Facts & Figures 2019

Medicinal Products and Health Care in Austria

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

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Imprint

Owned and published by
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Production
Grasl FairPrint
Druckhausstraße 1, 2540 Bad Vöslau

Currency
All indicated values are stated in Euro. Sum totals relating to the national economy are generally indicated in millions of Euro. Individual amounts and microeconomic data are generally stated in Euro.

Gender neutrality
All terms referring to individuals are generic and refer to both genders.

Laws and technical terms
Quotations and technical terms were inserted between parentheses or in inquotation marks.

Pharmig at a glance

Pharmig – the Association of the Austrian Pharmaceutical Industry – is a voluntary and party-politically independent representation of interests of the pharmaceutical industry in Austria.

Pharmig represents about 120 member companies with approximately 18,000 employees in total. These companies make up more than 95 per cent of the medicinal product market.

Pharmig and its member companies are committed to secure the supply of medicinal products in the health care system to the best effect. Through quality and innovation Pharmig and its member companies ensure both social and medical progress.

The pharmaceutical industry is dedicated to strengthening Austria's role as a pharmaceutical and research location. It constitutes an excellent example for the successful cooperation of economy and science which ultimately aids the further development of our knowledge society.

As a recognised and competent partner, Pharmig uses its great expertise to support decision makers in the healthcare system and relevant policy areas. In so doing, Pharmig demands fair, reliable and calculable framework conditions for the pharmaceutical industry which serve all stake holders and the entire population.

It is the primary aim of the association and of the businesses of the pharmaceutical industry to ensure the best possible supply of medicines for the population of Austria.

Dear readers,

Photo: Photo Simonis

I am delighted to be able to present you the latest issue of Facts & Figures 2019 in digital format.

In this issue we once again incorporated few new features, these include:

- **Social insurance reform**
  In 2018, the Social Insurance Organisation Act was used as the basis for the new structure of social insurance in Austria. By 2020, the 21 social insurance providers will be reduced to 5 and will be coordinated by an umbrella association thereafter.

- **Burden of cancer at a glance**
  Improved diagnostics and new therapeutic methods counteract the burden of cancer. Medical advances are significantly reducing the risk of new incidences and the mortality risk. A detailed overview of the burden of cancer can be found on pages 25 to 27.

- **Vaccines**
  The 2018 newly introduced chapter on vaccines and their production has been extended for this issue – with parts about the take-up of vaccines and the effect of herd immunity on TBE, measles and influenza in Austria.

In addition to this electronic issue of Facts & Figures 2019, selected graphics and the German version of this document are available on our website www.pharmig.at as a downloadable document.

I hope you enjoy reading and learning from our new Facts & Figures!

Best Wishes

Mag. Alexander Herzog
Secretary General, Pharmig

1 Health care system in Austria

The Austrian health care system is characterized by the federalist structure of the country. Through the multitude of decision-makers (federal, state, municipality, social insurance), health care financing is not regulated from one source, but rather depends on multiple sources of financing (including taxes, social insurance premiums through social insurance, federal, state, municipality etc. – see chapter 1.3). Agreement among those responsible is important due to the fragmented responsibilities. An important general framework therefore determined in mutual agreements and contracts (for example, agreements according to Art. 15a Austrian Constitutional Law – B-VG).

1.1 Economic basic information

The population of Austria in 2018 was 8,795,073 (see also chapter 3). 99 % are covered by one of the 21 social insurance institutions (status 2018), in addition to 15 special health care institutions (see chapter 1.4).

1.2 Social expenditures

Social expenditures in total amounted to Euro 105.9 billion in 2017. 70 % of social expenditures consist of retirement benefits and health care services.

Social expenditures* acc. to function in 2017

	million Euro	percent
Age	46,954.68	44.3
Illness/health care	27,497.70	26.0
of which sickness benefits	724.90	0.7
of which continued payment of wages during illness	2,983.39	2.8
of which in-patient care	12,937.44	12.2
of which out-patient care	9,447.35	8.9
of which prevention of illness/rehabilitation	1,096.10	1.0
of which other benefits in cash/in kind**	308.53	0.3
Family/children	10,080.64	9.5
Surviving dependants	6,053.22	5.7
Invalidity/disability	6,570.06	6.2
Unemployment	6,106.13	5.8
Habitation and social exclusion	2,691.64	2.5
Total	**105,954.07**	**100**

Source: Statistics Austria

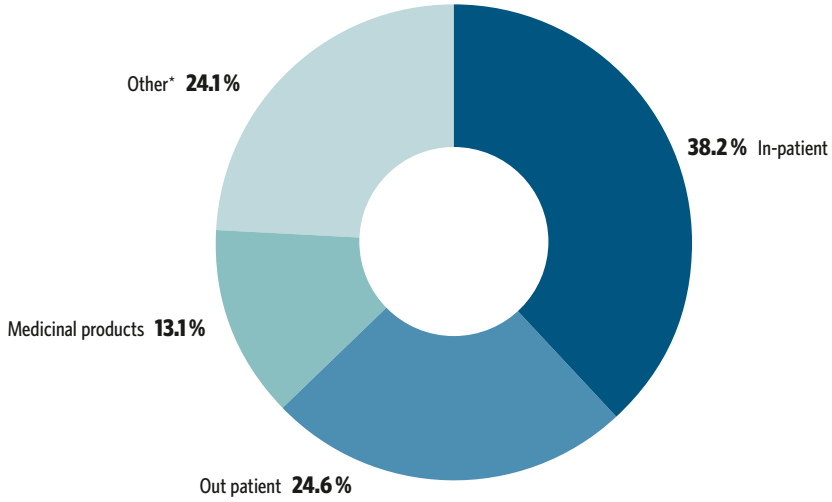
* social expenditures of functional organisation are the sum of social beneftis, without transfers between social systems (redirected social contributions and other transfers) and without other expenditures (administrative expenses, other not attributable expenditures)

** other social benefits: treatments for accidents, benefits in cash from other health care institutions, benefits in kind from welfare/minimum income; data from 2000 onwards can only partially be compared to earlier data.

1.3 Health care expenditures

According to the "System of Health Accounts" (SHA), health expenditure consists of running health costs and investments in the healthcare sector.

In 2017, health expenditures in Austria amounted to some Euro 41.3 billion, which corresponds to a share in GDP of 11.2 %.



Source: calculated by the Institute of Pharmaeconomic Research (IPF) with reference to the following data: IQVIA, Austrian statistics, HV

* Expenditures for long-term care, ambulance services, public health services, administration, medical products and equipment, private insurance.

The largest proportion of 38.2 % was spent on in-patient care. At the same time, expenditure on out-patient care made up 24.6 % and expenditure on medicinal products 13.1 %.

Expenditure on medicinal products includes consumption in pharmacies and hospitals, incl. VAT. The proportion between expenditure on medicinal products and total health expenditures in % is defined as the pharmaceutical ratio.
The pharmaceutical ratio also mirrors the varying significance of the health care settings (in-patient, out-patient, drug therapy) at national level.

Health care financing	2016		2017	
	million Euro	percent	million Euro	percent
Public health care financing	28,723	72.5	29,984	72.6
In-patient care*	12,605	31.8	13,009	31.5
Out-patient care	6,922	17.5	7,290	17.7
Long-term care at home**	2,357	6.0	2,403	5.8
Ambulance and emergency medical services	372	0.9	381	0.9
Pharmaceutical products, medical equipment	3,675	9.3	3,935	9.5
Prevention and public health services	576	1.5	604	1.5
Health care administration: State incl, social insurance	824	2.1	838	2.0
Public investments	1,392	3.5	1,524	3.7
Private health care financing	10,873	27.5	11,305	27.4
In-patient care*	2,505	6.3	2,746	6.7
Out-patient care	3,114	7.9	2,886	7.0
Pharmaceutical products, medical equipment	2,564	6.5	2,651	6.4
Health care administration private insurance	724	1.8	626	1.5
Investments (private)	1,328	3.4	1,307	3.2
Non-profit private organisations***	569	1.4	1,012	2.5
Services provided by company physicians	69	0.2	77	0.2
Total	**39,596**	**100**	**39,596**	**100**

Source: Statistics Austria

* Includes in-patient health care services in nursing homes.

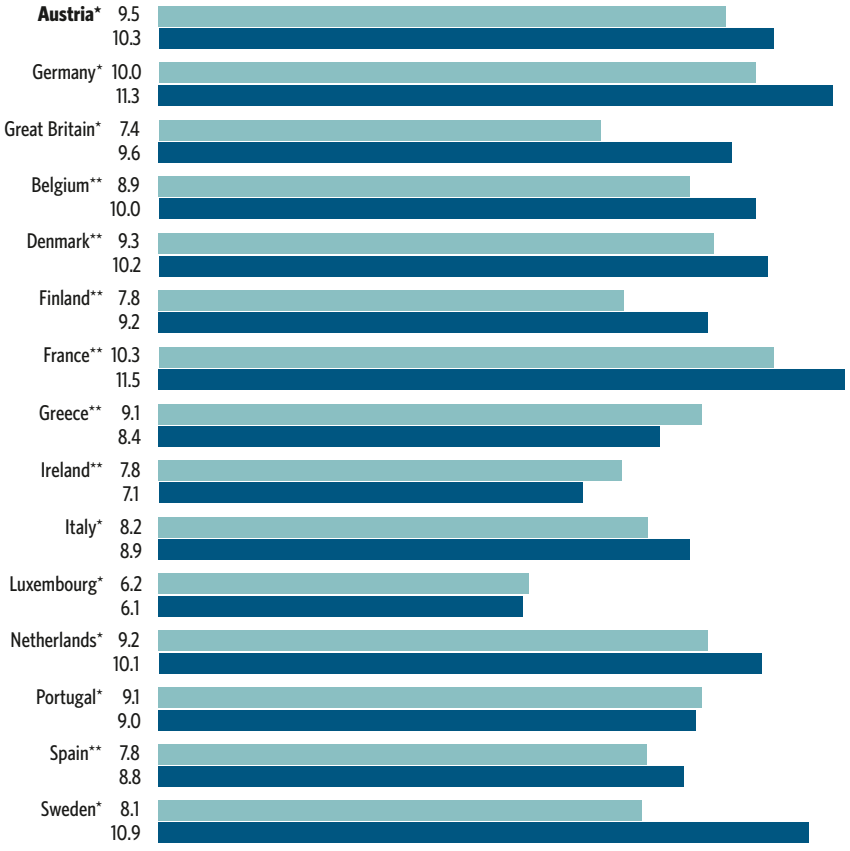
** Public spending for long-term care at home also includes federal and provincial nursing allowances.

*** Includes information about the non-profit private organisations for rescue services and other health services.

When broken down into public and private expenditure on health care, nearly three-fourths of the expenses are financed by public funds. In the period between 2010 and 2017, expenditure on health care rose on average by 3.7 % each year.

Comparative health care expenditures

Health care expenditure in % of GDP[1]



[1] graphical illustration of selected OECD countries

2007 2017

Source: Statistics Austria, OECD

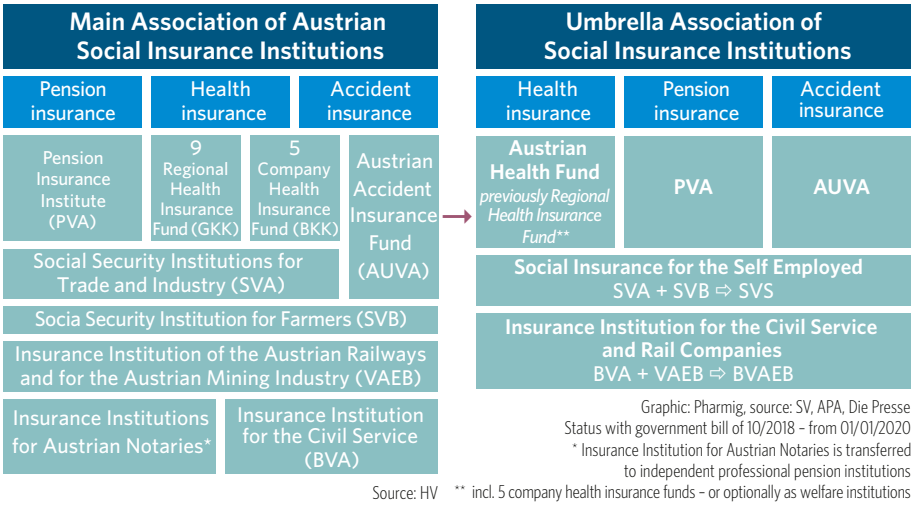
* provisional value

** estimated value

Due to national differences in the health care systems, however, and in view of varying data availability in the individual countries, international comparisons can only be indicative.

1.4 Social security system

The Austrian system of social security



Graphic: Pharmig, source: SV, APA, Die Presse
Status with government bill of 10/2018 – from 01/01/2020
* Insurance Institution for Austrian Notaries is transferred to independent professional pension institutions

Source: HV ** incl. 5 company health insurance funds – or optionally as welfare institutions

The **2018 Social Insurance Organisation Act** is reorganising the Austrian social insurance system from top to bottom through structural reform. The 21* social insurance providers will be reduced to 5 insurance providers, and they will be coordinated by an umbrella association (previously the Main Association of Austrian Social Insurance Institutions) in the future. The new structure will be in place from 01/01/2020. From 01/04/2019 to 31/12/2019 a transitional committee will prepare the system for the new structure. The Austrian Social Insurance System covers 99 % of the population and rests on three pillars:

- Health insurance
- Pension insurance
- Accident insurance

Everyone is compulsorily insured with the respective institution for their branch of industry or with their competent Regional Health Insurance Fund (Austrian Health Fund in the future).
In addition to statutory health insurance, 15 health care institutions provide health insurance to employees working in regional or municipal administrations.

