



## An analysis of potential costs of adverse events based on Drug Programs in Poland. Pulmonology focus

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### ABSTRACT

The project was performed within the Polish Society for Pharmacoeconomics (PTFE). The objective was to estimate the potential costs of treatment of side effects, which theoretically may occur as a result of treatment of selected diseases. We analyzed the Drug Programs financed by National Health Fund in Poland in 2012 and for the first analysis we selected those Programs where the same medicinal products were used. We based the adverse events selection on the Summary of Product Characteristics of the chosen products. We extracted all the potential adverse events defined as frequent and very frequent, grouping them according to therapeutic areas. This paper is related to the results in the pulmonology area. The events described as very common had an incidence of  $\geq 1/10$ , and the common ones  $\geq 1/100$ ,  $<1/10$ . In order to identify the resources used, we performed a survey with the engagement of clinical experts. On the basis of the collected data we allocated direct costs incurred by the public payer. We used the costs valid in December 2013. The paper presents the estimated costs of treatment of side effects related to the pulmonology disease area. Taking into account the costs incurred by the NHF and the patient separately we calculated the total spending and the percentage of each component cost in detail. The treatment of adverse drug reactions generates a significant cost incurred by both the public payer and the patient.

### INTRODUCTION

The project was performed within the Polish Society for Pharmacoeconomics (PTFE) Task Force group interested especially in the Drug Programs. Currently in Poland in order to ensure access to medicines, it is mandatory to perform an HTA analysis for each reimbursement dossier submission [6,8]. Part of the HTA is related to cost-effectiveness or cost-utility analysis. Such pharmacoeconomic analysis should be done from the public payer perspective and take into account all potential direct costs [1]. The objective of the project performed by the PTFE task

force group was to estimate the potential costs of treatment of side effects, which theoretically may occur as a result of selected diseases treatment. The Drug Programs selected for the first part of the project were related to immune diseases, like rheumatoid arthritis, psoriasis and juvenile idiopathic arthritis. This paper aims to present the potential costs incurred by the public payer and the patients in relation to pulmonology related events.

### MATERIAL AND METHODS

We analyzed the Drug Programs financed by National Health Fund in Poland in 2012 and for the first analysis we selected those Programs where the same medicinal products were used. The first phase of the analysis was focused on immunology and the Programs concerning rheumatoid

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arthritis, psoriasis and juvenile idiopathic arthritis. In the analysis, it is not important which specific medicinal product was the cause of adverse event. The important issue we focused our efforts on was the treatment patterns to cure patient from the experienced adverse event. We based the adverse events selection on the Summary of Product Characteristics of the chosen products. We extracted all the potential adverse events defined as frequent and very frequent, grouping them according to therapeutic areas. Due to a large number of affected therapeutic areas in this paper we decided to present the results related to the pulmonology area. The events described as very common had an incidence of  $\geq 1/10$ , and the common ones  $\geq 1/100$ ,  $<1/10$  [7].

Initially, the Internet was searched in attempt to identify published treatment standards in Poland. Unfortunately, we were not able to identify such specific Polish standards.

In the next step in order to identify the resources used, a survey was performed with the engagement of clinical experts. The survey was based on an excel questionnaire sent to the clinical experts. The questions were related to the standard treatment patterns in their experts practice in case of a patient suffering from the analyzed adverse event. It included medicinal products and all other resources used, like diagnostic procedures, specialist ambulatory visits, hospitalization. With regard to the products, questions on the doses, formulation used, and time of treatment were asked. With regard to other resources used like diagnostic test, ambulatory visits, we collected information about the frequency and for hospitalization about the time of hospitalization.

The provided information was discussed with the experts and all the questions were clarified at the data collection phase. We compared all 4 pulmonology experts' opinions in order to ensure proper understanding and alignment between experts. As the next step, on the basis of the collected data, we allocated direct costs incurred by the public payer. We used the data about costs incurred by the public payer valid in December 2013.

The costs of the resources identified in the questionnaires were allocated taking into account the public payer perspective and the payer perspective including public payer and patient's spending on the adverse event treatment.

The hospitalization costs, diagnostic tests and ambulatory visits were based on the NHF costs published in 2013. For the medicinal products listed in the reimbursement list and acquired by the patient in open pharmacies, the cost incurred by public payer was also included in the analysis. When the experts indicated ambulatory treatment or an additional treatment was required after hospitalization for the broader perspective analysis, the costs incurred by the patient were calculated.

