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Article type : Original Article-Asthma and Rhinitis

## Heterogeneity of the pharmacologic treatment of allergic rhinitis in Europe based on MIDAS and OTCims platforms

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/CEA.13884](https://doi.org/10.1111/CEA.13884)

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**Short title: Heterogeneity of medications for allergic rhinitis**

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**Word count:** 2813

**Data availability:** The data is the property of IQVIA

## Abstract

**Background:** The practice of allergology varies widely between countries, and the costs and sales for the treatment of rhinitis differ depending on practices and health systems. To understand these differences and their implications, the rhinitis market was studied in some of the EU countries.

**Methods:** We conducted a pharmaco-epidemiological database analysis to assess the medications that were prescribed for allergic rhinitis in the years 2016, 2017 and 2018. We used the IQVIA platforms for prescribed medicines (MIDAS® - Meaningful Integration of Data, Analytics and Services) and for OTC medicines (OTC International Market Tracking - OTCims). We selected the five most important markets in the EU (France, Germany, Italy, Poland and Spain).

**Results:** Intra-nasal decongestants were excluded from the analyses because they are not prescribed for allergic rhinitis. For both Standard Units (SU) and costs, France is leading the other countries. In terms of SU, the four other countries are similar. For costs, Poland is lower than the three others. However, medication use differs largely. For 2018, in SU, intra-nasal corticosteroid is the first treatment in Poland (70.0%), France (51.3%), Spain (51.1%) and Germany (50.3%) whereas the Italian market is dominated by systemic anti-histamines (41.4%) followed by intra-nasal corticosteroids (30.1%). Results of other years were similar.

**Discussion:** There are major differences between countries in terms of rhino-conjunctivitis medication usage.

**Key words:** allergic rhinitis, medications, MIDAS, costs, units

## Abbreviations

AR: Allergic rhinitis

ARIA: Allergic Rhinitis and its Impact on Asthma

ATC: Anatomical Therapeutic Chemical

DDD: Defined daily dose

EphMRA: European Pharmaceutical Market Research Association

EU: European Union

INCS: intranasal corticosteroids

LEU: Local Currency Euro

MASK: Mobile Airways Sentinel network

MIDAS: Meaningful Integration of Data, Analytics and Services

MNF: Manufacturer Price Level

OTC: Over-the-counter

OTCims: OTC International Market Tracking

SU: Standard Unit

## Introduction

Allergic rhinitis (AR) is one of the most common chronic conditions . Available treatments include allergen avoidance, pharmacotherapy with H<sub>1</sub>-antihistamines or intranasal corticosteroids (INCS), and allergen-specific immunotherapy (AIT) (1). Many patients are dissatisfied with their treatment for many reasons. Management does not consider the patient's needs, no cure is available, adherence to long-term therapy is poor and/or the patients do not fully understand their condition. Real-world data obtained via mobile technology have suggested that there are differences in medication use between countries (2, 3)

MASK-air (4-6) is a Good Practice of DG Santé concerning the digital transformation of health (7, 8). The practice of allergology varies widely between countries, and the costs and sales for the treatment of rhinitis differ depending on practices and health systems. To understand these differences and their implications, it is important to have an overall view of the rhinitis market in some of the EU countries.

The goal of the paper was to assess practices in different EU countries in order to better implement the Good Practice of DG Santé (MASK-air). The secondary goal was to understand some of the differences to propose mitigation strategies. This study will serve as a baseline status for possible future measures to be taken at the country level.

## Methods

### Study design

This ARIA study evaluated the market for allergic rhinitis (AR) treatment (prescribed and over-the-counter - OTC medications) in five EU countries in the years 2016-18. We conducted a pharmaco-epidemiological database analysis to assess the medications that were prescribed for allergic rhinitis during the years 2016, 2017 and 2018. We used the IQVIA (collaboration between Quintiles and IMS Health under the name "IQVIA") platforms for prescribed medicines (MIDAS<sup>®</sup> - Meaningful Integration of Data, Analytics and Services) (9-11) and for OTC medicines (OTC International Market Tracking - OTCims) (12). PharMetrics Plus database (IQVIA), a large health claims database captures demographics, physician visits, hospitalizations and prescription drugs. All medical diagnoses are captured through International Classification of Diseases, Ninth and Tenth Editions (ICD-9 and -10). This database also captures all outpatient prescription drugs. This includes drug identification, dose prescribed, and treatment duration. We used manufacturing costs and not the costs for the health care system as in some countries there are rebates that are not publicly available.

## Medications

### Definitions used

We used SU (Standard Units) and LEU/MNF (Local Currency Euro/ Manufacturer Price Level) to compare data between countries.

An SU is a unit defined by IQVIA to represent the smallest daily unit of consumption, e.g. one tablet, one vial/ampoule or 5 ml of liquid. As an example, a pack of 100 tablets with a dosage recommendation of 2 tablets a day will lead to: Unit = 1, Counting Units = 100 and SU = 50.

LEU/MNF per year represents the total sales in Local Currency Euro at Ex-Manufacturer Price Level per Calendar Year.

We chose Manufacturing Cost of the drugs and it was not possible to mention health care system costs because there are rebates that are not publicly available.

### Selection of medications

We selected medications registered for AR, as well as nasal or ocular decongestants since these medications may also be administered for AR.

The World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classifies drugs by their active ingredients (13) and their defined daily dose (DDD), a fixed attribute that allows the conduct of national or international drug use studies (14). This ATC system is based on the earlier Anatomical Classification System, which was intended as a tool for the pharmaceutical industry to classify pharmaceutical products (as opposed to their active ingredients) (15). This system was initiated in 1971 by the European Pharmaceutical Market Research Association (EphMRA) (16, 17). In the present study, we used the EphMRA system and we gave the ATC correspondence.

