

Decreased effectivity associated with the revised formulation of the salbutamol aerosol from Sandoz® -- an update of the reports

In the signal published in 2015 the Netherlands Pharmacovigilance Centre Lareb described nine cases of decreased effectivity associated with salbutamol aerosol from Sandoz®.

http://www.lareb.nl/Signalen/Signals_2015_Salbutamol_efficacy_lack.aspx

This signal has been discussed in the MEB Q-meeting of 28 October 2015 and the MEB 845th meeting on 23 December 2015 and an update on the 356th MEB meeting on 2 July 2016.

We hereby give a new update on the reports on this association.

From January 2015 until July 2016 the Netherlands Pharmacovigilance Centre Lareb received 63 reports considering possible decreased effectivity associated with the revised formulation of the salbutamol aerosol from Sandoz® (table 1). The cases describe 3 patients aged <1 year, 31 patients aged 1-11 years, 7 patients aged 11-20 years and 18 patients aged >20 years. Most reporters describe patients who experiences less effectivity compared to the salbutamol aerosol they used before (old version of Sandoz aerosol or another brand), in 21 cases leading to hospitalisation because of dyspnoea or asthma exacerbation. Some reporters mention, the aerosol fits less easy on the spacer they use. Also, reporters mention the output from the salbutamol aerosol from Sandoz® seems to be less than from the aerosol they used before. Most patients substitute to another brand after experiencing these complaints.

Table 1. Overview of reports decreased effectivity associated with the revised salbutamol aerosol from Sandoz