## RESULTS

The aim of the project was to investigate what is the standard practice of clinicians when treating different adverse events, which were identified as hypothetical based on the Product SPCs. It was not our intention to assess safety or efficacy of treatments and we did not focus the analysis on relationship between the adverse event and the product used

within the Drug Program. Our objective was to allocate costs to the resources we identified when performing the research with the use of a special questionnaire addressed to physicians. In our analysis we used the NHF costs published in December 2013 and the drug reimbursement costs incurred by public payer based on the data published by Minister of Health on 25<sup>th</sup> October 2013. The same source was used to calculate patients' co-payment [5].

If the doctor prescribed a medicinal product that was not reimbursed, we used for the analysis the cost of the pharmaceuticals wholesalers' price lists specified for December 2013.

The clinical experts provided names of the products used, the brand and international name.

If the most frequently used brand name was not indicated, then we included into calculations the less and the most expensive products available on the Polish market at the time of the analysis. Due to that reason, we presented the results as range of values, with a maximum and minimum value. The analysis is based on direct medical costs calculation, including the usage of resources like pharmacotherapy, diagnostics, nursing care, ambulatory visits to doctors and hospitalizations. In the case in which the experts indicated that the same adverse event could be treated in both ambulatory and hospital setting, we presented the results for both scenarios, with and without hospitalization and the hospitalization cost was calculated based on the scoring system used by NHF in the last quarter of 2013 [10].

All the results are presented in tables and the Table 1 shows all the costs components included in the analysis. We present the direct costs incurred by public payer and by patients and the minimum and maximum values for the treatment costs as well. The presentation of costs as a percentage of the total cost of the adverse event treatment is shown in the Table 2.

Table 3 presents the detailed costs of pharmacotherapy incurred by public payer and by the patient in the ambulatory setting.

Based on the analysis results it can be observed that the highest cost for the public payer was related to the hospital treatment of the adverse events (Table 1). Those events related to pulmonary infections, as interstitial pneumonia, interstitial alveolitis or typical mycobacterial infections generated the highest cost for the payer, as maximum the calculated value was 4184.69 PLN, 3931.30 PLN and 3415.56 PLN respectively. Asthma exacerbation treatment within the hospital ward could lead to a cost of even 2059.54 PLN from the public payer perspective. A remarkable observation concerns the patients who incurred significant costs due to the pulmonary adverse events treatment. The highest cost calculated was in case of mycotic infections (70922.13 PLN) and atypical mycobacterial infections, including tuberculosis (maximum cost 1581.60 PLN in case of hospitalization need).

The lowest cost from the public payer perspective was incurred due to runny nose and cough (29.75 PLN per episode of treatment). For the patient the minimum cost was related to those cases where the prescribed medicines were acquired in open pharmacy and reimbursed with a patient co-payment of 3.20 PLN as a lump sum, like for sinusitis treatment, bronchitis or other respiratory tract infections without hospitalization need.

**Table 1.** Total direct costs of pulmonology related adverse events treatment – public payer and patient perspective

Adverse event			Public payer		Patient	
			Cost min (PLN)	Cost max (PLN)	Cost min (PLN)	Cost max (PLN)
(Allergic) Pneumonia with symptoms: dry cough without sputum, shortness of breath and fever	Acute		81.11	130.34	23.66	56.16
	Chronic		139.79	215.95	113.08	218.36
	Additional bronchial obturation or paroxysmal dry cough		59.31	69.75	4.39	92.36
Asthma exacerbation	Without hospitalization		43.56	83.54	29.63	198.98
	Observation in the rescue unit		459.56	499.54		
	3 days hospitalization		2019.56	2059.54		
Chronic asthma – 30 days therapy			44.62	177.22	10.44	12.80
Dyspnea			32.47	87.71	5.71	3.21
Upper respiratory tract infections	Runny nose, cough, fever – symptoms longer than 3 days		36.54	44.78	25.48	48.73
	Pharyngitis		44.78	48.11	12.36	34.08
	Nasopharynx inflammation		44.78		3.20	
	Sinusitis		44.78	50.79	3.20	23.72
	Mycotic infections		89.25	1167.12	2244.99	70922.13
	Atypical mycobacterial infections, including tuberculosis	Without hospitalization	540.83	1699.56	0.00	1564.60
		With hospitalization	2256.83	3415.56	0.00	1581.60
	Protozoal infections		205.87		176.29	
	Legionella infection		150.50	305.05	110.08	882.20
	Listeriosis		52.40	52.72	10.82	74.30
Cough			29.75		12.65	60.45
Runny nose			29.75		13.19	45.44
Symptoms indicating possible serious injury of the lungs (interstitial pneumonia): dry cough without sputum, shortness of breath and fever	Without hospitalization		110.25	440.69	17.10	477.20
	With hospitalization up to 32 days		3854.25	4184.69	21.35	477.20
Interstitial alveolitis / pneumonia often combined with eosinophils increase	Without hospitalization		88.00	187.30	21.35	36.73
	With hospitalization up to 32 days		3832.00	3931.30	25.60	40.98
Lower respiratory tract infections (e.g. bronchitis, pneumonia)	Without hospitalization		50.36	64.61	16.17	66.62
	With hospitalization up to 16 days		1350.36	1364.61	20.42	70.87
Bronchitis			44.78	61.85	3.20	32.11
Pneumonia	Without hospitalization		57.39	105.08	30.50	5.44
	With hospitalization		1357.39	1405.08	34.75	9.69
Herpes Pneumonia			54.66		24.92	
Respiratory tract infections (including upper and lower respiratory tract)	Without hospitalization		44.78	64.61	3.20	66.62
	With hospitalization up to 16 days		1350.36	1364.61	20.42	70.87