For prescribed medications, the study was performed by IQVIA Ltd., London, England using de-identified prescription data from MIDAS<sup>®</sup> for 2016, 2017 and 2018 (in € for sales as well as numbers of treatments). MIDAS<sup>®</sup> provides connectivity and international standardization of national-level pharmaceutical audits to allow cross-country analysis of company and product performance, as well as additional insights and attributes not available at a local level. MIDAS<sup>®</sup> captures and harmonizes the data from 92 countries worldwide mainly for registered medicines (prescription and non-prescription) in pharmacy and hospital channels. MIDAS<sup>®</sup> integrates and extends IMS National Audits that accurately detail estimated product

volumes, trends and market share by product and therapy class, through retail and non-retail channels. MIDAS<sup>®</sup> tracks the direct sales (i.e., sales invoices) of pharmaceuticals from the manufacturer to pharmacies or hospitals. MIDAS<sup>®</sup> also tracks indirect sales (sales going through a middleman i.e., the wholesaler) to pharmacies and hospitals. MIDAS<sup>®</sup> tracks inflow or what these different channels are purchasing (i.e., the sales made into those outlets). It represents the full European market through representative panel projections for both retail and hospital channels.

The following subgroups include symptomatic AR drugs and ophthalmic drugs (since rhinitis is often associated with conjunctivitis). Montelukast was not used as it is both an anti-asthma and rhinitis treatment and is only indicated in patients with both rhinitis and asthma. The following medications were considered (Table 1A).

For OTC medications, the QuintilesIMS OTCims (OTC International Market Tracking) database was used. OTCims is a Customised Global Information Offering providing granular data for the effective tracking of company and competitor performance in the Consumer Health marketplace. It uses IQVIA Consumer Health Classification based on Market Positioning. Data are available across four main market segments: OTC, Personal Care, Patient Care and Nutrition. Data are included for 36 countries from Europe, Asia Pacific, North and Latin America. Clients are supported in both own as well as competitor product/pack performance tracking against key performance indicators.

The MIDAS<sup>®</sup> database does not identify the disease for which the medication has been used. This is the case for systemic antihistamines (R06A0) which include treatments for the nose, skin and other organs. They cannot be distinguished. INCS (R01A1) can also be administered for AR, non-allergic rhinitis and rhinosinusitis.

The list of OTC medications is given in Table 1B. The four OTC therapy classes include “oral H1-antihistamines” and “INCS”. The list is too far from ATC to propose any correspondence.

### **Allergen specific immunotherapy**

The only country where AIT is mostly delivered in pharmacies is Germany. We only provided data for AIT in Germany

### **Selection of countries**

The market for prescribed medications (in costs for patients) for 2018 in all EU countries was ranked in order to choose the markets with the highest sales (Table 1 online). OTC medications were not considered

in the country selection because a single database cannot be used in all countries. AIT was not considered in the country selection since large variations exist between countries in terms of supply (pharmacies, hospitals, Named-Patient Products ...).

The first six countries with the highest sales for AR medications and nasal decongestants were France, Germany, Italy, Spain, Poland and the UK. There was a big gap between UK N°6 and Sweden N°7. Thus, we considered only the first six countries. In the UK, a significant proportion of sales took place in supermarkets and these were not considered by IQVIA. Thus, the country had to be excluded.

The “Sell-Out” (Medication dispensed in pharmacies) data and, if not available, the “Sell-In” (Medication delivered in pharmacies) data were obtained from IQVIA. For the countries selected, the databases were from different origins and the data type differed taking into account the country specificities on drug dispensing (Table 2).

### **Collection of information**

There are different methods of collecting the information and we needed to make assumptions.

It is possible to compare “Sell-in” (from wholesaler to retail pharmacy, effects like stocking are included) and “Sell-out” (from retail pharmacy to patient) data bearing in mind some biases. . Therefore, for one quarter, the “Sell-in” data might be higher when compared to “Sell-out” due to stock, but these effects are minimized for yearly data. In the countries tested, “hospital” means hospital consumption from hospital to patient.

For the OTCims Panel, all panels are “Sell-out”.

### **Analyses**

We conducted a descriptive analysis to evaluate the medications used in different countries. To derive figures for anti-rhinitis consumption per person over the three years, we linked consumption by SU to population estimates.

**Stratification:** The analyses were performed for prescription data and OTC data separately. In some countries, the same products could be prescribed and also available OTC. Thus, in order to prevent multiple counts, a complex merger process between prescriptions and OTC was necessary.

**Data periods:** The analyses covered the periods 2016, 2017 and 2018. Results were processed on a yearly basis.

**Analyses** were performed once at the same time.

**Projection:** The results were projected yearly per country.

## Results

### **Intra-nasal decongestants (R1A7 and 01B2)**

Intra-nasal decongestant sales (R1A7 and 01B2) are extremely variable, with low sales in France (from 612,073 to 751,739 kSU per year, 12.6% to 14.8% of total sales) and high sales in Germany (from 6,586,460 to 6,890,822 kSU per year, 71.6 to 79.6%) (Table 3). We checked the monthly variation of R1A7 in Germany in 2018 and found that they were purchased less often during the pollen season than outside (Figure 1 online). In Germany, although the majority of products were available in pharmacies, they were non-prescribed. We therefore excluded R1A7 and 01B2 from further analyses as they are unlikely to represent patients with allergic rhinitis.

### **Overall results without intranasal decongestants (R1A7 and 01B2)**

The results are presented in Tables 2 online and 4 and in Figure 1. For both SU and costs, France is leading the other countries. In terms of SU, the four other countries are similar. For costs, Poland is lower than the three others. However, medication use differs largely. For 2018, in SU, INCS is the first treatment in Poland (70.0%), France (51.3%), Spain (51.1%) and Germany (50.3%) whereas the Italian market is dominated by systemic anti-histamines (41.4%) followed by INCS (30.1%). Results of other years are similar. MPAze-Flu (DYMISTA) represented from less than 1% in Spain to 1.5% in Poland and Germany and around 2.6 % in France of SU in 2018.

In costs for 2018, INCS represent 20.7% of the market (Poland), around 26-28% (Germany, Italy, Spain) and up to 38.6% (France). Systemic antihistamines represent from 45.8% (Italy) to 49.3% (France), 57 to 59% (Germany, Spain) and 67% (Poland).

## Rhino-conjunctivitis medication consumption per person in Europe

There are very large differences in medication consumption (SU) per person in Europe depending on the country (Table 5). In France, there are 4.3 times more INCS sold per inhabitant than in Germany. On the other hand, in Germany, there are 9.25 times more nasal decongestants sold per inhabitant than in France.

Although the proportion of reimbursement/out of pocket differs between countries, and even, in the same country, for different classes of drugs, reimbursement and OTC availability of medications differ in EU countries (Table 3 online).