* Liquidation BKK tobacco per 01/2017

Development of persons entitled to claim against a health insurance policy by insurance provider

Annual average 2013/2017	2013	2017
Total* persons	**8,342,875**	**8,677,278**
All insurance providers (insurance ratio)**	**9,013,541**	**9,409,569**
Regional health insurance fund – Vienna	1,588,174	1,709,053
Regional health insurance fund – Lower Austria	1,168,439	1,221,300
Regional health insurance fund – Burgenland	202,420	211,640
Regional health insurance fund – Upper Austria	1,192,331	1,241,986
Regional health insurance fund – Styria	924,281	960,045
Regional health insurance fund – Carinthia	427,291	435,519
Regional health insurance fund – Salzburg	449,072	464,159
Regional health insurance fund – Tyrol	568,018	591,175
Regional health insurance fund – Vorarlberg	312,552	326,727
Company health insurance fund Austria Tabak BKK	2,201	-
Company health insurance fund Transport companies	19,506	19,445
Mondi	2,795	2,575
Company health insurance fund VABS	13,106	13,116
Company health insurance fund Zeltweg	4,286	4,045
Company health insurance fund Kapfenberg	10,025	9,905
Insurance Institution of Austrian Railways and Mining Industry	231,088	219,383
Insurance Institution for public servants	779,948	814,725
Social Security Institution for Trade and Industry	748,194	811,991
Social Security Institution for Farmers	369,814	352,780

in absolute

Source: HV

* Each individual is counted once.

** The statistics do not count the number of persons with health insurance but rather the health insurance ratios. Persons with more than one insurance provider are counted once with each insurance provider.

Number of employees in health insurance institutions

Annual average 2017	Number of staff in total	Administration and invoicing	General medical services	Special institutions*
Total	**13,833**	**8,191**	**907**	**4,735**
Regional health care insurance funds	10,511	5,943	766	3,802
Company health care insurance funds	140	69	11	60
Insurance Institution of Austrian Railways and Mining Industry	555	294	29	232
Insurance Institution for Public Servants	1,617	936	40	641
Social Security Institution for Trade and Industry	579	551	28	-
Social Security Institution for Farmers	431	398	33	-

in absolute

Source: HV

* general out-patient clinics, out-patient dental clinics, other treatment institutions, out-patient clinics for children and teenagers, institutions for prevention and teenagers, as well as rehabilitation centres and sanatoria

Special health care institutions

In Austria the Insurance Institution for Public Servants is the only competent social insurance agency concerning health and accident insurance for civil servants in federal government, and for most civil servants in federal state government and municipial administration. In addition, there may exist further institutions for health care of civil servants in federal state government and municipical government. Therefore there are 15 other special health (and accident) insurance institutions for civil servants in federal state and municipal government, in addition to the Insurance Institution for Public Servants.

These special health care institutions are no social insurance agencies and are not part of the Main Association of Austrian Social Insurance Institutions and are not subject to surveillance through authorities.

Federal state	Number	Special health care institutions and/or accident insurance institution
Carinthia	1	of civil servants of the city of Villach
Lower Austria	1	of civil servants of the town of Baden
Upper Austria	6	of civil servants of the city of Linz
		of the towns of Upper Austria
		of civil servants of the federal state government of Upper Austria
		of teachers of Upper Austria
		of civil servants of the magistracy of Steyr
		of civil servants of the city of Wels
Salzburg	2	of civil servants of the town of Hallein
		of municipal employees of the magistracy of Salzburg
Styria	1	of civil servants of the city of Graz
Tyrol	3	of teachers of Tyrol (on federal state level)
		of civil servants of the federal state government of Tyrol
		of civil servants of the municipal governments of Tyrol
Vienna	1	of civil servants of the city of Vienna
Austria	**15**	

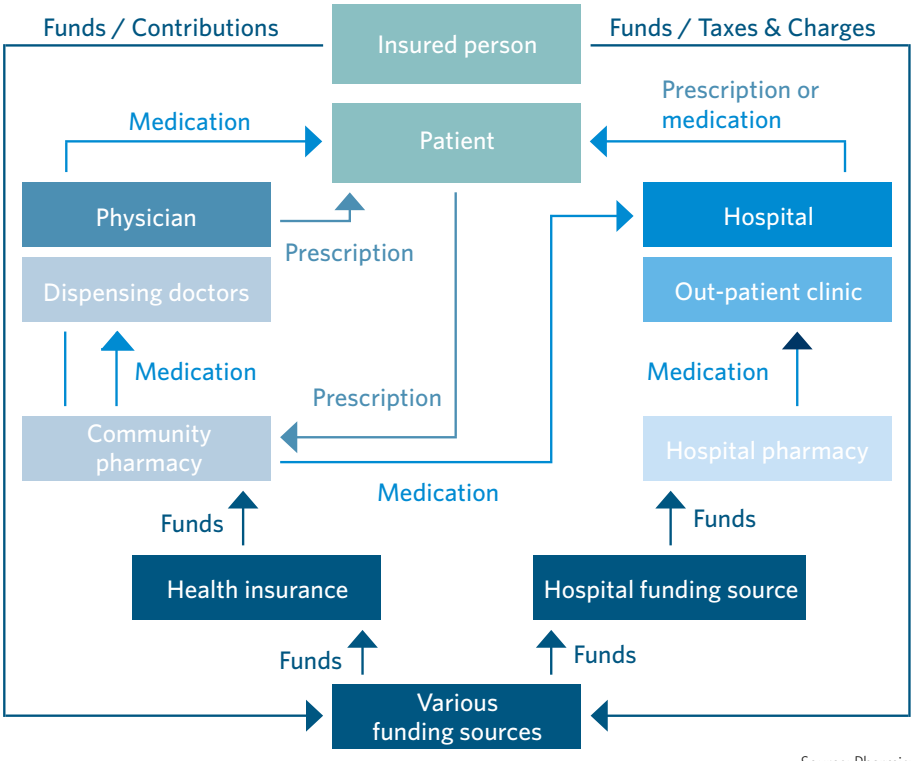
Source: Hofmacher, M.M (2013). Das österreichische Gesundheitssystem. Berlin: Medizinisch Wissenschaftliche Verlagsgesellschaft
§ 2 Officer, Health and Accident Insurance Act (B-KUVG)

1.5 Health care structure

Austria has a dense network of medical care institutions. Patients have four different levels of health care providers at their disposal:

- Physicians (general practitioners and specialists), dispensing or non-dispensing as well as primary care centres (PHC "primary health care")
- Hospitals and out-patient wards
- Community pharmacies
- Other medical/therapeutic services

Structure of Austria's health care system



Source: Pharmig

1.6 Employees in the health care system

As per December 31, 2017, Austria's 8.8 million inhabitants were supplied by 1,362 public pharmacies (with 29 branches), 43 hospital pharmacies and 919 dispensing doctors (who dispense medicines directly to patients).

	Number
Practicing physicians	**50,605**
General practioners	13,745
of whom solely employed physicians	5,642
Medical specialists	24,218
of whom solely employed physicians	11,663
Dentists	5,009
of whom solely employed physicians	634
Physicians in training	7,633
of whom solely employed physicians	7,633
Pharmacy employees	**17,001**
Pharmacists, employed or self-employed	5,867
Qualified staff	7,203
Other employees	3,931
Medical experts in hospitals	**117,982**
Physicians	24,646
Nursing staff	93,336

Source: Statistics Austria, Austrian Chamber of Pharmacists

In total about 185,000 people are employed in the healthcare sector.

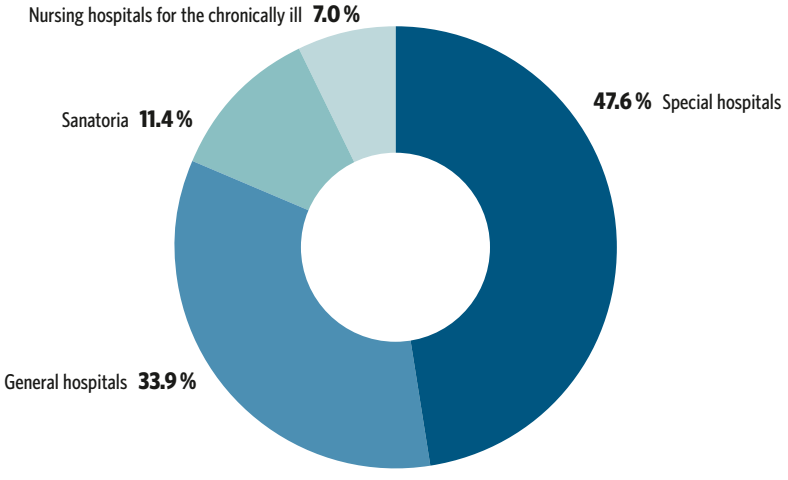
2 Hospitals in Austria

In Austria, hospitals totalled 271 at the end of 2017.
The hospital system is of federal nature, i. e. the jurisdiction is with the provincial governments.
The legal basis for all hospitals is the Federal Hospitals Act (KAKuG). This Act serves as the basis for the 9 provincial acts, which represent implementing statues.

Hospitals as per § 2 of the Federal Hospitals Act include:

- **General hospitals:** for persons irrespective of their gender, age or the type of medical care they receive.
- **Special hospitals:** for the examination and treatment of persons with specific diseases or of persons of a particular age or for certain purposes.
- **Convalescent homes:** for people who require medical treatment and special care.
- **Nursing hospitals for chronically ill:** Persons requiring medical treatment and special care.
- **Sanatoria:** Hospitals with special equipment for special care and accommodation.
- **Independent out-patient clinics:** Independent institutions (e. g. X-ray institutes, dental clinics) for the examination and treatment of persons who do not require in-patient treatment.

Types of hospitals (without independent out-patient clinics) 2017



Source: Statistics Austria, BMASGK

Hospitals run by social insurance institutions

In 2017 the Austrian social insurance institutions (health, accident and pension insurance institutions) ran a total of 190 own hospitals:

- 116 independent out-patient clinics
- 29 other out-patient clinics/examination centres
- 45 own hospitals for inpatient treatment (= 6,351 beds)

Independent out-patient clinics
37 general hospitals with 115 out-patient or specialist wards
77 dental out-patient wards
2 centres for out-patient rehabilitation

Other out-patient clinics
29 other out-patient clinics (to carry out adolescent, convalescent and other medical examinations)

Own hospitals for inpatient treatment	Beds
1 general hospital and 37 out-patient wards	455
7 accident and emergency hospitals	908
28 special hospitals/rehabilitation centres	4,145
5 sanatoria	447
4 convalescence and recovery homes	396

Source: HV, Statistical Handbook Austrian Social Insurance 2018

2.1 Structural details of hospitals

Of these 271 hospitals, 112 (41 %) are hospitals with public status and 159 (59 %) without public status. Hospitals with public status are not to be confused with hospitals of public agencies and institutions.

Approximately 55 % of hospitals are run by public agencies and institutions.