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
A. 188606 F, 41 - 50 years Consumer	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone for inhalation	Therapeutic response decreased	Unknown minutes, Dose increased, Unknown	Not with spacer, Used before (Actavis)
B. 189045 M, 51 – 60 years Other health professional (Received through the MAH), Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Drug ineffective, Dyspnoea	Unknown, Dose not changed, Recovering	Unknown, Used before (brand unknown)
C. 196661 M, 0 - 1 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Dyspnoea, Therapeutic response decreased	Unknown Month, Drug withdrawn, Recovering	With spacer, Used before (old Sandoz)
D. 196662 M, 2 - 4 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Dyspnoea	Unknown month, Drug withdrawn, Unknown	With spacer, Used before (old Sandoz)
E. 196663 M, 8 - 10 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Dyspnoea	Unknown, Drug withdrawn, Unknown	With spacer, Used before (old Sandoz)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
F. 196664 F, 11 -20 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Dyspnoea	Unknown, Drug withdrawn, Unknown	With spacer, Used before (old Sandoz)
G. 196665 M, 5 - 7 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Dyspnoea	Unknown, Drug withdrawn, Unknown	With spacer, Used before (old Sandoz)
H. 197688 Unknown sex and age, Other health professional (Received through the MAH), Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Asthma exacerbated, Drug ineffective	Unknown, Unknown, Unknown	Unknown, Used before (brand unknown)
I. 199973 M, 11 - 20 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased, Dyspnoea	2 days, Drug withdrawn, Recovering	Unknown, Used before (brand unknown)
J. 201436 F, 11 - 20 years Consumer	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased	Unknown minute, Unknown, Unknown	With spacer, Used before (Ventolin®)
K. 202411 Unknown sex and age, Specialist doctor (Received through the MAH), Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Drug effect decreased	Unknown, Unknown, Unknown	Unknown, Unknown
L. 203145 M, 2 - 4 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Drug effect decreased, Dyspnoea	Unknown days, Drug withdrawn, Recovered	With spacer, Used before (old Sandoz)
M. 203812 M, 8 - 10 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Salmeterol/ fluticasone for inhalation	Therapeutic response decreased, Dyspnoea	1 Hour, Dose not changed, Recovered	With spacer, Used before (Ventolin®)
N. 206136 F, 5 - 7 years Consumer	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased, Asthma	Unknown, Drug withdrawn, Recovering	With spacer, Unknown
O. 208432 F, 2 - 4 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased, Dyspnoea	Unknown day, Drug withdrawn, Recovered	Unknown, Used before (brand unknown)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
P. 211057 M, 11 - 20 years Specialist doctor, Other	Salbutamol aerosol 100ug/do Sandoz	Non specified inhalation corticosteroid	Therapeutic response decreased	2 Weeks, Drug withdrawn, Recovered	Unknown, Used before (brand unknown)
Q. 212053 F, 31- 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Ipratropium for inhalation, Formoterol for inhalation, Beclomethasone for inhalation, Laxation suspension	Dyspnoea, Therapeutic response decreased	20 Minutes, Drug withdrawn, Recovered	With spacer, Used before (old Sandoz)
R. 212058 F, 0 - 1 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone for inhalation	Asthma exacerbated, Therapeutic response decreased	2 Hours, Dose increased, Recovering	Unknown, Used before (brand unknown)
S. 212123 F, 0 - 1 years Consumer, Hospitalisation, Lifethreatening	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Respiratory failure	1 Day, Dose not changed, Recovering	With spacer, Used before (PCH)
T. 212579 F, 71 years and older Consumer	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone/ formoterol for inhalation	Therapeutic response decreased	Unknown Minute, Dose increased, Not recovered	With spacer, Used before (Ventolin® and other unspecified generic brands)
U. 212588 F, 2 - 4 years year, Consumer	Salbutamol aerosol 100ug/do Sandoz	Fluticasone for inhalation	Therapeutic response decreased	2 Hours, Drug withdrawn, Recovered	With spacer, Used before (old Sandoz)
V. 212589 M, 61 - 70 years Consumer	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone/ formoterol for inhalation	Therapeutic response decreased	Unknown, Dose increased, Not recovered	Unknown, Used before (brand unknown)
W. 212590 F, 31 - 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz	Salmeterol/flutic asone for inhalation	Therapeutic response decreased	2 Hours, Drug withdrawn, Recovered	Unknown, Unknown
X. 212636 F, 21 – 30 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone/ formoterol for inhalation, Ipratropium for inhalation	Therapeutic response decreased, Asthma exacerbated	Unknown minute, Drug withdrawn, Recovering	With spacer, Used before (Ventolin®, PCH)
Y. 212644 F, 2 - 4 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Fluticasone for inhalation	Therapeutic response decreased	0 days, Dose increased, Recovered	With spacer, Used before (CF)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
Z. 212706 F, 31 - 40 years Consumer, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone/ formoterol for inhalation, Ipratropium for inhalation, Tiotropium for inhalation	Therapeutic response decreased Asthma exacerbated	30 Minutes, Dose not changed, Recovered with sequel	Unknown, Unknown
AA. 212717 F, 11 - 20 years Pharmacist	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased	0 days, Drug withdrawn, Recovering	With spacer, Used before (Mylan, RP)
AB. 212863 M, 51 - 60 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone/ formoterol for inhalation	Therapeutic response decreased, Dyspnoea, Dizziness, Nausea	10 Minutes, Drug withdrawn, Not recovered	With spacer, Used before (PCH)
AC. 212931 F, 41 - 50 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Formoterol for inhalation, Ciclesonide for inhalation	Therapeutic response decreased	Unknown Minute, Drug withdrawn, Not recovered/	With spacer, Used before (Actavis)
AD. 213192 F, 41 - 50 years General Practitioner	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone/ formoterol for inhalation	Therapeutic response decreased, Dyspnoea	1 Minute, Dose not changed, Recovered	With spacer, Used before (Actavis)
AE. 213678 F, 51 - 60 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased	Unknown minute, Dose increased, Not recovered	With Spacer, Used before (old Sandoz)
AF. 213720 M, 0 - 1 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased, Dyspnoea	Unknown Hour, Drug withdrawn, Recovered	With spacer, Used before (Ventolin®, CF)
AG. 213789 Unknown sex and age, Other health professional (Received through MAH), Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Drug ineffective	Unknown, Unknown, Unknown	Unknown, Used before (Ventolin®)
AH. 214460 F, 31 - 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz	Salmeterol/ fluticasone for inhalation	Therapeutic response decreased, Dyspnoea	Unknown, Dose increased, Unknown	Unknown, Used before (Ventolin®)
AI. 214468 F, 31 - 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased	1 Minute, Dose increased, Unknown	With spacer, Used before (old Sandoz)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
AJ. 214542 F, 11 - 20 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone for inhalation	Dyspnoea, Cough	Unknown Minute, Dose reduced, Recovered	With spacer, Used before (old Sandoz)
AK. 215021 M, 31 - 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Carbamazepine	Therapeutic response decreased, Dyspnoea	1 Minute, Unknown, Recovered	With spacer, Unknown
AL. 215331 F, 5 - 7 years Other health professional	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Fluticasone for inhalation	Drug ineffective	Unknown Day, Drug withdrawn, Unknown	With spacer, Used before (brand unknown)
AM. 215718 M, 0 – 1 years Consumer	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased	Unknown Minute, Drug withdrawn, Recovered	Unknown, Used before (brand unknown)
AN. 216043 M, 5 - 7 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Drug ineffective	Unknown Hour, Drug withdrawn, Recovered	With spacer, Used before (PCH)
AO. 216493 F, 31 – 40 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone for inhalation	Therapeutic response decreased, Dyspnoea, Fatigue, Listless	20 Minute, Drug withdrawn, Not recovered	With spacer, Used before (PCH)
AP. 216589 F, Age unknown, Other health professional (Received through MAH), Other	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424) (prednisolone suspect as well)		Drug ineffective, Maternal exposure during pregnancy	Unknown, Unknown, Unknown	Unknown, Unknown
AQ. 216732 M, 5 – 7 years Physician NOS	Salbutamol aerosol 100ug/do Sandoz	Budesonide	Drug ineffective	6 Month, Unknown, Recovering	Unknown, Unknown
AR. 217765 F, 2 - 4 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz	Fluticasone for inhalation	Asthma exacerbated	Unknown, Unknown, Recovering	With spacer, Used before (old Sandoz)
AS. 218220 M, 0 – 1 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Beclomethasone for inhalation	Asthma exacerbated, Dyspnoea	Unknown Month, Drug withdrawn, Recovered	With spacer, Used before (brand unknown)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
AT. 218283 M, 2 – 4 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Prednisolone	Dyspnoea	1 Day, Drug withdrawn, Recovering	With spacer, Used before (Ventolin®)
AU. 219019 U, 8 – 10 years Other health professional (received through MAH), Hospitalisation	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Drug ineffective	Unknown, Unknown, Recovered	Unknown, Unknown
AV. 219491 F, 41 - 50 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34432)		Drug effect decreased	5 Minute, Drug withdrawn, Recovered	With spacer, Used before (Mylan)
AW. 220305 (duplicates: 219971) F, 2 - 4 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Drug ineffective, Asthma exacerbated	Unknown hours, Drug withdrawn, Recovered	Unknown, Used before (brand unknown)
AX. 220365 M, 5 – 7 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone for inhalation	Drug ineffective	4 Week, Drug withdrawn, Recovered with sequel	With spacer, Used before
AY. 221153 F, 51 – 60 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased	Unknown, Unknown, Unknown	Unknown, Used before (brand unknown)
AZ. 221202 M, 0 -1 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased	Unknown hour, Drug withdrawn, Recovering	With spacer, Unknown
BA. 221347 F, 11 – 20 years Consumer	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone for inhalation	Asthma exacerbated	10 Minute, Drug withdrawn, Not recovered	Unknown, Used before (Airomir®)
BB. 221464 F, 5 – 7 years Pharmacist	Salbutamol aerosol 100ug/do Sandoz		Dyspnoea	1 Hour, Drug withdrawn, Recovered	Unknown, Unknown
BC. 221542 M, 2 – 4 years year, Other health professional, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased, Dyspnoea	8 Hour, Drug withdrawn, Recovered	Unknown, Unknown
BD. 221846 M, 5 – 7 years Consumer	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)	Fluticasone for inhalation Levocetirizine	therapeutic response decreased	30 Minute, Drug withdrawn, Recovering	With spacer, Used before (Ventolin®)