## Allergen immunotherapy

In Germany, AIT represents an between 33.2 to 37.3% of LEU/MNF (Table 3).

## Discussion

The present paper shows that there is a great heterogeneity in AR medications across Europe. Some explanations may be proposed including reimbursement strategies.

## Limitations

Although the IQVIA platform appears to be a good source of data for estimating drug consumption in different countries, there are several limitations.

First, we can only use the classification of medications proposed by IQVIA and some classes are assessing medications for multiple diseases such as “Systemic anti-histamines”. It is likely that their use differs between countries and that the results reported in this paper may not be totally comparable.

Second, In the IQVIA database, medications are not classified by disease and there are overlaps between skin and respiratory diseases as well as for respiratory diseases, there are different indications such as allergic and non-allergic rhinitis or rhinosinusitis.

Third, we had to make assumptions that were discussed in the methods. It does not seem that these estimations may have led to significant problems.

Third, another limitation is non-adherence to prescribed drugs in patients that cannot be estimated. Thus, the results of the study do not consider lack of adherence to medication that was reported to be quite high (18).

Fourth, exclusion of nasal decongestants was proposed because they are not indicated in AR and they are largely used for common cold and cough in some countries. The BSCAI guidelines (the only European guidelines) (19) and ARIA (global guidelines) (20) that are used in most European countries do not recommend the regular use of intra-nasal decongestants. In ARIA, the last recommendation was in 2010 since there has not been any other important paper on the subject since then. “In adults with AR and severe nasal obstruction, we suggest a very short course (not longer than 5 days and preferably shorter) of intranasal decongestant while co-administering other drugs (conditional recommendation, very low-quality evidence). We suggest that clinicians do not administer and parents do not use intranasal decongestants in preschool children (conditional recommendation j very low-quality evidence).” A report by Statista (<https://www.statista.com/statistics/417727/cough-and-cold-self-medication-market-sales-in-europe/>) showed the same ranking order for cold and cough drugs as the IQVIA data for nasal decongestants with Germany ranking first (1,557 million € for 2017), followed by Italy (718), Poland (609), Spain (552) and France (490). In Germany, in 2018, the months with the highest pollen counts were those with the lowest use of nasal decongestants.

## Interpretation

Although many papers dealt with AR costs, we were not able to find any that analyzed the units sold. Moreover, costs are difficult to compare between papers as OTC and prescribed drugs vary between countries and AR direct costs reduced considerably when medications became OTC. In the present paper, we found large differences between EU countries, and particularly between France (low nasal decongestants, high INCS consumption) and Germany (the opposite).

In a Swedish study, it was found that 71.6% of patients with AR were using OAH, 44% INCS and 41% nasal decongestants (21).

In France, most medications are reimbursed if prescribed. A long wait to consult French medical specialists encourages quick purchases of OTC drugs, during pollen seasons for example. French pharmacists are often well trained for offering OTC drugs: easy-to-use, inexpensive oral OAH, nasal sprays and eye drops. ENT physicians and allergists traditionally prescribe these molecules and train general practitioners to do so too. These molecules were prescribed very early by paediatricians, also in children of atopic families who present nasal signs. The children are used to these methods from the age of 3.

In Germany, the situation is more complex than in other countries. The general reimbursement strategy is outlined in Table 3. 8.7% of the population are privately insured, this is only possible for people who are self-employed or for employees who earn an above-average salary. For privately-insured patients, all allergic rhinitis medications are usually reimbursed but it depends very much on the individual contracts. Some privately-insured patients for instance have a contract where they are only reimbursed for medication and other healthcare costs above a chosen limit, e.g. 1,000€ per year. This is a contract which young people very often choose, the monthly costs being lower and with the speculation of not having to use this fixed rate in the year. These patients often tend not to buy medications recommended by the physician. The rest of the population is under the statutory health insurance (Gesetzliche Krankenversicherung) but can choose between different companies offering policies. Also, the official healthcare insurance companies have different reimbursement strategies and details vary. The general reimbursement strategy is outlined in Table 3 but another variable comes into play. Physicians treating patients under the statutory health insurance scheme in Germany have a fixed budget for medication costs and can be made liable if they do not adhere to the very strict economic prescription pathways. Although OAH can be reimbursed for severe allergic rhinitis, even if over-the-counter products are available, physicians often choose not to prescribe these medications on a panel prescription which allows reimbursement but to give a private prescription to the patient which means that he/she has to cover the full costs. Last but not least, another limiting factor in Germany is the fact that all patients above 12 years of age also have to pay a cost share fee for every drug at the pharmacy which is 10% of the price of the product, with a minimum of 5 € and maximum of 10 €.

In Italy, most medications for rhinoconjunctivitis are provided through medical prescription. OAH are reimbursed by the NHS - National Healthcare System, whereas INCS (including INCS+INAH ) are not, except in one region, Tuscany.

In Poland, the situation is similar to France. The medications for Allergic Rhinoconjunctivitis are reimbursed if prescribed by the physician. Everyone is covered by the National Health Fund (NHF), but the private sector is also very active. Patients can visit specialists working under (NHF) for free but must wait a few months to consult or can choose to visit a private doctor and pay out-of-pocket for the service without having to wait. Physicians in private and public sectors can prescribe reimbursed medications. Many medications which are reimbursed if prescribed also have an OTC version, including INCS and OAH. Similar to France, these molecules were prescribed very early by paediatricians, also in children of atopic families who present nasal symptoms. The children are used to these methods from the age of 2. In Poland, nasal washing with isotonic saline is also very common.

In Spain, most medications for rhinoconjunctivitis are provided through medical prescription. Nevertheless, there are a few formulations which may be acquired as OTC, including some OAH, such as cetirizine, and INCS, such as fluticasone propionate. A recent study has calculated the direct and indirect costs of AR in patients attending specialized clinics in Spain (22). Data showed that the mean drug treatment per year was significantly higher in persistent AR ( $77.88 \pm 134.22\text{€}$ ) compared to intermittent AR ( $45.62 \pm 78.93\text{€}$ ). On the other hand, no significant differences were found when comparing mild, moderate and severe AR ( $41.77 \pm 86.02\text{€}$ ,  $70.36 \pm 127.07\text{€}$  and  $72.16 \pm 114.60\text{€}$ , respectively). Direct costs accounted for 24% of total costs, and drug therapy was only 10-13% of the direct costs.