Ownership/responsible bodies – public law status in 2017

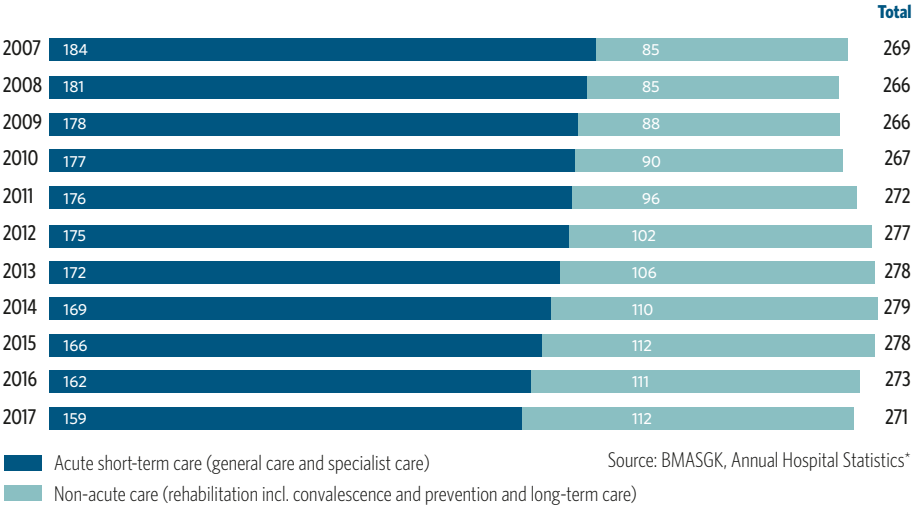
Number of hospitals and beds actually set up		
	With public law status* 147 hospitals (45,235 beds)	Without public law status** 124 hospitals (19,570 beds)
Public ownership 112 hospitals (43,172 beds)	88 hospitals (36,419 beds)	24 hospitals (7,753 beds)
Private ownership 159 hospitals (21,633 beds)	59 hospitals (8,816 beds)	100 hospitals (12,817 beds)

Source: BMASGK, Hospital Statistics

* federal government, provincial and municipal hospital companies, social insurance institutions

** religious orders and congregations, private persons, private companies and associations

Development of hospitals according to care function

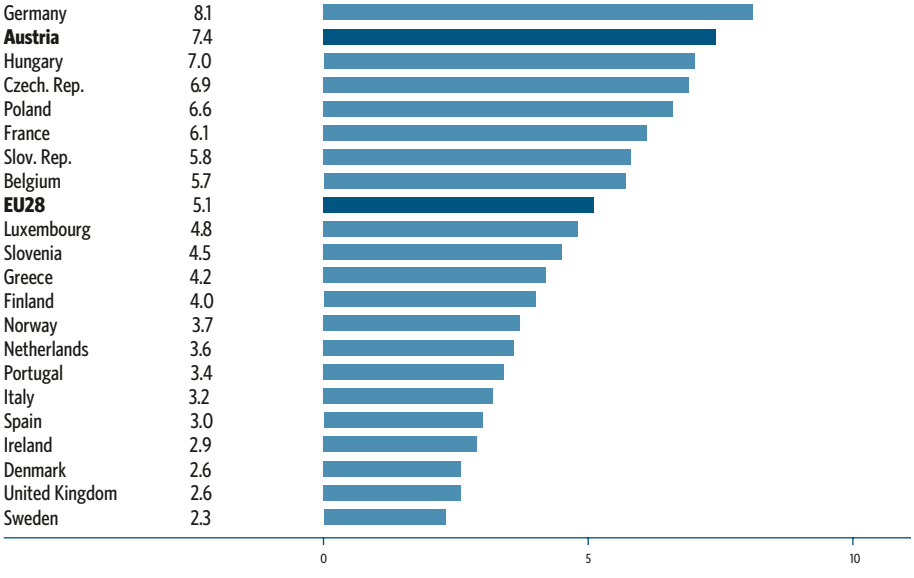


Source: BMASGK, Annual Hospital Statistics*

Throughout the years, the number of institutions in the area of acute short-term care has decreased from 184 (2007) to 159 institutions (2017). In comparison to this, the area of non-acute care has increased from 85 institutions (2007) to 112 (2017).

Hospital care in international comparison

Hospital bed capacity per 1,000 inhabitants, 2016*



* graphic representation of selected EU countries

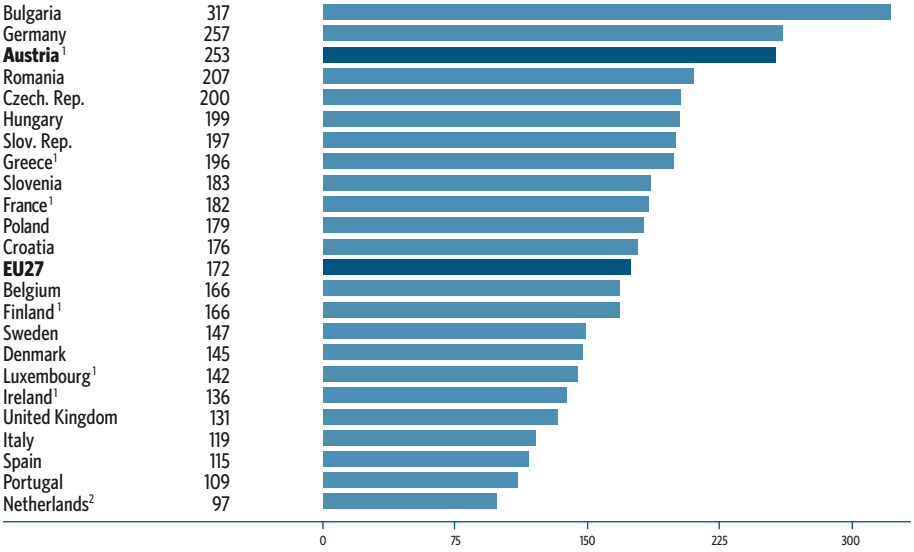
Source: OECD, Health at a Glance, Europe 2018,

With 7.4 beds per 1000 inhabitants, Austria is in second place behind Germany (8.1) in the 2016 European OECD country comparison.

Austria has 46 % more hospital beds than the average of the EU 28 member states. There is a slight decline compared to 2006 (7.7 beds per 1,000 inhabitants).

Along with the large availability of hospital beds Austria also has the third highest number of hospital treatments per number of inhabitants after Bulgaria and Germany compared to other European countries (253 vs EU 27-average 172).

Hospital discharges per 1,000 inhabitants, 2016*



* graphic representation of selected EU countries

Source: OECD, Health at a Glance, Europe 2018

[1] not including discharges of healthy new-born babies from hospitals (between 3 % and 10 % of all discharges).

[2] including discharges of day-care cases

Development of bed capacity in Austria

The overview also indicates the actually set up beds in Austria's hospitals (64,805). In relation to Austria's population, the bed coverage was 7.37 beds per 1,000 inhabitants.

- In 2017, 2.8 million hospitalisations for in-patient treatment were reported in Austrian hospitals.
- The hospitalisation frequency (= hospital stays per 100 inhabitants) amounted to 32.2 % (1991: 23.9 %, 2005: 31.8 %).
- In 2017 the average stay in acute hospitals was 6.4 days.

2.2 Hospital funding

The expenditure of Austrian hospitals operating on the "LKF" basis (system of performance-oriented hospital financing) amounted to 13.8 billion Euro in 2017. Of these, about 60 % were funded by the Regional Health Fund.
The remainder had to be paid by the hospital operators using other means. Patients also directly contributed to the funding, e. g. through private insurances.

The most important numbers for hospitals financed through the regional health fund in 2017

	million Euro
Share from regional funds	**8,123**
Social insurance*	5,262*
The federation	1,299
Federal states (VAT-funded)	230
Municipalities (VAT-funded)	162
Funder means	1,170
Share from hospital funders	**4,306**
Federal states, municipalities	2,760
Religious orders and others	1,500
Social insurance	46
Share from private parties	**1,405**
Patients, private insurances	1,405
Total	**13,834**

in Euro million

Source: calculated by the Institute of Pharmaeconomic Research (IPF) with reference to the following data: HV, BMGF/BMASGK, Austrian Statistics

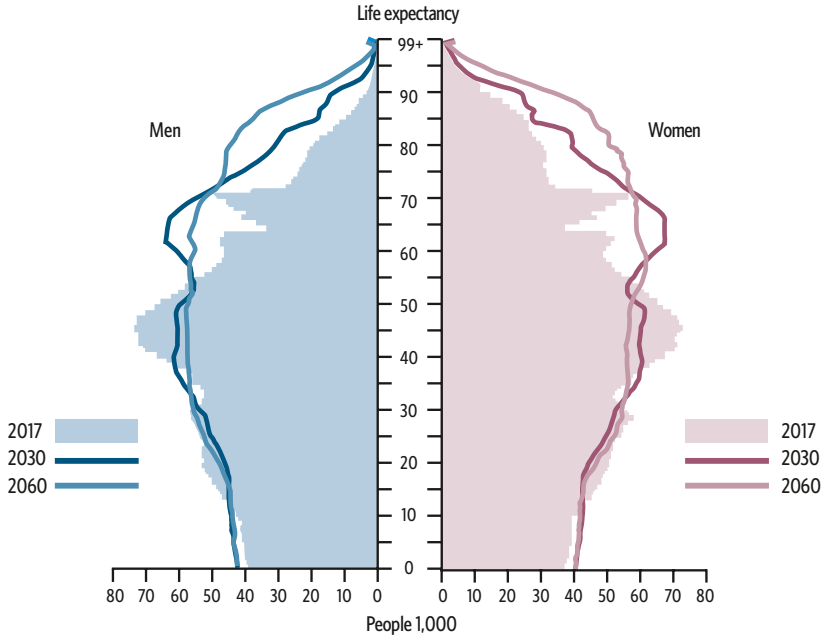
* In the Austrian social insurance system the area of hospital care incorporates the following expenses: proportionate money transfers to regional health care funds and the Federal Health Agency for Inpatient Care, payments to the remaining hospitals (funds for private hospitals, emergency hospitals, etc.) and payments for hospitals abroad. It does not include expenses for outpatient care. These expenses are recognised as medical attention and equivalent services (outpatient services in hospitals).

**Social insurance makes a large contribution of the hospital funding.
Of Euro 8.0 billion which are financed by regional health insurance funds, 65 % are covered for by the social insurance system.**

3 Population structure and demographic trends

3.1 Population structure

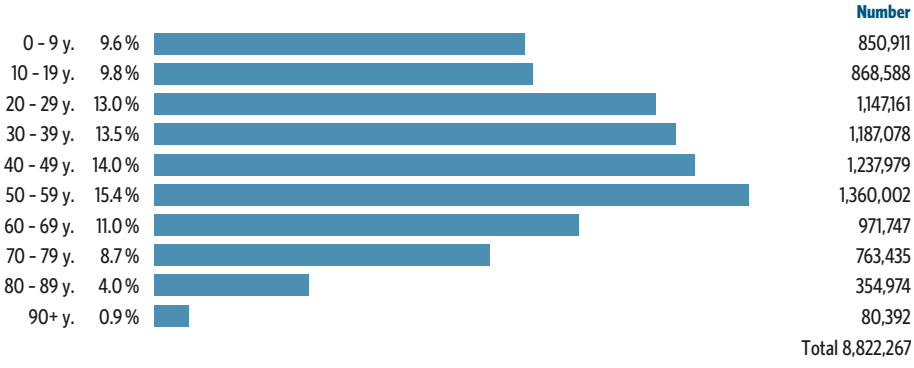
Population pyramid 2017, 2030 and 2060



Source: Statistics Austria

Statistics Austria forecasts a strong population growth until 2060 and a further shift in the age structure towards higher ages. Life expectancy has increased significantly in the last few decades and is currently at 79 for men and 84 for women. According to projections, Austria will have a population of 9.74 million in 2060.

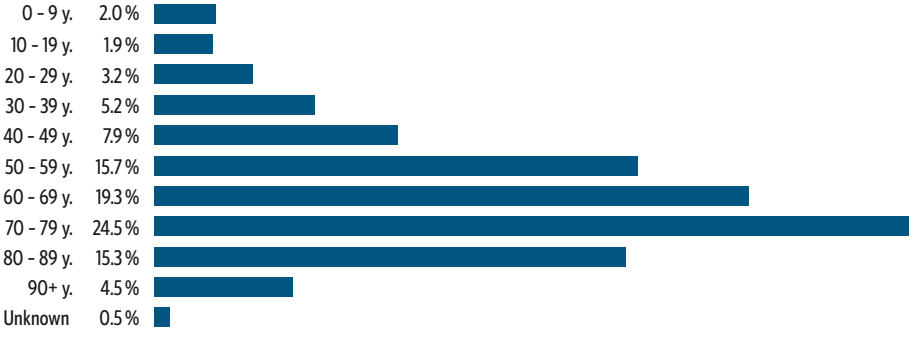
Share of age groups in total population in %



In 2018, the percentage of the population over 65 years of age was 19 %. According to projections by Statistik Austria, this percentage will increase by half in the next 20 years.

3.2 Need for medicinal products by age group

The need for medicinal products in % (national health insurance patients, by no. of packages)



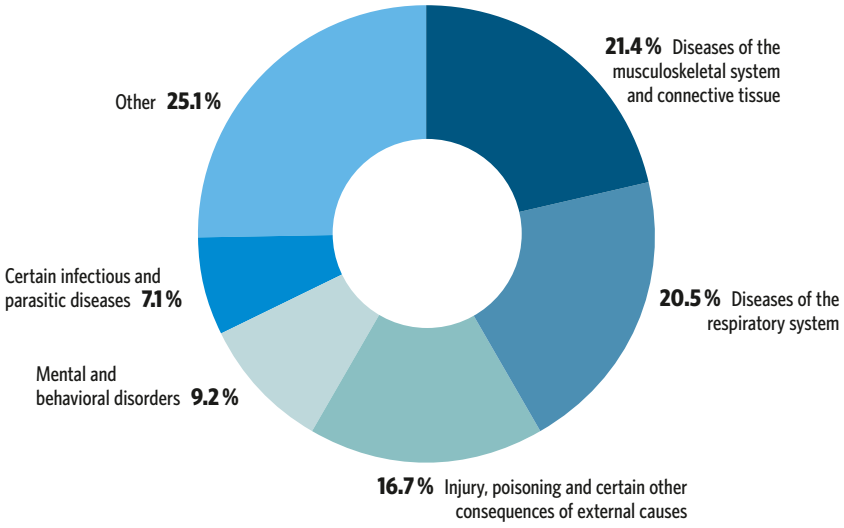
Source: Austrian Chamber of Pharmacists, 2018

There will also be an increase in the need for medicinal products in the course of the demographic transition. The demand for medicinal products increases considerably from the age of 60.