**Table 2.** Single cost components contribution from public payer's perspective

Adverse event		Pharmacotherapy (%)	Diagnostics (%)	Hospitalization (%)	Ambulatory visits (%)	Nursing procedures (%)
(Allergic) Pneumonia with symptoms: dry cough without sputum, shortness of breath and fever	Acute	71.6-84.1	-	-	15.9-28.8	-
	Chronic	88.2-93.2	-	-	6.8-11.8	-
	Additional bronchial obturation or paroxysmal dry cough		21.9-57.0	30.1-62.8	-	-
Asthma exacerbation		8.8-75.3	-	59.2-96.2	1.5-40.6	1.1-14.2
Chronic asthma – 30 days therapy		46.0-84.3	-	-	15.7-54.0	-
Dyspnea		22.1-67.3	-	-	32.7-77.9	-
Upper respiratory tract infections	Runny nose, cough, fever – symptoms longer than 3 days		52.0-68.2	-	31.8-48.0	-
	Pharyngitis		47.9-63.8	-	36.2-52.1	-
	Nasopharynx inflammation		38.0	-	62.0	-
	Sinusitis		38.0-60.1	-	39.9-62.0	-
	Mycotic infections		96.2-99.9	-	0.1-3.8	-
	Atypical mycobacterial infections, including tuberculosis		22.5-99.1	-	34.3-76.0	0.9-6.3
	Protozoal infections		92.2	-	7.8	-
	Legionella infection		88.6-97.5	-	2.5-11.4	-
Listeriosis		52.9-76.6	-	-	23.4-47.1	-
Cough			-	-	56.2-80.2	-
Runny nose			-	-	65.5-69.3	-
Symptoms indicating possible serious injury of the lungs (interstitial pneumonia): dry cough without sputum, shortness of breath and fever			0.4-0.5	80.3-96.6	0.7-23.4	-
Interstitial alveolitis / pneumonia often combined with eosinophils increase			-	94.3-97.1	0.9-27.2	-
Lower respiratory tract infections (e.g. bronchitis, pneumonia)			-	90.6-94.8	2.2-44.7	-
Bronchitis			-	-	30.3-60.5	-
Pneumonia			-	91.9-93.4	2.4-33.8	-
Herpes Pneumonia			-	-	37.4	-
Infections of the respiratory tract (including the lower and upper respiratory tract)			-	90.6-94.8	2.4-62.0	-

The percentage of different cost components is presented in the Table 2 and in most of the cases only pharmacotherapy and ambulatory visits or hospitalization were the components included in the analysis as those provided by the experts.

Diagnostic costs were only included in case of allergic pneumonia with additional bronchial obturation or paroxysmal dry cough (30.1-62.8% of total cost was allocated to diagnostic procedures) and diagnosis of symptoms possibly related to interstitial pneumonia (0.4-0.5% of total treatment cost of this adverse event).

Pharmacotherapy was the most important cost component from the public payer perspective, from minimum contribution of 8.8% in case of asthma exacerbation episode, in some cases a maximum of 75.3%, to even the maximum contribution of 96.2-99.9% in case of the mycotic infections.

However in case of hospitalization, the pharmacotherapy costs contribution to total treatment cost was much lower in comparison to the cost generated by the hospitalization episode. The hospitalization cost was related to the length of hospitalization and can reach 94.3-97.1% of the total costs in case of interstitial alveolitis or pneumonia.

According to the experts, nursing procedures were required only in case of asthma exacerbation and equaled to 1.1-14.2% of total costs of the mentioned adverse event.