Cultural and reimbursement differences between countries may explain trends in treatment.

Many studies reported that OAH are more often used than INCS (23-25) and this accords with the results of the present study. However, this is the first multi-national study comparing medication delivery.

The large differences between countries in INCS use are surprising since the guidelines of ARIA (26), the British Society of Allergy and Clinical Immunology (19) or the US Practice parameters (27) recommend INCS as the first line treatment for moderate to severe AR and it is likely that AR severity is similar between countries. However, the reimbursement strategies of some countries may impair the implementation of guidelines. Moreover, although most AR patients consulting a physician have moderate to severe rhinitis, the low level of INCS prescribed is surprising. These data may, at least partly explain the poor satisfaction of AR patients.

There are also very large differences between countries in intra-nasal decongestants. Although the indications cannot be assessed using the IQVIA database, it is likely that many patients in Germany use intra-nasal decongestants for AR. This does not accord with guidelines. In ARIA, “In adults with AR and severe nasal obstruction, we suggest a very short course (not longer than 5 days and preferably shorter) of intranasal decongestant while co-administering other drugs (conditional recommendation, very low-quality evidence)” (20). In the BSCAI.....

## **Conclusions**

With the limitations discussed, this study is of great interest for assessing the heterogeneity of pharmacotherapy in some European countries and can be used as a baseline for future studies to show treatment trends.

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**Table 1A: Codes of prescribed medications**

Description	EphMRA code	ATC code	Application form
Nasal corticosteroids without anti-infectives	R01A1	R01AD	Nasal spray, drops, ointment
Nasal anti-allergic agent	R01A6	R01AC	Nasal spray, drops, ointment
Nasal decongestant*	R01A7	R01AA + R01AB	Nasal spray, drops, ointment
Other topical nasal preparation	R01A9	R01AX	Nasal spray, drops, ointment
Systemic rhinologic preparations (including oral decongestants)	R01B0	R01BA	Systemic
Systemic anti-histamines	R06A0	R06AA + R06AB + R06AD + R06AE + R06AX	Systemic
Ophthalmologic anti-allergic anti-histamines	S01G1	S01GX	Eye drop
Ophthalmologic anti-allergic mast cell stabilizers	S01G2		Eye drop
Other ophthalmologic anti-allergic agents	S01G3		Eye drop
Ophthalmologic decongestants with sympathomimetics*	S01G5	S01GA	Eye drop

\*: included although not indicated in allergic rhinitis but may be used

**Table 1B: Codes of OTC medications**

Description	OTC class
Nasal Decongestants	.01B2
Respiratory & General Antiallergics	01E1
Eye Antiallergics	.07A2
Eye Decongestants & Anti-Inflammatories	.07A5

**Table 2: Origin of the databases**

Countries/Panels:	Country	Channel	Data Type
OTCIMS	France	Pharmacy	Sell-out
		Para-pharmacy	Sell-out
	Germany	Pharmacy	Sell-out
		Pharmacy Mail Order	Sell-out
		Discounter	Sell-out
		Drugstores	Sell-out
		Supermarkets	Sell-out
	Italy	Pharmacy	Sell-out
		Para-pharmacy	Sell-out
		Supermarkets & Hypermarkets-Corner	Sell-out
		Supermarkets & Hypermarkets-Non Corner	Sell-out
	Poland	Pharmacy	Sell-out
	Spain	Pharmacy	Sell-out
		Para-pharmacy	Sell-out
MIDAS	France	Hospital	Sell-in
		Retail	Sell-in
	Germany	Retail/Mail Order	Sell-out
		Hospital	Sell-in
	Italy	Hospital	Sell-in
		Retail	Sell-in
	Poland	Hospital	Sell-in
		Retail	Sell-in
	Spain	Hospital	Sell-in
		Retail	Sell-out
Retail		Sell-in	

**Table 3: Overall units and costs obtained by MIDAS and OTCims**

	Annual SU (thousands)			Annual LEU/MNF (million €)		
	2016	2017	2018	2016	2017	2018
<b>France</b>						
All without R1A7+01B2	4,345,542 (85.2%)	4,232,505 (85.8%)	4,262,629 (87.4%)	297,502 (91.1%)	289,445 (91.7%)	290,265 (92.6%)
R1A7+01B2	751,739	697,063	612,073	29,107	25,742	23,134
Total	5,097,281	4,929,568	4,874,702	326,609	315,187	313,399
<b>Germany</b>						
All without R1A7+01B2	1,873,427 (28.4%)	1,813,819 (20.4%)	1,988,758 (22.4%)	148,607 (50.2%)	136,762 (46.9%)	154,858 (48.8%)
R1A7+01B2	6,586,460	6,763,831	6,964,445	147,137	155,700	162,511
R1A7 prescribed	4	2	0	14	6	0
Total	8,459,887	8,577,650	8,879,580	295,744	292,462	317,369
Allergens (V1A0)	896,439	841,312	1,796,473	107,746	18,953	107,138
<b>Italy</b>						
All without R1A7+01B2	1,584,524 (63.5%)	1,560,315 (63.5%)	1,560,179 (62.3%)	163,988 (75.6%)	163,317 (74.8%)	167,595 (74.5%)
R1A7+01B2	908,777	897,072	945,276	52,739	55,042	57,843
Total	2,493,301	2,457,387	2,505,455	216,727	218,359	225,438
<b>Poland</b>						
All without R1A7+01B2	1,725,720 (62.4%)	1,804,554 (63.5%)	1,806,021 (63.7%)	98,413 (69.1%)	98,622 (67.5%)	101,771 (67.8%)
R1A7+01B2	1,039,763	1,037,053	1,029,205	44,063	47,571	47,989
Total	2,765,483	2,841,607	2,835,226	142,476	146,193	149,960
<b>Spain</b>						
All without R1A7+01B2	1,659,893 (71.1%)	1,696,172 (72.4%)	1,746,283 (73.4%)	158,275 (83.5%)	160,797 (83.5%)	168,842 (72.8%)
R1A7+01B2	675,098	645,544	631,286	31,317	31,703	32,392
Total	2,334,991	2,341,716	2,377,569	189,592	192,500	232,852