3.3 Frequent causes of illness

Illness groups as percentage of sick leave days

Survey group: blue collar and white collar



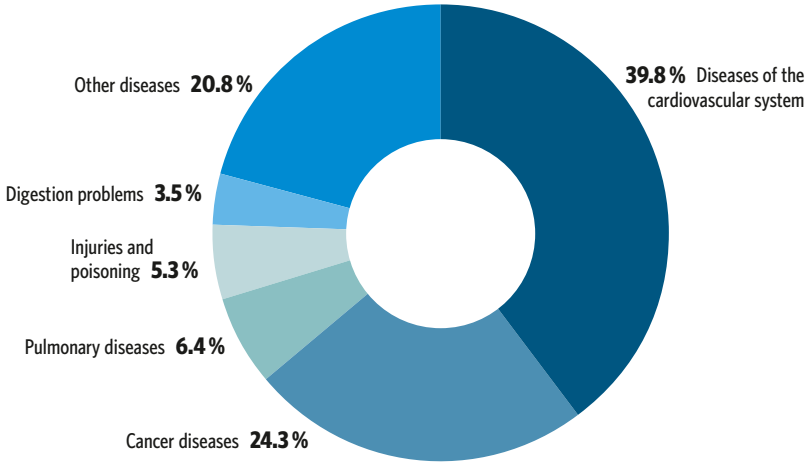
Source: HV, 2018

The 4,266,219 cases of illnesses causing absence from work and the 41,522,418 days of employee absence in 2017 show that illnesses of the respiratory system and of the musculoskeletal system are the main causes for notifications of sickness.

Diseases of the respiratory system together with diseases of the musculoskeletal system represent the cause for approximately 42 % of the notifications of illness.

3.4 Mortality

Mortality by causes of death



Source: Statistics Austria, 2017

The two most frequent causes of death – cardiovascular diseases and cancer – cause almost two thirds of all deaths between them.

Along with the increase in life expectancy (see chapter 3.1), mortality has fallen for both genders in the last 10 years, although the mortality risk for both main causes of death is still significantly higher for men.

Source: Statistics Austria

Classification of ICD 10:

- diseases of the cardiovascular system: heart attack, stroke, hypertension etc.
- malignant growths: cancer (lungs, stomach, breast, prostate, blood)
- other deseases: nutritional and metabolic deseases (Diabetes Mellitus), virusinfections (AIDS), psychiatric disorders, nervous system etc.

Overview of the burden of cancer

Worldwide burden of cancer – for 2018, the WHO is anticipating

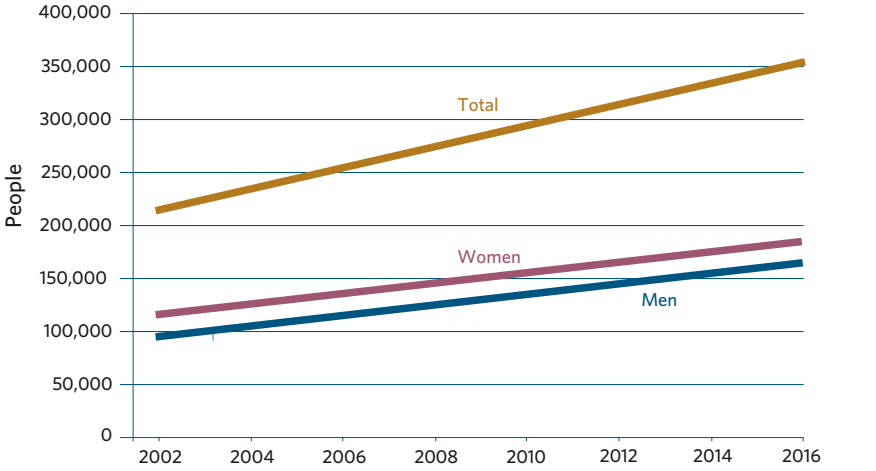
- 18.1 million new cases of cancer
- 43.8 million people living with cancer
- 9.6 million deaths because of cancer

Due to population growth and increasing life expectancy, the WHO is also projecting further growth in the number of new cancer diagnosis in the future. The 3 most common types of cancer relate to the lung, breast, and stomach.

Cancer in Austria

- There were 350,600 people living with cancer (of which 53 % were women, 47 % were men) at the end of 2016.
- This represents a significant increase compared to 2002 (213,620 people with cancer), and can be attributed to the following factors all working in conjunction with each other:

  ➔ **demographic ageing, a general rise in life expectancy, and the improved survival chances of afflicted persons.**



Source: Statistics Austria

- By the end of 2016, 40,718 new cancer diagnosis had been documented, fewer than in 2015

  ➔ The risk of a new diagnosis and the risk of mortality both decreased significantly. At the same time, the survival rate for people with cancer increased.
  This is due to improved diagnostics – screening programmes, earlier diagnosis – medical advances, and new treatment methods

- The most common types of cancer in women relate to the breasts, stomach and lungs
- The most common types of cancer in men relate to the prostate, lungs and stomach

In an international comparison, cancer mortality rate in Austria has declined significantly: according to the latest calculations from a Eurocare study for the years 2000–2007, Austria is in 5th place with a comparative 5-year survival rate of 60.1 % (the comparative 5-year survival rate was 51 % for the period 1989–1993).

Comparative 5-year survival rate

in percent

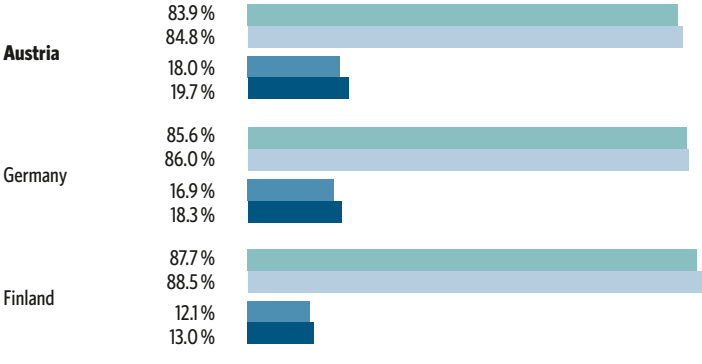
Source: Statistics Austria 2019, Eurocare

This development can be attributed to the following factors: greater health consciousness, especially with regard to nutrition, a reduction in damaging environmental influences, better medical care and advances in treatment.

Source: WHO, Globocan, Statistics Austria, OECD Health Statistics

5-year survival rate of certain types of cancer in comparison with other European countries

Ranked against other European countries, Austria is among the Top 5 countries regarding 5-year survival rates for certain types of cancer.



Source: Concord-3, Global surveillance of cancer survival (The Lancet, 30.1.2018)

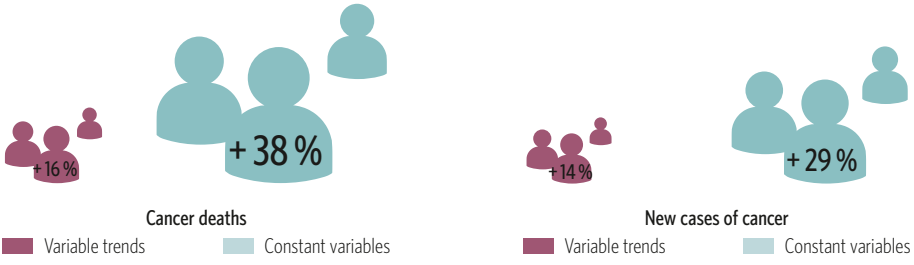
Patients can take part in clinical trials early on and therefore gain access to innovative active substances which increase the chances of curing the disease. About a third of all clinical trials are conducted in the field of oncology. Therefore oncology is the field which is most intensively researched into in the Austrian pharmaceutical industry. This means that on frequent occasion cancer patients have access to medication with innovative active substances from an early stage (see chapter 4.6).

Projection for Austria

According to projections, the number of illnesses with malignant growths will continue to increase. However, thanks to medical advances (increased screening programmes and improved diagnostics), this projected growth is significantly lower than would have been expected due to the demographic development:

- Long-term increase in new cases of cancer according to constant variables (only demographic development considered in projections) + 29 % vs. + 14 % taking medical advances into consideration
- A similar development is shown in cancer deaths which grew by 38 % according to constant variables (only ageing) vs. just 16 % growth when taking medical advances into consideration

Projection 2030



Source: Statistics Austria

4 Pharmaceutical research and development

Research location Austria

Ranked 7th place in the "Innovation Union Scoreboard 2017" published by the European Commission, Austria leads the "Strong Innovators" group; this represents a significant improvement to the previous year – Austria took 10th place in 2016. The proportion of Gross Domestic Product (GDP) spent on Research and Development (R&D) expressed as a percentage is called the research quota. In 2017 the research quota was 3.16 % above the European target value of 3 %. For the last 10 years it has grown continuously (2008: 2.57 %).

In 2018 the research quota is expected to grow again by + 0.03 % to 3.19 % (as of April 2018)*.

- The largest proportion of the research expenditures (amounting to Euro 12.34 billion) was incurred by companies, taking up 49.5 %
- 34.6 % of spending was provided by the public sector, and
- 15.8 % from abroad.

In particular the domestic pharmaceutical industry in Austria contributes to the added value with research tasks. In 2015, Euro 294 million were invested by the pharmaceutical industry in Austria for research and development**.

In addition to excellent universities, Austria has outstanding and internationally recognised research institutes in the field of Life Science, such as the Research Institute for Molecular Pathology (IMP), the Institute for Molecular Biotechnology (IMBA), or the Research Center for Molecular Medicine (CEMM). Since 2008, there is also Europe's first "Research Center Pharmaceutical Engineering" (RCPE) located in Graz, whose aim is to optimise product and process development in the pharmaceutical industry. Austria is also the location of the European biobanks research infrastructure which is aimed at connecting existing and future biobanks in Europe in order to facilitate access to biological samples for research. In 2014 the Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC), located in Graz, has become operational.

* Austrian Research and Technology Report 2018
** EFPIA The Pharmaceutical Industry in Figures 2018

4.1 Active substances

As soon as a new active substance candidate has been identified, it is developed further on a broad scientific basis. In order to ensure continued economic exploitation, a patent is generally taken out for an active substance after it has been identified. The patented active substance then goes through several stages of clinical research.
The following categorisation of active substances is based only on the primary classification of investigational medicinal products in accordance with the EudraCT form used for the submission of clinical trials without further pharmacological differentiation.

Active substances of chemical origin

Chemical substances are natural chemical agents or products obtained through chemical synthesis. Simple chemical medicinal products frequently have a moar mass of no more than 1,000 g/mol. They make up the lion's share of the medicinal products approved in recent years.
They include medicinal product groups such as antibiotics, cholesterol-lowering agents (e. g. statins), analgesics (e. g. acetylsalicylic acid) or cytostatics.

- **Generics** (see also chapter 9.4) are copies of originator products that are offered in the market once the patent of the original expires. They may be approved in a pertinent marketing authorisation procedure once a patent or data exclusivity no longer applies for the originator products. Only minor bioequivalence studies are needed to prove the efficacy and safety of conventional generics.

Active substances of biological or biotechnological origin (biopharmaceuticals or biologicals)

Biopharmaceuticals (see also chapter 9.5) are medicinal products produced in genetically modified organisms using biotechnological procedures. As opposed to traditional chemical active substances, biotechnologically produced active substances are complex, high-molecular and large proteins with a moar mass of several 1,000 g/mol, in some cases even up to 500,000 g/mol. Biopharmaceuticals are subdivided into various classes, such as immunomodulators, monoclonal antibodies, enzymes, hormones and vaccines.

- **Biosimilars** are biological medicinal products which are similar to another biological medicinal product ("reference medicinal product") which has already been approved for use. In order to bring a biosimilar on the market, it must be as similar as possible to the reference medicinal product in terms of its quality, safety, and efficacy. Yet also the biosimilar, just like the reference medicinal product, is to a certain extent naturally variable due to the manufacturing process. The active substance of a biosimilar is essentially the same biological substance as the one of the reference medicinal product. Biosimilars can only be similar to the originator product and cannot be identical due to the complex structure of the molecules which are often very large and due to the individual manufacturing process with specific cell lines for each biological medicinal product. Therefore biosimilars are not the same as generic products: Generic products are identical copies of the originator medicinal product which consist of the same active substances to an equal amount.

  Biosimilars adhere to the same regulations of EU-legislation which has determined high standards of quality, safety and efficacy. The authorisation procedure for biosimilars involves a multi-stage clinical testing programme which aims to prove that there is no significant difference in the efficacy and safety compared to the originator product. As a rule, biosimilars are approved for the same indications as the reference medicinal product once the patent for the originator product has expired.

  For many illnesses biopharmaceuticals provide new treatment opportunities (these include rheumatic diseases, cancer, diabetes, multiple sclerosis, ...). The importance of biopharmaceuticals for the treatment of numerous and, in many cases, life-threatening diseases has increased in previous years. Biosimilars have been in use in the European Union since 2006 in clinical practice.The market share of biosimilars has increased in EU member states and has also increased overall in each product category to different extents depending on market access provisions and pricing mechanisms (see chapter 9.5).

4.2 Clinical research

Clinical research means the testing of medication and forms of treatment on people by means of clinical studies. The objective is to prove the effectiveness and tolerability of these forms of treatment and to improve the medical care of future patients. In principle, a distinction is made between clinical trials (intervention studies) and non-interventional studies.