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome	Combined with spacer, Used salbutamol before (brand)
BE. 221854 M, 5 – 7 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz	Fluticasone for inhalation	Therapeutic response decreased	1 Day, Drug withdrawn, Not recovered	With spacer, Used before (Ventolin®)
BF. 221970 M, 2 – 4 years Specialist doctor, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz		Asthma exacerbated	Unknown Month, Drug withdrawn, Recovering	Unknown, Unknown
BG. 222123 M, 2 – 4 years Specialist doctor, Hospitalisation, Lifethreatening	Salbutamol aerosol 100ug/do Sandoz		Asthma exacerbated, Therapeutic response decreased	2 Month, Drug withdrawn, Recovering	Unknown, Used before (Ventolin®)
BH. 222243 F, 0 – 1 years General Practitioner	Salbutamol aerosol 100ug/do Sandoz (RVG: 34424)		Therapeutic response decreased	1 Day, Drug withdrawn, Recovered	Unknown, Not used before
BI. 222494 F, 5 – 7 years Other health professional	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone for inhalation	Therapeutic response decreased, Dyspnoea	Unknown, Drug withdrawn, Recovering	Unknown, Unknown
BJ. 222495 F, 2 – 4 years Specialist doctor	Salbutamol aerosol 100ug/do Sandoz		Therapeutic response decreased	10 days, Drug withdrawn, Recovered	Unknown, Unknown
BK. 222596, F, 2 – 4 years Other health professional, Hospitalisation	Salbutamol aerosol 100ug/do Sandoz	Beclomethasone for inhalation	Asthma exacerbated	Unknown days, Drug withdrawn, Recovered	Unknown, Unknown