**Table 4: Standard units (SU) and costs of medications (LEU/MNF, absolute for fiscal year) in five European countries based on MIDAS and OTCims**

Accepted Article

	Standard Units 2016 (Absolute)	Standard Units 2017 (Absolute)	Standard Units 2018 (Absolute)	LEU/MNF 2016 (Absolute)	LEU/MNF 2017 (Absolute)	LEU/MNF 2018 (Absolute)
<b>France</b>	<b>5 097 280 885</b>	<b>4 929 568 274</b>	<b>4 874 702 206</b>	<b>326 609 288</b>	<b>315 187 283</b>	<b>313 398 985</b>
<b>HOSPITAL</b>	<b>24 443 211</b>	<b>22 347 969</b>	<b>24 131 960</b>	<b>3 994 101</b>	<b>3 930 879</b>	<b>4 164 317</b>
R1A1	4 430 987	3 142 635	3 408 948	323 730	307 361	336 467
R1A7	4 165 245	3 735 215	3 600 270	61 833	52 174	48 840
R6A0	12 383 393	12 163 848	12 668 770	3 124 229	3 209 892	3 284 036
* <b>DYMISTA</b>	<b>0</b>	<b>720</b>	<b>144 840</b>	<b>0</b>	<b>74</b>	<b>13 948</b>
S1G1	14 980	13 119	20 349	1 198	1 095	1 636
S1G2	3 376 938	3 251 404	4 251 647	126 016	124 745	153 377
S1G3	63 456	35 431	170 362	2 455	1 587	7 990
<b>RETAIL</b>	<b>4 690 535 231</b>	<b>4 530 115 204</b>	<b>4 493 777 976</b>	<b>303 069 376</b>	<b>292 933 322</b>	<b>290 997 700</b>
R1A1	2 281 980 628	2 205 997 152	2 182 679 986	119 602 835	114 537 298	111 803 786
R1A7	382 849 348	334 644 594	289 028 123	12 324 480	10 578 877	9 086 817
R6A0	1 259 075 253	1 250 282 248	1 284 035 579	140 023 134	137 490 816	139 313 337
* <b>DYMISTA</b>	<b>796 680</b>	<b>34 165 320</b>	<b>114 622 080</b>	<b>113 530</b>	<b>3 444 710</b>	<b>11 462 208</b>
S1G1	50 009 780	47 470 270	48 741 660	4 633 682	4 569 464	4 788 785
S1G2	592 278 142	570 187 400	570 438 348	20 262 676	19 507 566	19 794 182
S1G3	124 342 080	121 533 540	118 854 280	6 222 569	6 249 301	6 210 793
<b>OFF-TAKE</b>	<b>360 521 721</b>	<b>352 837 569</b>	<b>333 455 785</b>	<b>19 074 984</b>	<b>17 810 498</b>	<b>17 700 707</b>
O1B2	343 489 664	332 041 918	297 306 639	16 300 087	14 656 459	13 563 859
O1E1	5 346 125	7 039 683	23 249 372	821 915	938 080	1 998 837
07A2	400	0	0	13	0	0
07A5	11 685 532	13 755 968	12 899 774	1 952 969	2 215 959	2 138 011
<b>PARA PHARM</b>	<b>21 780 722</b>	<b>24 267 532</b>	<b>23 336 485</b>	<b>470 827</b>	<b>512 584</b>	<b>536 261</b>
O1B2	21 236 429	23 640 960	22 138 035	421 973	454 114	434 148
O1E1	341 703	422 512	978 770	44 419	52 036	96 827
07A2	400	0	200	8	0	4
07A5	202 190	204 060	219 480	4 427	6 434	5 282
<b>GERMANY</b>	<b>8 474 999 252</b>	<b>8 595 106 633</b>	<b>8 898 547 120</b>	<b>691 220 202</b>	<b>686 781 024</b>	<b>707 408 598</b>
<b>HOSPITAL</b>	<b>249 496 527</b>	<b>255 184 305</b>	<b>250 282 157</b>	<b>8 711 628</b>	<b>7 863 795</b>	<b>8 272 906</b>
R1A1	5 474 147	5 439 325	5 575 688	324 277	282 455	299 298
R1A7	228 397 070	234 976 448	229 199 632	2 923 767	2 942 361	2 909 478
R6A0	13 346 015	12 761 105	13 384 968	2 066 290	1 923 863	2 484 365
V1A0	17 442	12 954	13 269	3 335 043	2 668 134	2 524 879
* <b>DYMISTA</b>	<b>64 240</b>	<b>44 400</b>	<b>72 120</b>	<b>10 675</b>	<b>7 400</b>	<b>12 154</b>
S1G1	291 274	303 232	410 628	10 349	11 407	11 025
S1G2	1 387 085	1 278 129	1 156 591	16 949	13 627	14 754
S1G3	583 494	413 112	541 381	34 953	21 948	29 107
<b>PHMSCOPE</b>	<b>7 867 016 585</b>	<b>7 966 630 528</b>	<b>8 257 235 986</b>	<b>674 286 284</b>	<b>669 888 195</b>	<b>689 539 848</b>
R1A1	775 921 033	755 819 069	829 008 199	37 308 422	37 331 516	42 471 934
R1A7	6 231 082 998	6 396 953 648	6 486 356 795	139 382 223	148 708 228	155 314 296
R6A0	564 852 155	543 717 940	608 321 693	92 324 525	80 342 707	88 917 806
V1A0	15 095 779	17 444 001	18 953 549	392 140 744	391 651 448	387 486 192
* <b>DYMISTA</b>	<b>36 562 768</b>	<b>34 240 092</b>	<b>36 755 760</b>	<b>6 093 972</b>	<b>5 706 703</b>	<b>6 165 471</b>
S1G1	39 119 160	33 719 080	44 437 320	2 479 823	2 128 481	2 849 695
S1G2	106 793 840	94 276 360	104 978 800	2 957 406	2 544 410	2 862 850
S1G3	134 151 620	124 700 430	165 179 630	7 693 141	7 181 405	9 637 075
<b>PHARMACY</b>	<b>193 137 402</b>	<b>210 177 201</b>	<b>216 417 121</b>	<b>5 093 515</b>	<b>5 681 215</b>	<b>5 846 784</b>
O1B2	83 858 450	98 444 811	103 622 407	2 281 585	3 043 918	3 246 814
07A5	100 576 690	104 101 960	105 335 380	2 088 516	2 002 415	2 000 027
O1E1	5 926 522	4 475 960	4 168 654	578 025	481 892	452 820
07A2	2 775 740	3 154 470	3 290 680	145 389	152 990	147 123
<b>DISCOUNTER</b>	<b>8 832 814</b>	<b>8 353 946</b>	<b>8 590 854</b>	<b>257 229</b>	<b>197 507</b>	<b>193 400</b>
O1B2	8 832 814	8 353 946	8 590 854	257 229	197 507	193 400
<b>DRUGSTORE</b>	<b>113 170 473</b>	<b>114 023 434</b>	<b>124 054 013</b>	<b>1 999 975</b>	<b>2 237 524</b>	<b>2 572 119</b>
O1B2	86 313 303	89 465 439	100 583 488	1 727 111	1 780 528	1 795 086
O1E1	26 857 170	19 024 460	15 197 810	272 864	184 562	174 842
07A2	0	4 272 160	4 959 840	0	71 889	80 231
07A5	0	1 261 375	3 312 875	0	200 545	521 960
<b>S/MARKET</b>	<b>38 898 835</b>	<b>36 600 671</b>	<b>37 537 948</b>	<b>778 642</b>	<b>823 753</b>	<b>893 062</b>
O1B2	30 506 765	30 122 121	32 530 143	733 210	724 048	766 362
O1E1	8 392 070	4 216 660	3 629 200	45 432	51 778	51 792
07A2	0	2 176 640	1 022 880	0	34 308	18 346