Legal foundations

Every clinical trial in Austria has to be approved by the Federal Office for Safety in Healthcare and needs a positive opinion of the ethics committee. Details on terminological definitions and on the requirements and implementation of clinical trials are set out in the Medicinal Products Act in § 2a and § 28 to § 48.

Within the EU, standardised administrative rules are set out for clinical trials by Regulation 2001/20/EC. However, deviating approaches among different member states in implementing this regulation have led to insufficient harmonisation within the EU. For this reason in Europe the carrying out of multinational clinical trials in particular has proven to be difficult. This should change in the future with the new EU Regulation 536/2014 on clinical trials on medical products for human use. The aim is to standardise and simplify the implementation of clinical trials in Europe by means of a central approval system with standardised applications that will be submitted via a central portal.

Preclinical studies

Before an active substance can be tested in humans, its safety must be proven in cell models (in-vitro tests) and animal models (in-vivo tests). Some tests can be conducted using cell cultures, but most can only be carried out on the entire organism. The animal experiments needed for this purpose are required by law and, in particular, involve pharmacological studies, as well as studies on toxicity, toxicokinetics, and pharmacokinetics.
Preclinical studies are often conducted in suitable animal disease models (e. g. knock-out mice) in order to study the effectiveness of an active substance in vivo. Relevant proof of efficacy can not always be provided and is therefore not mandatory. Only when an active substance concluded positively all preclinical tests it can be used in humans for the first time. This marks the beginning of the development stage called clinical trials.

Clinical trials

Thanks to the willingness of many volunteers, new medication can be developed on an ongoing basis, in order to ease the suffering of many patients and provide hope in cases of severe illness. But by participating in a clinical trial, many patients also receive the opportunity to have early access to innovative and in some cases life-saving medicinal products – often many years before these are available on the market. However, each clinical trial also carries a certain risk. Therefore, every person involved does everything possible in order to keep the risks to participants in a clinical trial to an absolute minimum. For this reason, clinical trials for the development of new medicinal products are carried out with the greatest care and under strict conditions. One essential prerequisite of every clinical trial is that participation is always voluntary and may be ended at any time.

The sequence of the individual clinical phases

The relevant information for the marketing authorisation of a medicinal product is collected in phases I and IIIa of the clinical study. Further testing conducted after submission of an application for marketing authorisation or after the authorisation has been awarded (e. g. long-term studies of influencing factors of the course of illnesses or detailed investigations on pharmacokinetics with renal or hepatic insufficiency patients) is implemented in the so-called phase IIIb or phase IV studies.

- **Phase I: Testing of pharmacokinetics**

  In Phase I, the medicinal product is administered for the first time in order to determine its behaviour in a healthy person (so-called "first-in-man" studies). Objective: information regarding tolerability, resorption, elimination and any metabolites. Phase I testing is conducted with a limited number (10 to 50) of healthy persons. Healthy trial participants are preferred because the pharmacokinetics of the substance under examination should not be distorted by pathological conditions. However, if the active agent is expected to have any toxic properties (such as substances used for oncological diseases), only persons with the respective disease are included in Phase I trial.

  In order to reduce the risks to the trial participants to a minimum, especially in Phase I trials, a special EU directive was adopted in 2007. It stipulates that every Phase I trial must be based on a thoroughgoing risk analysis, in order to categorise high-risk products and take the necessary measures. It is also essential that a new substance

must not be administered to a number of persons simultaneously. Close diagnostic monitoring must be safeguarded for every single trial participant, and emergency intensive care must be on stand-by at all times.

- **Phase II: Ascertaining the dosage**
  In the next stage, the controlled phase II test, the substance's pharmacodynamic effect is examined. Objective: to ascertain the therapeutic dosage and obtain a biological signal proving the efficacy of the substance. Moreover, the aim is to obtain information regarding tolerability and any interactions. In this phase, the group of trial participants with the relevant illness consists of 50 to 200 patients. The trials are generally controlled, i. e. they include a control group and are double-blind trials (neither physician nor patient know whether the active agent or control is administered). This is intended to prevent any influences on treatment results.

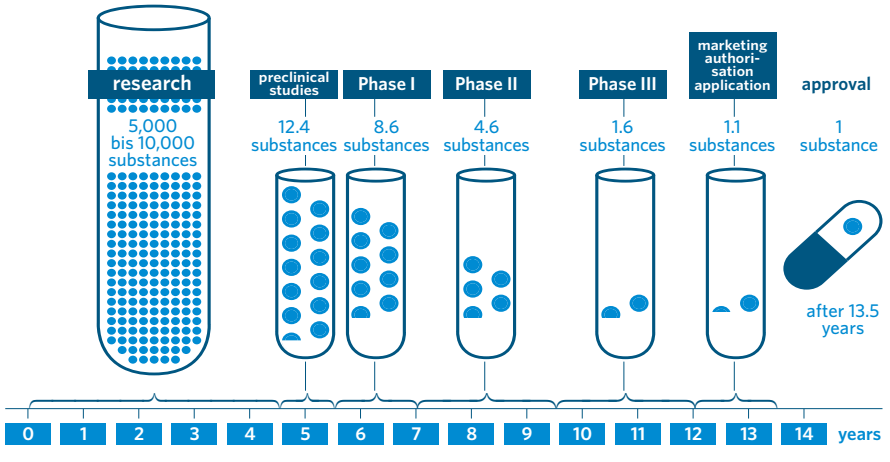
- **Phase III: Establishing the therapeutic efficacy**
  Unlike the previous phases, the test in phase III is carried out on a large group of patients (with the relevant illness). The size of the patient group is determined depending on the indication in order to ensure reliable proof of the effectiveness and to detect any rarely occurring side effects. The duration of treatment of the individual patients in the course of the clinical trial depends on the illness; in the case of chronically progressing disorders, the treatment may even last several years. As a rule, these multi-centre trials are conducted in several countries at the same time (multinational) in order to keep the duration of the overall trial as short as possible. The phase III trials are controlled and double-blind in nature just like the trials in phase II. Once phase III of the clinical trial has been positively concluded, an application can be submitted to the appropriate authorities for authorisation of the medicine.

- **Phase IV: Clinical trial after authorisation**
  In this phase, conducted in the form of a clinical trial, further data is collected after marketing authorisation has been granted. The trials in phase IV are subject to the same conditions as the clinical trials in phases I through III.

Non-interventional study (NIS)

A NIS (e. g. Case-control study, Cross-selectional study, Observational study, Analysis of administrative registers) is the systematic examination of an approved medicinal product administered to patients. The type and duration of the administration correspond to the approved summary of product characteristics and patient information leaflet. Therefore no additional diagnostic, therapeutic or strainful measures may be taken. A NIS is suited for proving the efficacy of a medicinal product in practice and for documenting side effects which have not occured in clinical trials due to limited numbers. Prior to its implementation each NIS has to be reported to the BASG or the Risk Assessment Committee of the Pharmacovigilance (PRAC).

Development phases of a medicinal products



Source: Paul, S.M., et al.: Nature Reviews Drug Discovery 9, 203–214 (2010)

Development costs

Drug developing is a high-risk process: on average, only one in between 5,000 to 10,000 initial substances is actually approved in the end. According to recent studies, the average cost of developing new, innovative medication is up to US$ 2.6 billion (DiMasi et al. 2016). These costs include the direct costs for developing the medication, the associated failures and the opportunity costs; i. e. the indirect costs of financing such long and cost-intensive development projects. These high costs arise from the documentation and safety requirements for clinical trials and the large number of trial participants required.

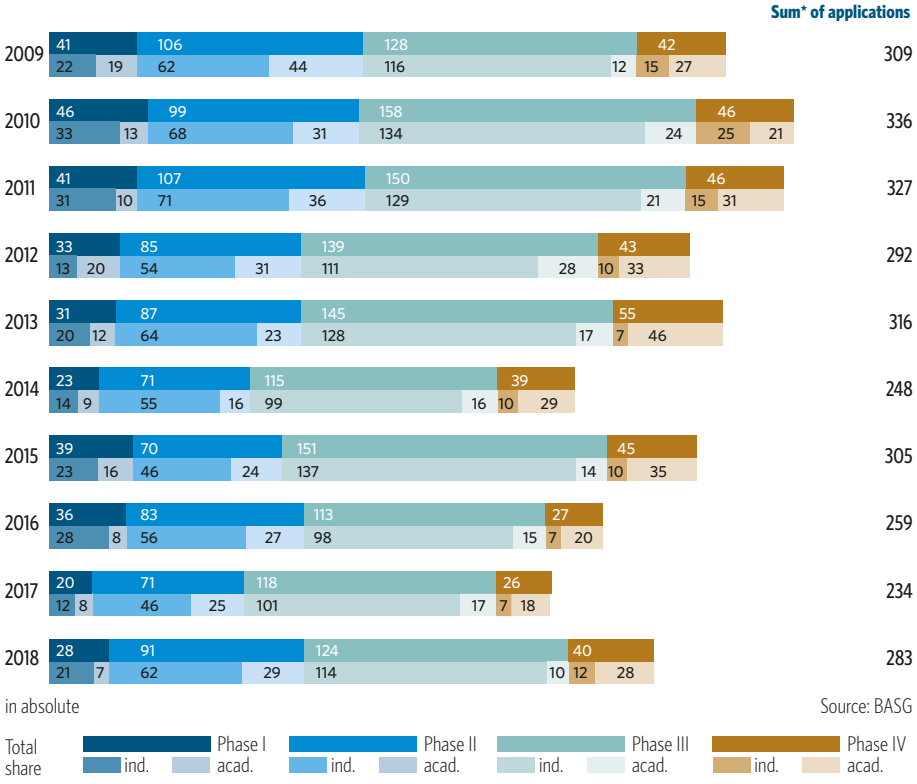
In many cases, it cannot be determined whether active substances are effective enough and whether their side effects are not too onerous until extremely complex multinational phase III studies have been performed. The costs incurred by the many unsuccessful development projects need to be factored in and borne by the companies as well.

Source: EFPIA/PhRMA 2016

Clinical trials in Austria – a statistical overview

In recent years, around 4,400 clinical trials have been applied for annually in the EU/EEA, almost 300 of these in Austria. Overall, applications for clinical trials in Austria have remained constant within the fluctuation range in the years 2007–2011. But a clear decline has been recognised since 2012.
After the low in 2017 fortunately more applications were filed in 2018. The increase can mainly be attributed to commercial studies. The proportion of multi-national studies reached its highest level in 2018.

Distribution of clinical trial applications in Austria according the phases



* Since multi-phase trials (e. g., Phase I/II trials) count twice in this survey, the sum of phases exceeds the indicated sum of applications. The deviations indirectly indicate the number of dual-phase trials.

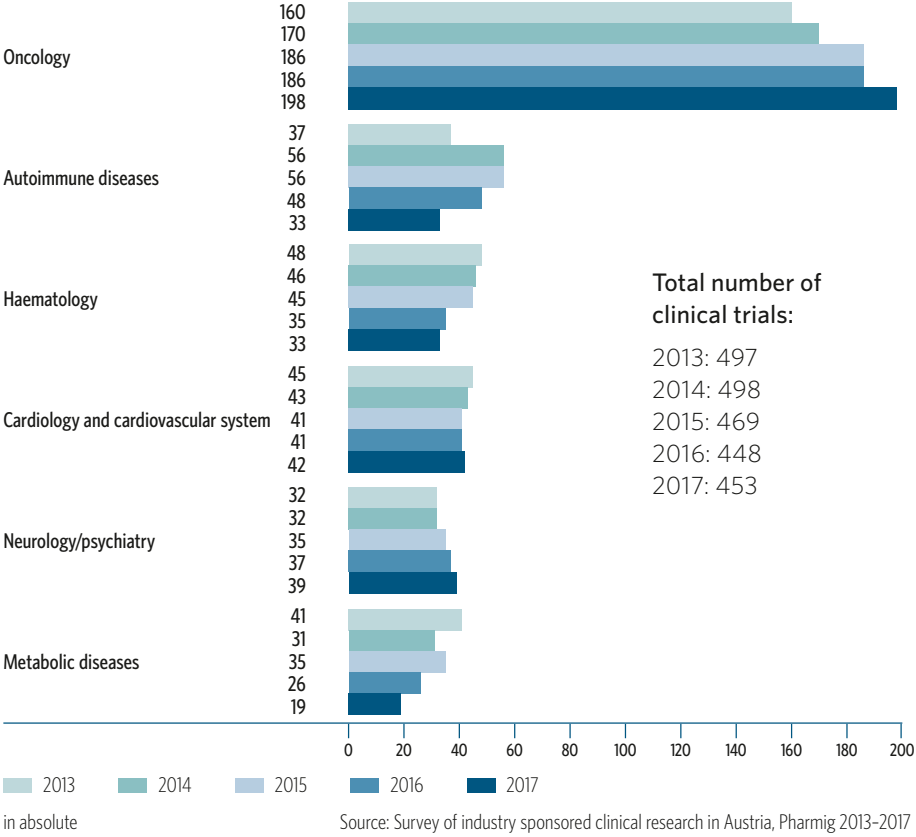
In the EU an average of around 60 % of clinical trials are carried out by the pharmaceutical industry (industry sponsored), 40 % are implemented by academic researchers (academic sponsored). In Austria this ratio lies at 70 : 30 % as an annual average (two thirds of clinical trials are multinational, one third of trials is conducted in Austria only).

