reliever were counted as duplicate prescriptions. More likely however this may reflect over-reliance on reliever use rather than guideline guided COPD or asthma care.

Duplicates by two different physicians in the 14 weeks period with first supply of 90 days (N3) package may also represent a different problem than mistake of the prescriber: we suspect in many cases missing information of the second prescriber. In the German statutory healthcare system in 14 weeks period patients can consult several FP's and specialists and can get new prescriptions. The prescriber is usually not informed about former prescriptions. This can dramatically improve if in the next years digital prescription will be introduced provided that the prescribers information of personal health record on electronic patient files will not be limited by data protection rules.

It is important to note that it is the pharmacist who can immediately detect same-day duplicate prescriptions. Usually, the pharmacists will fill the duplicate prescription. DocMorris provides written notice that in such cases the patients should re-consult the prescribing physician.

► **Table 7** Results of the overall and duplicate prescriptions of SABA.

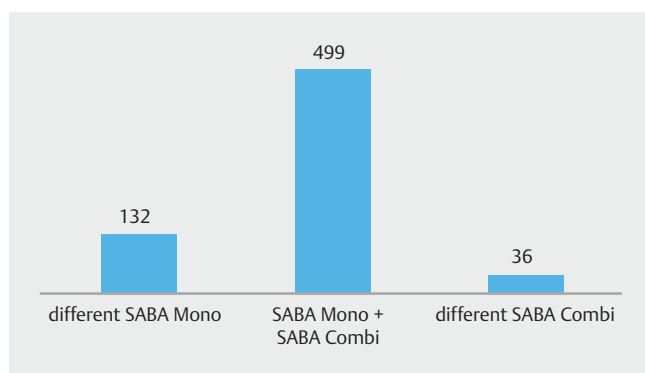
Survey period January 1 st 2018–October 31 st 2018	Number of overall prescriptions	Percentage duplicate prescriptions of overall prescriptions	Number of overall prescriptions by FP, RP, OP	Percentage of overall prescriptions by FP, RP, OP
Overall prescriptions SABA				
A.) all package sizes	43 503		A.)	A.)
			FP 27 888	FP 64.11
			RP 12 827	RP 29.49
			OP 2788	OP 6.41
B.) large package size	16 427		B.)	B.)
			FP 11 611	FP 70.68
			RP 3839	RP 23.37
			OP 977	OP 5.95
Duplicate SABA prescriptions Same physician	667	1.53	FP 391	FP 1.40
			RP 229	RP 1.79
			OP 47	OP 1.69
Duplicate SABA prescriptions Different physicians	380	2.31	FP+RP 255	FP+RP 67.11
			RP+RP 3	RP+RP 0.79
			FP+FP 53	FP+FP 13.95
			other constellation 69	other constellation 18,16

FP: family physician, RP: respiratory physician, OP: physician other than family physician or respiratory specialist

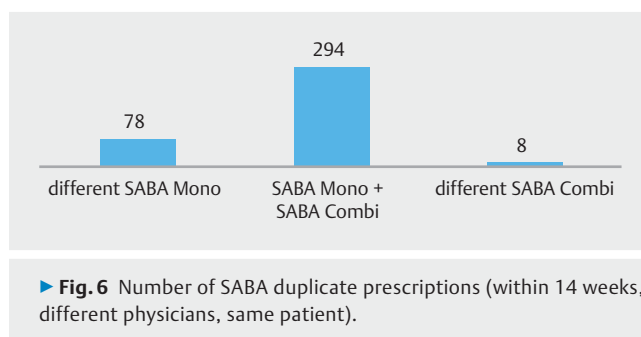
Numbers in the table are either numbers or percentages of prescriptions or of duplicate prescriptions by the respective physicians or numbers of duplicate prescriptions of the respective drug groups as outlined in the heading of the respective column of the table.

For calculation of the respective percentages see explanation in brackets

Explanation of the column "number of duplicate prescriptions of the respective drug groups": Example from the same physician perspective: there were 132 duplicate prescription by the same physician of two different SABA Mono containing inhalatives, e. g. one containing Fenoterol and the other one Salbutamol. 499 duplicates were seen with one of the inhalatives containing a SABA Mono ingredient the other one a SABA Combi. See table 5 for details of the respective drug groups.



► **Fig. 5** Number of same day duplicate prescriptions of SABA.



► **Fig. 6** Number of SABA duplicate prescriptions (within 14 weeks, different physicians, same patient).

Limitations of the survey

The most important limitation of the study is the possibility that patients can fill their prescriptions in different pharmacies. Therefore, the captured data can be incomplete and duplicate prescriptions may be underestimated. To check generalizability of our data extracted from the database of a large mail-order phar-

macy we would need comparable centrally aggregated data from a large number of on-site pharmacies. To our knowledge, there is no such database available. Another possible source for validation is data from a health care provider database.

Duplicate prescriptions were found at an unexpectedly low level; any differences in duplicate prescribing habits between FP and RF should be interpreted with caution.

Conversely, clinical aspects cannot be captured in the pharmacy database which may lead to an overestimation of dupli-

cate prescriptions. Some patients could stop their medication due to side effects and get another prescription, e. g. in COPD an ICS/LABA treatment can be changed to LABA/LAMA if oral candidiasis appears.

Some patients with escalation or de-escalation of their treatment can have a “duplicate” prescription, e. g. if an ICS/LABA treatment was escalated to triple therapy.

Conclusions

Despite a confusingly high number of recently introduced branded and generic drugs on the inhalative market and the inherent weakness of the current prescribing system the surprisingly low number of duplicate prescriptions as detected in this study is reassuring. Nonetheless, irrespective the low percentage number of all prescriptions we saw in just one large mail order pharmacy several thousands of erroneous prescriptions.

Prescribers should be aware of the issue of duplicates – especially when prescribing combination products. The pharmacist can also detect same time duplicate prescriptions. Moreover, looking the filling history of the patient the pharmacist can detect duplicates from different prescribers, provided that the individual patient fills his prescription always in the same pharmacy.

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Conflict of interests

According to this paper the authors PK and HW declare no conflict of interest.

FG, JS and CF are employees of DocMorris, Heerlen.

UB is Executive manager of the German Airways League.

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