07A5 E	0	85 250	355 725	0	13 619	56 562
<b>SMALL SMKT</b>	<b>4 446 616</b>	<b>4 136 548</b>	<b>4 429 041</b>	<b>92 929</b>	<b>89 035</b>	<b>90 479</b>
01B2	3 781 336	3 682 438	3 562 601	89 961	85 649	82 075
01E1	665 280	372 290	680 470	2 968	1 762	3 051
07A2	0	81 120	172 320	0	1 512	3 166
07A5	0	700	13 650	0	112	2 187

<b>ITALY</b>	<b>2 493 701 426</b>	<b>2 460 288 900</b>	<b>2 508 148 909</b>	<b>221 605 769</b>	<b>224 095 406</b>	<b>230 723 070</b>
<b>HOSPITAL</b>	<b>19 268 623</b>	<b>20 624 634</b>	<b>22 896 801</b>	<b>7 307 742</b>	<b>8 225 054</b>	<b>7 737 864</b>
R1A1	2 637 698	3 097 120	6 309 450	215 073	247 465	522 799
R1A7	6 402 915	6 575 175	6 376 050	152 228	158 388	162 177
R6A0	6 641 693	7 132 653	6 905 066	2 345 114	2 494 632	2 189 101
V1A0	2 307 100	2 676 768	2 454 872	4 557 923	5 291 088	4 839 904
* <b>DYMISTA</b>	<b>12 628</b>	<b>18 840</b>	<b>90 240</b>	<b>1 854</b>	<b>2 762</b>	<b>13 228</b>
S1G1 O	1 120 848	1 033 981	791 298	31 163	27 931	20 146
S1G2	8 931	18 846	3 785	448	750	179
S1G3	149 438	90 091	56 280	5 793	4 800	3 558
<b>RETAIL</b>	<b>1 883 436 191</b>	<b>1 844 094 607</b>	<b>1 881 117 488</b>	<b>176 870 734</b>	<b>177 557 354</b>	<b>184 265 292</b>
R1A1	496 427 232	485 212 020	499 795 900	43 107 606	42 304 966	44 205 554
R1A7	683 174 377	678 502 447	689 459 915	40 119 423	42 168 247	44 414 520
R6A0	372 064 000	370 177 978	377 874 748	73 414 490	72 901 327	74 732 272
V1A0	162 692	225 659	238 380	320 549	445 196	470 630
* <b>DYMISTA</b>	<b>30 759 112</b>	<b>31 069 200</b>	<b>36 225 840</b>	<b>6 041 621</b>	<b>6 102 510</b>	<b>7 115 358</b>
S1G1	230 409 525	214 051 423	215 322 465	10 608 676	10 101 835	10 384 357
S1G2	35 852 210	31 149 190	31 040 290	2 588 674	2 362 103	2 352 370
S1G3	65 346 155	64 775 890	67 385 790	6 711 316	7 273 680	7 705 589
<b>OFF-TAKE</b>	<b>420 390 759</b>	<b>426 548 277</b>	<b>441 534 997</b>	<b>29 617 267</b>	<b>30 277 427</b>	<b>30 776 362</b>
01B2	183 808 168	183 945 839	177 617 076	8 938 640	9 011 910	8 847 760
01E1	18 147 917	15 335 022	13 921 881	1 525 029	1 454 974	1 373 791
07A2	23 223 460	24 866 070	25 146 300	1 345 096	1 761 222	2 005 317
07A5	195 211 214	202 401 346	224 849 740	17 808 502	18 049 321	18 549 494
<b>PARA PHARM</b>	<b>41 399 851</b>	<b>42 567 200</b>	<b>42 588 137</b>	<b>2 863 821</b>	<b>2 865 082</b>	<b>2 796 401</b>
01B2	15 199 665	15 112 203	13 707 888	754 197	760 555	722 685
01E1	3 130 451	2 712 157	2 786 754	300 695	289 792	304 747
07A2	811 270	1 139 910	856 970	50 091	72 531	72 711
07A5	22 258 465	23 602 930	25 236 525	1 758 838	1 742 204	1 696 258
<b>MASS MARKET</b>	<b>113 035 642</b>	<b>110 123 888</b>	<b>104 234 591</b>	<b>4 326 080</b>	<b>4 470 655</b>	<b>4 382 715</b>
01B2	62 842 213	61 141 481	57 418 452	2 703 120	2 737 765	2 643 213
01E1	1 971 259	2 292 072	2 124 944	231 160	347 777	372 003
07A2	6 867 550	6 237 605	5 858 435	244 540	227 324	215 782
07A5	41 354 620	40 452 730	38 832 760	1 147 260	1 157 789	1 151 717
<b>MASS MKT-NC</b>	<b>16 170 360</b>	<b>16 330 294</b>	<b>15 776 895</b>	<b>620 125</b>	<b>699 834</b>	<b>764 436</b>
01B2	2 236 235	1 796 525	1 461 621	72 318	67 713	52 786
01E1	26 030	37 499	36 434	3 186	5 115	5 743
07A2	62 585	66 140	67 690	2 572	2 929	2 599
07A5	13 845 510	14 430 130	14 211 150	542 049	624 077	703 308