Industry sponsored clinical research in Austria 2017

On many occasions clinical trials run for several years after marketing authorisation has been granted. The numbers of ongoing clinical trials per year (incl. clinical trials which are running, which have been initiated and which have been completed) according to the specified indication areas, as well as the number of patients which actively participate in these trials give us an overview of the services of the pharmaceutical industry.

Pharmig carries out an annual survey among the member companies on industry-sponsored clinical research in Austria. Around 35 companies took place in the survey during the past five years retrospectively. This corresponds to a market coverage of approximately 80 % (measured on the sales of all Pharmig member companies).

Ongoing industry sponsored clinical trials according to indication groups

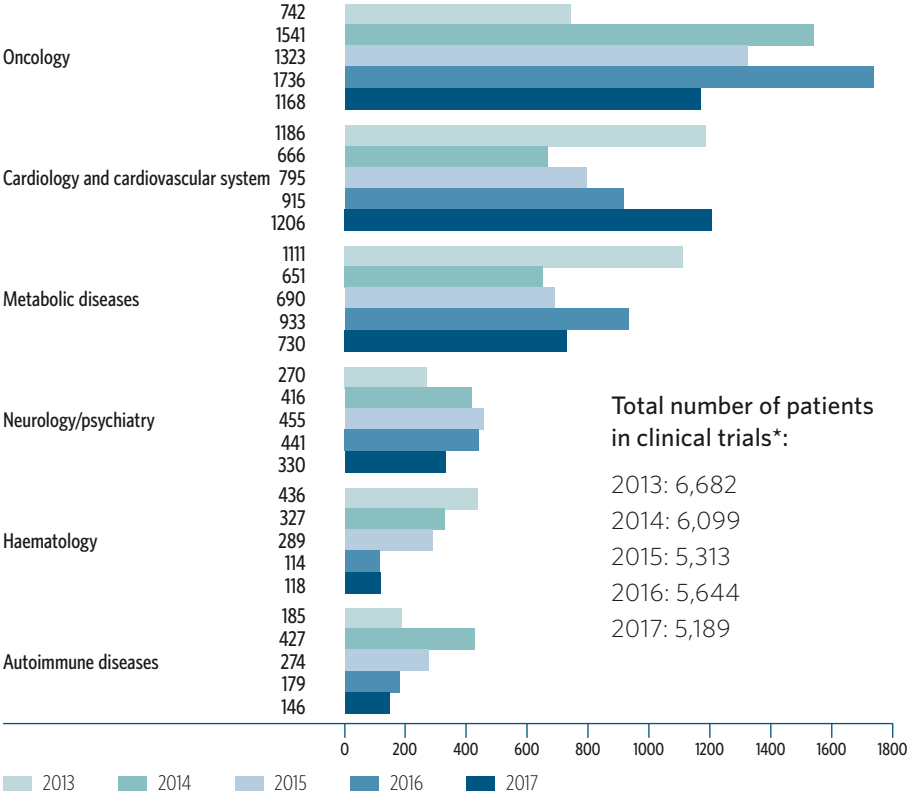


in absolute

Source: Survey of industry sponsored clinical research in Austria, Pharmig 2013–2017

The **total** of approximately **473** clinical trials per year includes all running, started and completed clinical trials

The number of patients in clinical trials according to the most researched indications



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Source: Survey on industry-sponsored clinical research in Austria, Pharmig 2013–2017

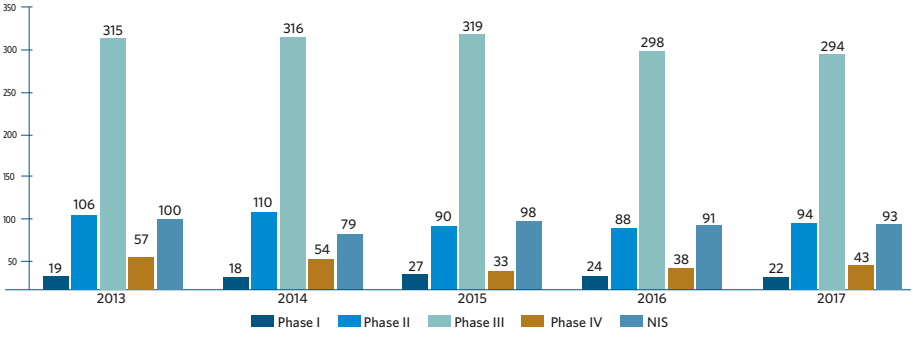
Around 5,800 patients participated annually in ongoing, started and completed clinical trials in Austria*.

* Information on the number of patients is available for an average of 88 % of clinical trials

Number of running clinical trials according to phases and non-interventional studies (NIS) in AT 2013 to 2016

Total number of clinical trials:

2013: 497 2015: 469 2017: 453
2014: 498 2016: 448



in absolute

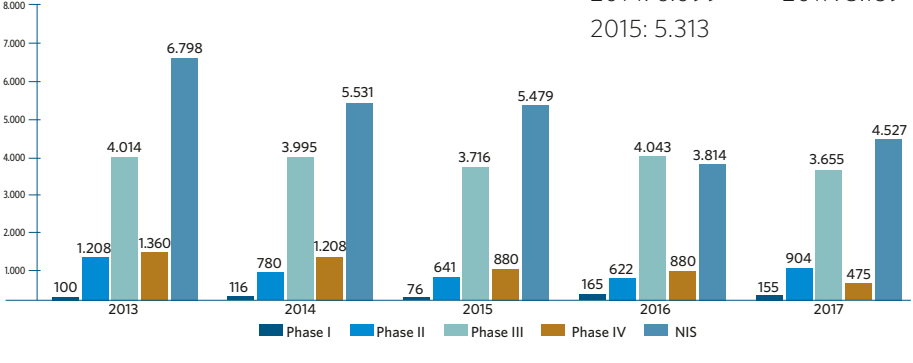
Source: Survey on industry-sponsored clinical research in Austria, Pharmig 2013–2017

Furthermore, through the support of the pharmaceutical industry, on average **138 "investigator initiated trials"** were made possible per year in the years 2013–2017.

Distribution of patients in ongoing clinical trials according to phases and non-interventional studies (NIS)

Total number of patients in clinical trials*:

2013: 6.682 2016: 5.644
2014: 6.099 2017: 5.189
2015: 5.313



in absolute

Source: Survey on industry-sponsored clinical research in Austria, Pharmig 2013–2017

* Information on the number of patients is available for an average of 88 % of clinical trials

Paediatric pharmaceutical research

50–90 % of medicinal products conventionally used in paediatrics are not authorised for children because paediatric trials were considered unethical until recently. However, a sufficient supply of children with medicinal products which have been adequately studied and authorized for use in children, is essential and has therefore been required by EU regulation since 2007.
All new marketing authorizations, changes in the indication, form of administration or composition of the medicinal product must be implemented within the framework of a development plan (Paediatric Investigation Plan (PIP). Clinical trials involving children and adolescents are essential for this purpose.

OKIDS – Child research network

OKIDS is a public-private partnership acting as a network for promoting pediatric studies in Austria (http://okids-net.at). It serves as a central contact point for sponsors of all important stakeholders in pediatric research (pharm. ind., university medical centers, coordination centers for clinical studies, specialty departments, etc.). Together with the Federal Ministry of Health and funds from the "joint health care objectives from the pharmaceutical framework agreement", the following 30 companies have been supporting OKIDS since 2013 with core funding for 5 years.

An important milestone in 2018/2019 was the commitment to a further period of funding from the following 24 companies, including Pharmig, and further funding for the OKIDS network from the "joint healthcare objectives" (2019–2022), which will, among other things, facilitate an expansion of the facilities in Linz.

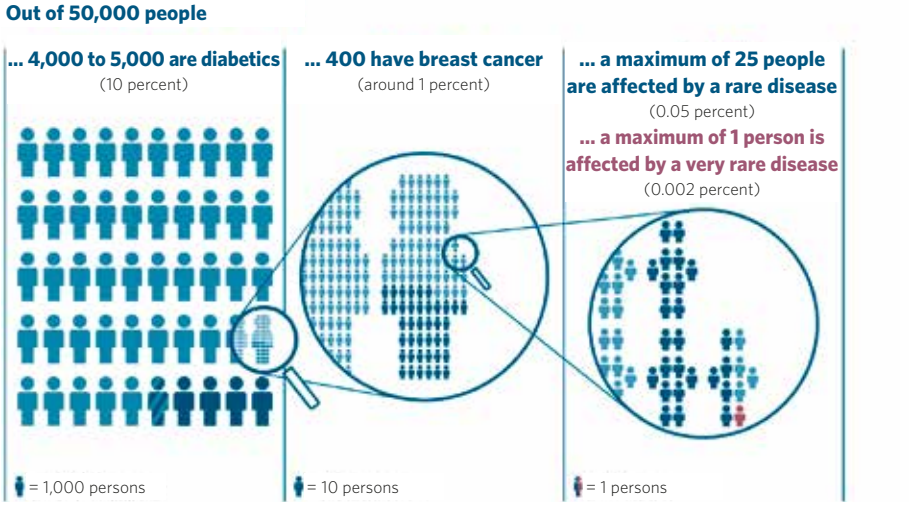
Since its foundation in May 2013, OKIDS has carried out 104 feasibility studies from CROs and pharmaceutical companies, and via Enpr-EMA and c4c (Collaborate Network for European Clinical Trials for Children). In total, 172 studies have been supervised by OKIDS, with the number of patients just under 200 people.
Following its successful admission into the European child research network Enpr-EMA (European Network of Paediatric Research at the European Medicines Agency) and as a project partner for PedCRIN (Paediatric Clinic Research Infrastructure Network) and c4c, OKIDS has taken on important tasks in European structure planning, thereby gaining increasing recognition in the study landscape children's medication in Europe.

Pharmaceutical research of rare diseases

Rare diseases are disorders which are life-threatening or chronically debilitating and which affect less than 5 in 10,000 people (in relation to the European average). Of around 30,000 diseases known to this day, 6,000 to 8,000 count as rare diseases and 50 % of these affect children. In Austria about 400,000 people (i. e. 6–8 % of the population) suffer from rare diseases; within the EU the estimated number of affected people amounts to 30 million.

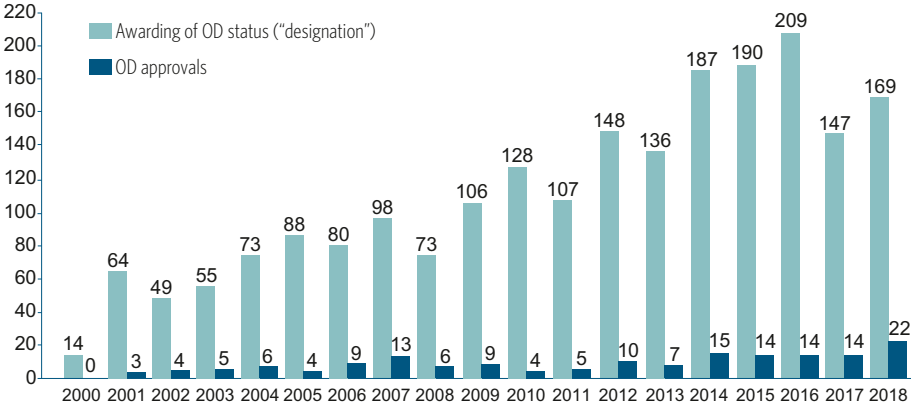
The European regulation concerning medicinal products for rare diseases (EC) No. 141/2000 was adapted in 2000 specifically to promote research and development of medicinal products for rare diseases (so-called orphan drugs) in pharmaceutical companies.Through this regulation the companies are offered reduced marketing authorisation costs, as well as exclusive marketing rights for ten years. The orphan drug status must be requested from EMA at any point during the development of such medicinal product before applying for marketing authorisation.The examination of the authorisation application, in the same manner as with other medicinal products, takes place via the centralised procedure of the Committee of Medicinal Products for Human Use.

What is rare? A comparison:



3,211 applications for orphan drug status were filed from 2000 to 2018. In 2,121 cases orphan drug status were awarded but, so far, only in 164 of these cases marketing authorisation has been granted. The great number of applications (3,211) reflects the high level of research work done in this area and it shows that the incentives offered by the regulation are recognized by the companies. However, the low success rate (164 approvals) demonstrates the high entrepreneurial risks for companies.

Awarding of orphan drug status vs. approval of orphan drugs (2000–2018)



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Source: Committee for Orphan Medicinal Products (COMP) meeting report on the review of applications for orphan designation, December 2018

The national action plan for rare diseases (NAP.se)

The NAP.se was published at the end of February 2015 with the objective of improving the life situation of all affected patients and their relatives. It was commissioned by the Federal Ministry for Health and written by the NKSE (National Coordination Office for Rare Diseases).

The starting point for the plan was drawn up European requirements (e. g. recommendations and guidelines), the national needs survey "Rare Diseases in Austria" (Voigtländer et al 2012), structured exchanges with national experts and current national points of reference such as the framework healthcare objective, the healthcare reform or the children and youth healthcare strategy.

The NAP.se combines plan and strategy, and defines new key thematic focuses that take consideration of both European recommendations and national requirements. A central element is the establishment of centres of expertise and their networking in order to combine knowledge and provide patients with rare diseases with faster and better diagnoses as well as the best possible therapy options. The research and development of new medical products, with the help of networked and combined expertise, is particularly important in the case of rare diseases. It is essential that patient care can continue to be provided near to the home.