**Table 3.** Pulmonology related adverse events pharmacotherapy cost in ambulatory setting – by payer perspective (public, patient)

Adverse event		NHF cost (PLN)	Patient cost (PLN)
(Allergic) Pneumonia with symptoms: dry cough without sputum, shortness of breath and fever	Acute	51.36-100.59	23.66-56.21
	Chronic	110.04-190.96	113.08-224.94
	Additional bronchial obturation or paroxysmal dry cough	0.00-9.56	4.39-92.36
Asthma exacerbation		8.56-9.56	33.88-203.23
Chronic asthma – 30 days therapy		14.87-147.47	10.44-12.80
Dyspnea		2.72-57.96	3.21-5.71
Upper respiratory tract infections	Runny nose, cough, fever – symptoms longer than 3 days	6.79-15.03	25.48-48.73
	Pharyngitis	15.03-33.39	12.36-37.28
	Nasopharynx inflammation	15.03	3.20
	Sinusitis	15.03-36.07	3.20-26.92
	Mycotic infections	0.00-1167.12	1167.12-72000.00
	Atypical mycobacterial infections, including tuberculosis	506.83-1563.56	0.00-1581.60
	Protozoal infections	176.12	176.29
	Legionella infection	18.30-20.00	110.08-882.20
Cough		0.00	12.65-30.70
Runny nose		0.00	13.19-15.69
Symptoms indicating possible serious injury of the lungs (interstitial pneumonia): dry cough without sputum, shortness of breath and fever		58.25-392.94	21.35-477.20
Interstitial alveolitis / pneumonia often combined with eosinophils increase		58.25-153.30	21.35-40.98
Lower respiratory tract infections (e.g. bronchitis, pneumonia)		16.36-28.97	20.42-91.29
Bronchitis		15.03-47.13	3.20-35.31
Pneumonia		27.64-75.33	5.44-30.50
Herpes Pneumonia		24.91	24.92
Infections of the respiratory tract (including the lower and upper respiratory tract)		15.03-28.97	3.20-91.29

When analyzing the costs incurred during treatment in the ambulatory setting from public payer perspective and patient perspective separately significant cost in both cases were generated by chronic (allergic) pneumonia treatment, 110.04-190.96 PLN, 113.08-224.94 PLN respectively.

Another costly treatment for both the public payer and the patient was protozoal infections therapy, equal to 176.12 PLN and 176.29 PLN respectively.

The highest cost for the patient was due to mycotic infections treatment, with a cost range between 1167.12 PLN-72000 PLN. This high cost for the patient is due to potential need to use not reimbursed medicinal products. Atypical mycobacterial infections, including tuberculosis could generate a maximum cost of 1581.60 PLN for the patient.

Analyzing only the pharmacotherapy costs (Table 3) we can observe that NHF had no costs in relation to runny nose and cough. The most expensive adverse events treatment for the NHF were atypical mycobacterial infections, including tuberculosis – 506.83-1563.56 PLN and mycotic infections treatment – up to 1167.12 PLN.

## DISCUSSION

Our analysis presents the level of the adverse drug reactions treatment cost in the light of the experts' opinion in respiratory diseases area. In the available literature, there are no Polish publications on the cost of adverse drug reactions. In the databases we analyzed we could find some publications from other countries. Those analyses are based on retrospective data, and performed following a different methodology. The only Polish work on the cost of side effects is the work of N. Wiśniewska. N. Wiśniewska calculates the costs of adverse reactions treatment in a sample size of patients hospitalized in the Clinic of Dermatology at the Military Medical Institute in Warsaw in the years 2002-2012 [9]. Using a different methodology N. Wiśniewska presented the average cost of hospitalization of patients with drug induced skin reactions in the dermatology clinic as amounted to 2834.95 PLN. It was a lower cost in comparison to the data available from other countries. The average cost of treating adverse events in Spain in 2013 on the basis of retrospective data in hospitals was estimated at the level of 5260 EUR [2], in France – at a range between 1300 EUR – 3244 EUR [3] and in India at 5556 EUR [4].

In this paper, we present the data related to pulmonology and we should pay particular attention to fungal infections of the upper respiratory tract, which generate very high cost for the patient. One of the interviewed experts mentioned that in opportunistic infections voriconazole is used in the treatment lasting from a few to several months. Currently available on the Polish pharmaceutical market preparations containing voriconazole are not reimbursed by the National Health Fund and therefore the cost to the patients is so high.

Referring to the available in the databases pharmaco-epidemiological research related to the adverse events of medicinal products and the amount of generated costs we should consider not only the safety aspect of therapy but also be conscious of the economic impact.



## CONCLUSIONS

Based on the analyzed data we can observe a significant patient contribution to the adverse events treatment cost in relation to pulmonologic diseases; often patients have to pay out of their pocket for the whole pharmacotherapy prescribed for the adverse events treatment.

The costs generated by the adverse events for the public payer are high, especially in the situation when hospitalization is required.

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