<b>POLAND</b>	<b>2 765 988 564</b>	<b>2 842 199 367</b>	<b>2 835 908 301</b>	<b>155 134 749</b>	<b>160 226 726</b>	<b>164 378 170</b>
<b>HOSPITAL</b>	<b>15 137 626</b>	<b>16 445 222</b>	<b>16 028 988</b>	<b>1 596 145</b>	<b>1 627 760</b>	<b>1 654 806</b>
R1A1	2 298 952	2 749 104	2 513 696	37 254	38 483	38 328
R1A7	7 500 858	8 190 886	7 891 661	132 630	154 203	158 718
R6A0	4 753 783	4 890 510	5 023 220	672 903	699 454	790 018
V1A0	18 573	17 682	17 331	745 406	726 527	658 504
* <b>DYMISTA</b>	<b>360</b>	<b>1 080</b>	<b>4 680</b>	<b>59</b>	<b>176</b>	<b>663</b>
S1G1	376 200	407 800	388 700	4 560	5 658	5 468
S1G2	160 400	154 620	162 200	1 578	1 622	1 783
S1G3	28 860	34 620	32 180	1 814	1 813	1 987
<b>RETAIL</b>	<b>2 366 366 557</b>	<b>2 417 153 496</b>	<b>2 431 208 428</b>	<b>146 144 714</b>	<b>150 426 738</b>	<b>153 779 672</b>
R1A1	653 132 400	703 686 012	713 149 704	22 924 341	20 705 341	20 673 273
R1A7	1 004 863 014	1 011 149 604	992 832 758	42 197 935	45 819 743	46 349 359
R6A0	486 694 708	493 734 398	503 733 894	64 423 901	66 049 824	67 696 276
V1A0	468 615	573 662	665 272	11 912 466	13 306 862	13 759 838
* <b>DYMISTA</b>	<b>6 561 360</b>	<b>8 876 280</b>	<b>21 715 680</b>	<b>972 582</b>	<b>1 273 403</b>	<b>2 772 401</b>
S1G1	32 080 900	28 343 000	26 681 800	565 844	519 091	490 397
S1G2	142 996 760	131 793 440	139 948 300	1 440 042	1 259 054	1 311 795

S1G3	46 130 160	47 873 380	54 196 700	2 680 185	2 766 823	3 498 734
<b>OFFTAKE</b>	<b>384 484 381</b>	<b>408 600 649</b>	<b>388 670 885</b>	<b>7 393 890</b>	<b>8 172 228</b>	<b>8 943 692</b>
O1B2	27 399 224	27 711 821	27 479 770	1 732 406	1 596 898	1 479 956
O1E1	70 555 480	59 164 147	59 134 467	2 684 702	2 764 934	3 395 491
O7A2	19 943 700	40 539 400	52 760 100	562 182	1 057 186	1 368 100
O7A5	266 585 977	281 185 281	249 296 548	2 414 600	2 753 210	2 700 145
<b>SPAIN</b>	<b>2 335 455 930</b>	<b>2 342 195 399</b>	<b>2 378 256 266</b>	<b>190 665 883</b>	<b>193 609 689</b>	<b>202 734 323</b>
<b>HOSPITAL</b>	<b>9 112 183</b>	<b>11 052 976</b>	<b>10 225 055</b>	<b>1 513 651</b>	<b>1 645 761</b>	<b>1 560 387</b>
R1A1	2 172 526	3 357 987	2 535 450	50 334	86 924	75 791
R1A7	2 005 927	2 283 341	2 158 777	88 131	93 613	92 522
R6A0	4 027 829	4 395 427	4 440 996	1 309 209	1 392 995	1 316 609
* <b>DYMISTA</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
S1G1	119 460	150 960	183 220	6 728	8 488	10 080
S1G2	9 300	5 300	11 700	378	208	459
S1G3	777 141	859 961	894 912	58 871	63 533	64 926
<b>SELL OUT</b>	<b>2 194 730 398</b>	<b>2 195 372 883</b>	<b>2 242 126 707</b>	<b>180 353 377</b>	<b>182 800 026</b>	<b>191 487 364</b>
R1A1	855 946 916	889 440 180	919 688 976	42 155 216	45 579 352	47 849 302
R1A7	627 535 576	601 079 486	590 371 990	28 513 887	29 012 900	29 795 483
R6A0	457 352 438	465 876 773	487 974 761	91 904 533	91 040 256	96 059 459
V1A0	465 028	479 164	686 600	1 074 098	1 110 096	1 584 551
* <b>DYMISTA</b>	<b>9 252 292</b>	<b>11 344 080</b>	<b>12 349 804</b>	<b>1 233 993</b>	<b>1 596 132</b>	<b>1 852 831</b>
S1G1	111 263 360	102 285 020	107 474 200	5 855 324	5 514 404	5 680 404
S1G2	33 539 100	29 905 100	29 050 300	772 194	681 761	669 877
S1G3	108 627 980	106 307 160	106 879 880	10 078 125	9 861 257	9 848 288
<b>OFF-TAKE</b>	<b>129 508 699</b>	<b>131 988 535</b>	<b>122 727 936</b>	<b>8 702 319</b>	<b>8 969 019</b>	<b>9 517 896</b>
O1B2	46 051 527	42 168 335	38 740 393	2 714 808	2 595 648	2 513 212
O1E1	4 814 504	4 447 039	5 056 991	1 025 215	760 457	834 638
O7A2	184 714	434 790	2 210 500	57 610	131 428	218 062
O7A5	78 457 954	84 938 371	76 720 052	4 904 686	5 481 486	5 951 984
<b>PARAPHARM</b>	<b>2 104 650</b>	<b>3 781 005</b>	<b>3 176 568</b>	<b>96 536</b>	<b>194 883</b>	<b>168 676</b>
O1B2	4 050	13 875	14 850	256	817	1 038
O1E1	1 640	4 660	11 710	308	1 505	3 941
O7A5	2 098 960	3 762 470	3 150 008	95 972	192 561	163 697