The NAP.se and information on the NKSE can be found under the following link: https://www.sozialministerium.at/site/Gesundheit/Krankheiten_und_Impfen/Krankheiten/Seltene_Krankheiten/

Transparency of study data

- The U.S. National Institutes of Health keep the largest public register since 1997. They publish study data from all 50 federal US states and from a further 180 countries:
  https://www.clinicaltrials.gov
- The European Clinical Trials Register (EudraCT) by the European Medicines Agency (EMA) has made study data from the EU, Iceland, Liechtenstein and Norway publicly accessible since 2011. As of 2014, the reports from clinical trials II-IV, as well as all trials which were carried out based on Directive 2001/20/EC, are to be retroactively published:
  https://www.clinicaltrialsregister.eu/
- Non-Interventional Studies which have been commissioned by authorities and which are conducted in several EU member states, so-called PASS (Post Authorisation Safety Studies), must be reported to he EU PASS register of EMA:
  http://www.encepp.eu/
- Full access to clinical trial data has, on the basis of the "EMA policy 0070 on publication of clinical data", been made possible by EMA's centralised approval procedure as of 1 January 2015. Upon completion of the first implementation phase, interested parties can access clinical reports by means of a registration process on the EMA website:
  http://www.ema.europa.eu/ema/ (Human Regulatory Faculty / Clinical data publication)
- Many companies have voluntarily committed to support the responsible use of clinical trial data and also enable full access to their study data. A summary of the principles of this voluntary commitment can be found here:
  http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.pdf
- In the NIS register of the medical market supervision of AGES (Austrian Agency for Health and Food Safety) you can find information on all NIS which have been reported in Austria:
  https://forms.ages.at/nis/listNis.do

4.3 Production and quality assurance

Scope of Pharmaceutical Production

Pharmaceutical production covers the manufacture of the pharmaceutical form of medicinal products (e. g. tablets, capsules, salves, injections, etc.) as well as the production of active pharmaceutical ingredients and the packaging of the final products plus quality assurance.

The manufacture of medicinal products is regulated by national, European and international legislations. Pharmaceutical manufacturers need an authorization by authority which requires dedicated and sufficient space, technical equipment and facilities for quality control. In the European Union a Qualified Person (QP) has to declare that each batch of a medicinal product has been produced and tested according to the specifications and instructions.

GMP – The basic rules of manufacture

Pharmaceutical production has to be performed in accordance to Good Manufacturing Practice (GMP), which specifies a methodical, hygienic, well documented and controlled manufacture.

GMP covers amongst others the following areas:

- Duty of care
- Training of staff
- Facilities
- Separation of production, packaging and storage area
- Testing
- Labelling
- Hygiene
- Quality of materials
- Rules for internal and external audits
- Supplier qualification
- In process controls
- Validation
- Quality Control
- Deviation management
- Change management (change control)
- Complaints and recall

National and international regulations

GMP defines guidelines for quality assurance of the production processes and surroundings when manufacturing medicinal products and active pharmaceutical ingredients. During pharmaceutical production quality assurance plays a central role, because deviations in quality can have direct influence on the health of the consumer.

Relevant guidelines were compiled by the European Commission, by the Pharmaceutical Inspection Co-Operation Scheme (PIC/S), by the US Food and Drug Administration (FDA), or by the "International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use" (ICH). In Austria GMP is transposed into national legislation mainly by the Medicinal Product Site Regulations (german: „Arzneimittelbetriebsordnung", AMBO).

Monitoring of the regulations is conducted by the health authorities of the respective countries. The Austrian Federal Office for Safety in Healthcare (BASG) is the responsible enforcement authority for Austria together with the Austrian Medicines and Medical Devices Agency (Medizinmarkaufsicht) from the Austrian Agency for Health and Food Safety (AGES).

Measures against falsified medication

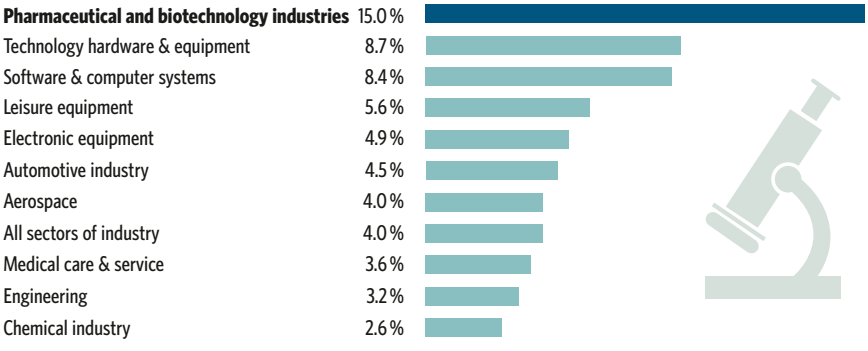
New security features on every pack of medication should make any tampering immediately apparent and ensure the medication is fully traceable from the manufacturer to the pharmacy.

see also chapter 7.2

4.4 Research and development – investments

The healthcare industry (biotechnology, healthcare providers, medical technology and medicinal products) is globally responsible for about a fifth of research and development expenditures.

Research rate, by industry (Europe)



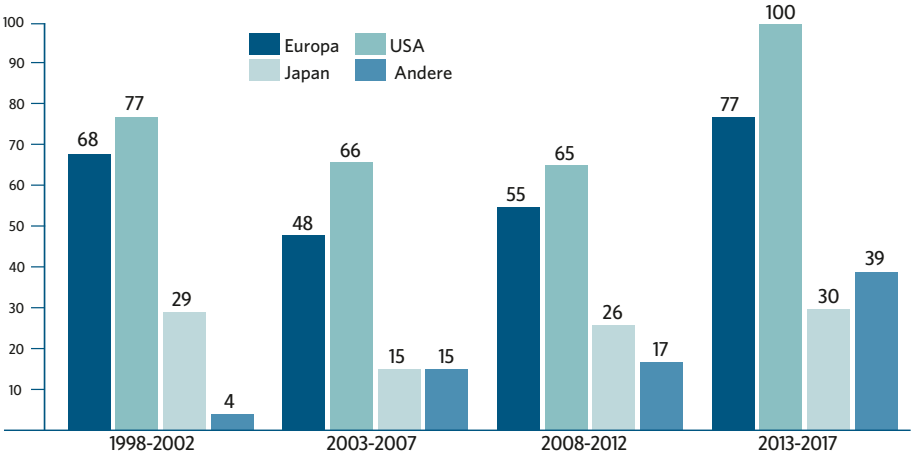
Source: The 2018 EU Industrial R&D Investment Scoreboard

The pharmaceutical and biotechnology industry is in first place in the field of research and development in the EU: Euro 138.9 billion (+ 7.6 % increase to last year) has been invested in research and development since 2017; that corresponds to 15 % of turnover.

With this research quota (= investment in research and development measured in terms of turnover), the pharmaceutical and biotechnology industry is significantly ahead of other industries like hardware, electronics, leisure goods, automotive, aerospace / air defence, etc, and above the EU industry average of 4 %.

4.5 Medicinal product innovations

New molecular entities by region



in absolute

Source: European Commission, VfA, SCRIP/EFPIA, 2017

- In 2018, 84 new medicinal products for human use were approved in Europe (EMA)
- 42 of these contain a new active substance
- The recently approved medicinal products treat cancer, infectious diseases, cardiovascular and inflammatory diseases of the skin, type 2 diabetes, etc.
- New products for treating cancer (just under a third of the new medication), for regulating blood clotting and for fighting bacterial infections are expected to be launched in 2019.

Source: EMA, VfA, IQVIA, EFPIA

Number of innovations in Austria

in absolute

Source: IQVIA DPMÖ incl. direct business, 2018

From 2014 to 2018, an average of 41 new products* were launched on the market in Austria per year (203 in total). The sales share for these new products across the entire pharmaceuticals market (pharmacy and hospital market) was to about 16 % in 2018.

* New Active Substance

Timeline of pharmaceutical developments

1848	Chloroform used as an anaesthetic in surgery
1891	First drug against diptheria, an infection of the respiratory tract that is usually lethal with children: diphtherpia antiserum
1899	Acetylsalicylic acid: analgesic, antipyretic and anti-inflammatory
1910	First antibacterial preparation: salvarsan against syphilis
1922	Insulin used to treat diabetes
1927	Active vaccine against tetanus
1944	Penicillin available as drug
1948	First strong anti-inflammatory: nature-identical cortisone
1956	First antidepressant (iproniazid)
1957/58	First cytostatic against leukaemia (chlorambucil) and lung cancer (cyclophosphamide)
1960	First immunosuppressant, azathioprine, made organ transplants possible
1960	First "pill" for contraception
1963	First vaccine against measles
1976	First inflammation-reducing asthma drug (derived from cortisone)
1980	Successful eradication of smallpox through vaccination
1980	First ACE inhibitor for the reduction of blood pressure
1982	First genetically engineered medicinal product in the German and US market: human insulin
1983	First (anti-)hormone therapeutic agent against the reoccurrence of breast cancer
1987	First preparation against HIV / AIDS
1993	First drug to slows down specific forms of multiple sclerosis (MS)
1996	First three-drug combination to delay the outbreak of AIdS in patients infected with HIV for years
1998	First oral drug for the treatment of erectile dysfunction
1999	Cure for hepatitis C based on a combination of drugs (an alpha interferon + a synthetic virustatic)
2000	First antibody therapy against breast cancer metastasis
2001	First specific drug against chronic myelotic leukaemia
2004	First anti-body preparation against intestinal cancer
2005	First drug to cut off tumour blood supply
2006	First vaccine against cervical cancer
2006	First drug for the treatment of morbus pompe, a rare hereditary disease
2007	First drug against liver cancer
2007	drugs with two new active principles against HIV infection
2009	First trifunctional antibody; for the treatment of ascites in patients with EpCAM-positive tumours
2011	Extending the life of patients suffering from melanoma by administering a drug with new mode of action
2011	High chances of recovery in difficult Hepatitis C (subtype 1 viruses) cases through new antiviral drugs (in combination with PEG-alpha interferon and an older antiviral drug)

2011/12	Enhanced life expectancy with metastatic black skin cancer (melanoma) with medications with new active principles
2012	First gene therapy with approval in industrial nations, for the relief of pancreatitis in patients with a deficiency of the lipid metabolism (LPLD)
2013	First vaccine against meningitis caused by meningococcal serogroup B
2013/14	Medications cure multiresistent tuberculosis with three active principles
2013/14	The chances of curing Hepatitis C over 90 % due to new antiviral drugs in combination with other medications
2015	Medication lowers the mortality of patients with chronic heart failure
2015	Medications, so-called PCSK-9-inhibitors, significantly lower the cholesterol level for patients with an extremely high cholesterol level
2016	First medication against spinal muscular atrophy (SMA)
2017	First medication against primary progressive multiple sclerosis
2017	First cancer treatment with genetically engineered T cells (CAR T cells)
2017	Vaccine against shingles with a very high protective effect
2018	New antiviral drug prevents cytomegalovirus (CMV) infections after a stem cell transplant
2018	Medication with a new effect for haemophilia A patients who have developed inhibitors to factor VIII medication (an antibody)

Source: VFA, excerpt – timeline of pharmaceutical developments
(All the information provided refers to the year in which the medicinal product was first marketed internationally.)

4.6 Achievements of innovative therapies

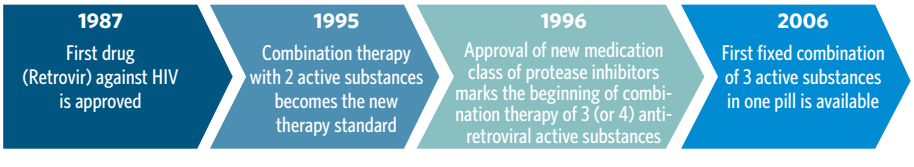
Medicinal products make an important contribution to our society: they help heal, relieve or protect against diseases. Medicinal products help in multiple ways: they relieve the patients of pain and stress and save the health care system and economy costs by reducing the days of sick leave, shortening or avoiding stays in hospitals (replacement for operations). Therefore, medicinal products and medical progress make a significant contribution to a longer life.

The following examples show how innovations in the development of medicinal products can change the entire health care system and what chances they offer – above all saving lives and giving people with diseases more quality of life.

HIV/AIDS

The once fatal infection of HIV became a chronic disease through innovative medicinal products: the mortality rate decreased significantly. Thanks to this development, those infected with HIV can live a mostly normal life and also have a much higher life expectancy than twenty years ago. With the first treatment possibilities, affected individuals still had to take countless pills and the stress caused by side effects was comparably high. In the meantime, there are antiretroviral therapies where the patient only has to take one pill a day.
Around 13,201 people in Austria live with diagnosed HIV, of which 397 were newly infected in 2018.