**Table 5: Rhino-conjunctivitis medication consumption in Europe per inhabitant (results in SU per year, 2018)**

	<b>Population 2015 (in thousands)</b>	<b>All without nasal decongestants</b>	<b>Nasal decongestants</b>	<b>INCS</b>
France	66,352	64.2	9.2	33
Germany	81,175	24.5	85.1	7.6
Italy	60,795	25.7	15.6	8.3
Poland	38,005	47.5	27.0	18.8
Spain	46,440	36.5	13.7	20.0

**Figure 1: Comparison between countries for 2018 of the number of standard units sold (SU) and costs (LEU/MNF)**

Incs include dymista

### **Conflict of interest :**

CB reports personal fees from Meda.

JB reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Purina, Sanofi-Aventis, Takeda, Teva, Uriach, other from KYomed-Innov, outside the submitted work.

VC reports personal fees from ALK, Allergopharma, Allergy Therapeutics, Diater LETI, Thermofisher, Stallergenes, outside the submitted work.

PD reports personal fees and non-financial support from Astra Zeneca, Chiesi, personal fees from Mylan, personal fees from Sanofi, GlaxoSmithKline, Menarini, outside the submitted work.

LK reports grants and personal fees from Allergopharma, LETI Pharma, MEDA/Mylan, Sanofi, personal fees from HAL Allergie, Allergy Therapeut, grants from ALK Abelló, Stallergenes, Quintiles, ASIT biotech, Lofarma, AstraZeneca, GSK, Immunotk outside the submitted work; and Membership:

AeDA, DGHN, Deutsche Akademie für Allergologie und klinische Immunologie, HNO-BV GPA, EAACI.

OP reports grants and personal fees from ALK-Abelló, Allergopharma, Anergis S.A., , Stallergenes Greer, HAL Allergy Holding B.V./HAL Allergie GmbH, Bencard Allergie GmbH/Allergy Therapeutics, Lofarma, ASIT Biotech Tools S.A., Laboratorios LETI/LETI Pharma, grants from Biomay, Circassia, Glaxo Smith Kline, personal fees from MEDA Pharma/MYLAN, Mobile Chamber Experts (a GA2LEN Partner), Indoor Biotechnologies, Astellas Pharma Global, EUFOREA, ROXALL, NOVARTIS, SANOFI AVENTIS, Med Update Europe GmbH, streamedup! GmbH, outside the submitted work.

BS reports grants from AstraZeneca, personal fees from Mylan, Polpharma, outside the submitted work.

GS reports personal fees from ALK- Abello, Mylan, GSK, Bayer outside the submitted work.

EVG reports personal fees from PELyon, outside the submitted work.

TZ reports : Organizational affiliations:Committee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA), Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI); Head: European Centre for Allergy Research Foundation (ECARF); President: Global Allergy and Asthma European Network (GA<sup>2</sup>LEN)

Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO).

### **Data Availability Statement**

The data is the property of IQVIA

### **Contribution statement**

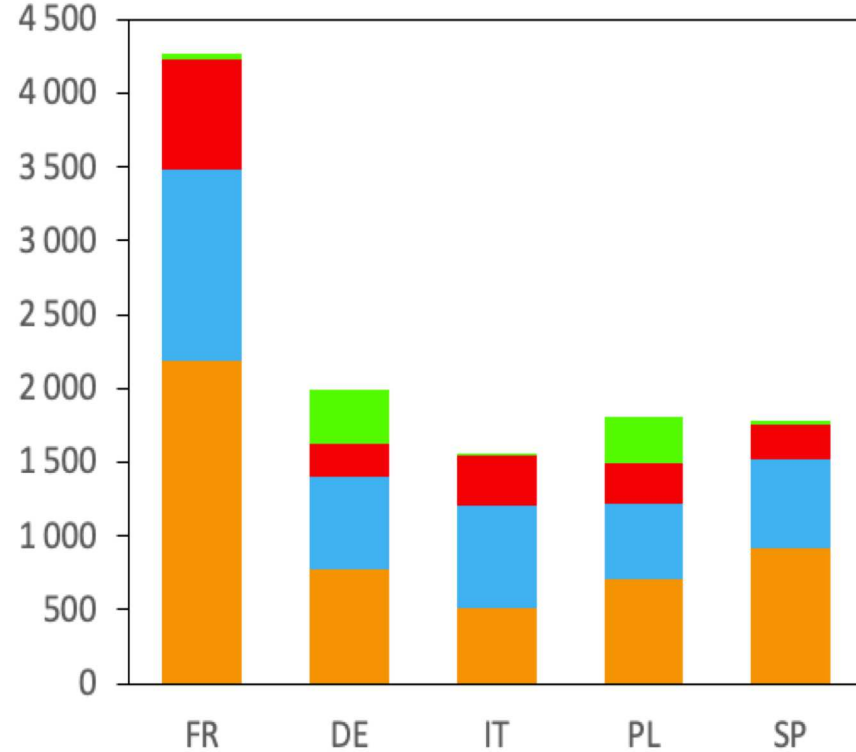
- Jean Bousquet designed and interpreted the study data and wrote the paper
- Detlef Schröder-Bernhardi co-designed the study and participated to the analysis interpretation
- Claus Bachert, Giorgio W Canonica, Victoria Cardona, Elisio M Costa, Wienczyslawa Czarlewski, Philippe Devillier, Joao Fonseca, Ludger Klimek, Piotr Kuna, Olga Lourenco, Joaquim Mullol, Oliver Pfaar, Nhn Pham-Thi, Boleslaw Samolinski, Glenis Scadding, Sophie Scheire, Eric Van Ganse, Torsten Zuberbier interpreted the data and reviewed the paper. They all gave their agreement for the publication
- Julia Saueressig, Ann-Kathrin Stroh analyzed the data

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**SU - absolute values ( $10^6$ ) 2018****Costs - LEU/MNF (k€) 2018**