Important milestones in the treatment of HIV:



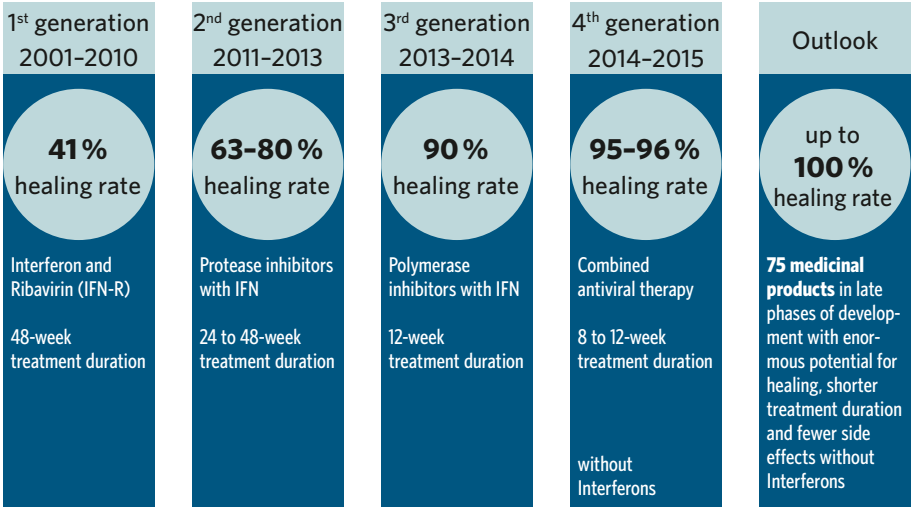
Now there are more than 35 medications available as individual active substances or fixed combinations of up to 4 active substances for HIV therapy.

Source: Aidshilfen Styria, Austria, Germany

Hepatitis C

Due to the often-inconspicuous signs of the disease, hepatitis C patients often do not notice their infection in the beginning. An infection with the hepatitis C virus (HCG) lasting more than six months is identified as a chronic HCV infection. While the only treatment option in the past was a liver transplant in the event of an advanced disease or inefficient treatment, there is now great progress in the therapy thanks to innovative medicinal products: shortened treatment duration (12–72 weeks), high healing rates (no viral load can be traced in the blood any more for more than 90 % of the treated patients), clearly less side effects, no more transplants in an advanced stage.

A chronic disease has become an infection that can be eliminated. This shows that the discussion about costs of innovative medicinal products should never disregard the benefits for the patients and the society.



Source. BPI Pharmadaten 2016

Cancer

In the past 10 years modern cancer treatments have helped patients to increase quality of life and gain valuable time of life. Cancer is increasingly turning into a chronic illness and can now often be healed in some areas. With new diagnostic and therapeutic possibilities the treatment of cancer also becomes easier and easier (see chapter 3.4). Furthermore, affected individuals can actively take part in working life for longer. The mortality-related loss of productivity has decreased throughout Europe by approximately 13 %. Medical progress was achieved over the past years in the treatment of breast, skin and lung cancer.

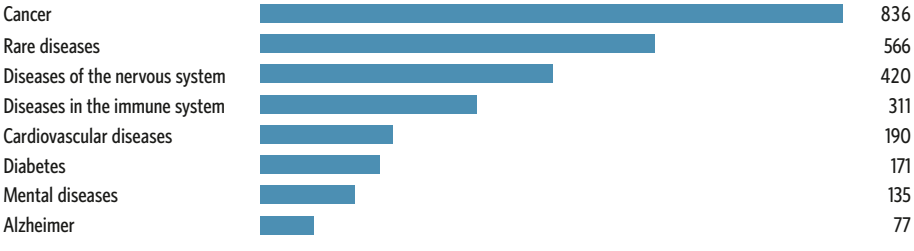
Cancer research and treatment is very different and complex. Today, one assumes that there are more than 250 types of cancer. Factors like form, structure, genetic modifications and molecular properties influence the growth of the tumour.
The use of monoclonal antibodies has also proven itself in therapy and diagnostics. The usage of active substances should support the immune system in detecting and killing off cancer cells.

- 76 new oncological products were registered globally between 2013 and 2017, 61 of them with new active substances or active principles
- 23 new cancer medicines came onto the market in Europe in 2018 – 11 of them with a new active substance
- Numerous new medicines are in development at the moment (see chapter 4.2 Clinical research)

The treatment of cancer diseases accounts for approximately 6.5 % of the total health expenses in Austria. This corresponds with the European trend, which has remained constant at around 6 % over the past 20 years. The cost-intensive hospital sector accounts for nearly 50 % of the expenses. Due to the new therapies, an increasing number of patients can receive outpatient treatment.

Source: IHE Comparator Report 2016, IQVIA 2017, Pharmig Factsheet Onkologie 2016

Currently more than 7,000 medications are being developed throughout the world:



Source: PhRMA, Chart Back, Biopharmaceuticals in Perspective, July 2017

4.7 Patent law

The value of a medicinal product is based on the research and development achievement, which receives special protection as intellectual property. This protection of intellectual property (IP) constitutes the foundation for any research-based company to bring innovative products onto the market.

The development of a medicinal product normally takes 10 to 12years (see chapter 4.2). Due to the long-term commitment of capital, patent protection is one of the most important basic conditions.

Patents have two primary functions:

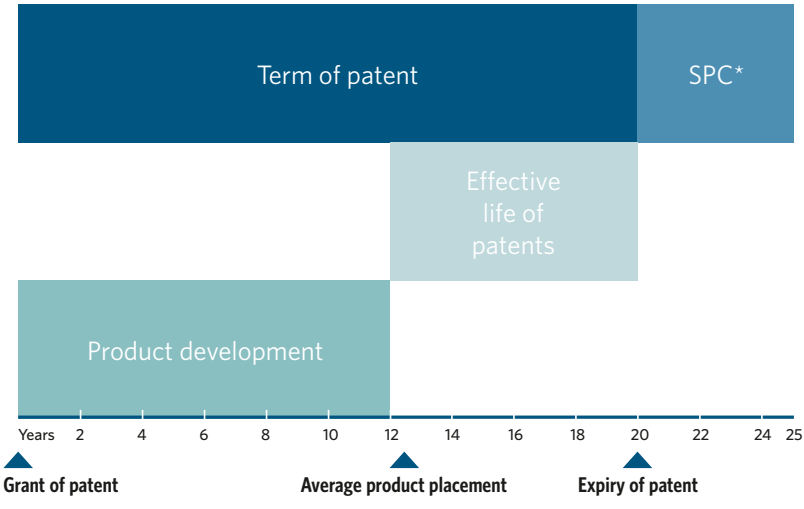
- Inventions are made accessible to the public through publication.
- The economic usage is protected against imitation for a legally defined period of time (in favour of the patent holder, who finances and executes the research and development).

With the patent-holder's consent, other manufacturers can use the patent as well (subject to license fees). Patents also guarantee that there will not be an absolute monopoly. The patent law does give the inventor a limited protection against imitation, however, the patent-holder still has to have their products and procedures prove themselves against other competitors: patent-protected medicinal products compete with medicinal products that are already on the market as well as other innovative medicinal products in the affected indications. A patent does not even illustrate the allowance to use the invention: the usage right is regulated through other laws, like the Medicinal Products Act. Patented medicinal products also have to run through regular approval procedures before they can be brought on the market.

The protective effect of the patent is the best incentive for investments in the area of research and development.

Duration of patent protection

Innovative medicinal products (as all other goods) are protected for 20 years under patent law. However, medicinal products must be patented as the intellectual property of the inventor at a comparatively early stage of their development.



* supplementary protection certificate max. 5 years

Source: Pharmig

From the time a medicinal product is patented until it becomes available to patients, an average of 12 years elapses. This period is necessary for pre-clinical testing and the official marketing authorisation process (see chapter 4.2). Thus, on average, the actual effective life of a patent is only about 8 years.

To extend the patent term, the patent holder (marketing authorisation holder) can apply for additional protection (Supplementary Protection Certificate, SPC) of his invention. The SPC grants an extension of the patent period for up to five years.

The effective useful life of a patent amounts to 8 years on average.

After expiration of the patent protection, other companies may produce and sell medicinal products with the same active substance (generics) or with similar active substances (biosimilars) – see chapter 4.1. After expiration of the patent, original medications can therefore no longer provide a contribution to refinancing research and development costs.

Data exclusivity

Irrespective of the patent protection, what is known as data exclusivity (data protection) has been uniformly provided for across the EU and has been applicable for all marketing authorisation applications since October 30, 2005. Data exclusivity specifies as of when a reference to the documents of an original product is allowed in an application for generics. Generally, this is not permissible until 8 years after the first-time authorisation in the EU. After expiry of another 2 years (i. e. after 10 years in total), the generic medicinal product may be placed on the market for the first time ("8+2 rule").

When the marketing authorisation holder of an original product successfully applies for new fields of application within the first 8 years after the first authorisation was awarded, data exclusivity is extended from 10 to 11 years ("8+2+1 rule").

Particularities in patent protection and data exclusivity

There are several particularities applicable for patent protection and data exclusivity in the EU, which promote the generic industry on the one hand while creating incentives for innovative research in the field of medicinal products on the other.

- **Roche-bolar rule**
  In the EU, studies and investigatory work for patent-protected medicinal products may – for the preparation of documents for generics applications for marketing authorisation – be conducted prior to the expiry of the patent protection already.

- **Pediatric medicinal products**
  Since January 2007, the suitability for children of all new medicinal products in the EU must be verified. New, patentprotected medicinal products which are suitable for administration to children (paediatric medicinal products), may assert an additional 6 months of patent protection. Any medicinal products whose patent protection has already expired, may apply for an additional year of data exclusivity – upon submission of new paediatric data within the first 8 years of data exclusivity.

- **Orphan Drugs**
  Companies can apply for an orphan drug status at the European Medicines Agency (EMA) for the development of medicinal products for rare diseases. Certain criteria determined in the EU Regulation on medicinal products for rare diseases no. 141/2000 must be fulfilled for this purpose. An orphan drug receives ten-year market exclusivity with the approval. This means other orphan drugs for the same rare diseases can only be permitted during these 10 years if they are either more effective or more tolerable or to overcome a supply bottleneck. This offers the approval holder a relative guarantee that they can exclusively sell their medicinal product in a small market for a limited amount of time.

5 Vaccination

Not only can 2 to 3 million lives be saved every year, but many disabilities can also be avoided through the widespread use of vaccinations. Vaccinations have multiple uses:

- they protect the vaccinated from illness – just under 30 illnesses can be prevented by vaccination today
- they reduce the long-term effects or disability resulting from it
- they help the healthcare system to save money by, among other things, reducing hospital stays and costs for doctor consultations

For some illnesses which can be prevented through vaccination, everyone getting a vaccination contributes to protecting the community. If enough people are vaccinated, so-called "herd immunity" is achieved. Then everyone who was unable to get vaccinated (such as vulnerable infants or elderly people) will also be protected. The number of people at which this "herd immunity" is reached differs from illness to illness.

In the long term, at least, epidemics can be reduced, and entire illnesses – such as smallpox or polio – can be repressed or exterminated.

Vaccines – just like all medical products on the market – are monitored for their safety (see chapter 7 Pharmacovigilance).

The vaccination system in Austria

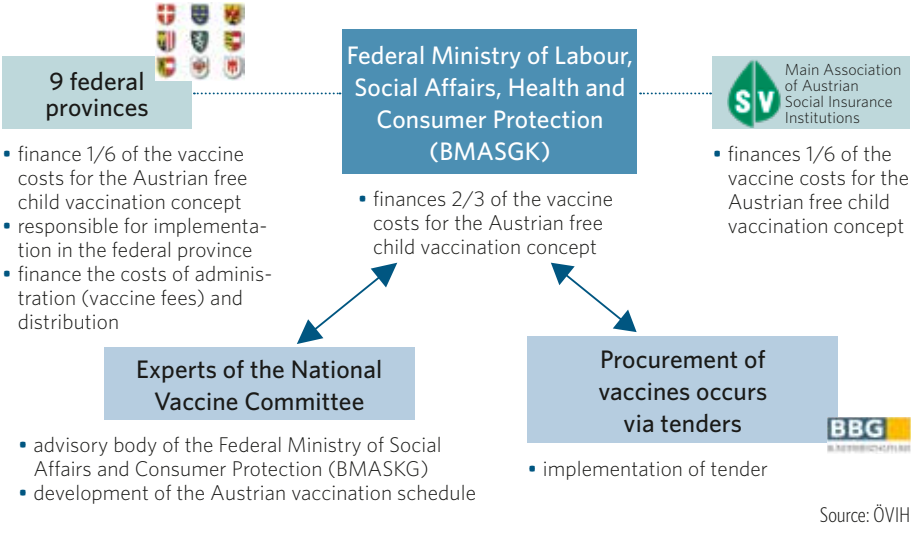
The Austrian vaccination schedule provides an overview of currently available vaccinations. It differentiates between vaccinations which are borne by public authorities within free child-vaccination programmes and those vaccinations which must be self-financed, but are recommended on the basis of scientific evidence. Selected health insurance schemes offer a subsidy for some vaccinations, such as TBE, flu or pneumococci.

You can find the vaccination plan for Austria in 2019 on the website of the Federal Ministry of Health:
https://www.sozialministerium.at/site/Gesundheit/Krankheiten_und_Impfen/Impfen/

Free child vaccination concept

The free vaccination programme of the federal government, federal provinces and social insurance institutions was introduced about 20 years ago. The objective was to enable all children up to age 15 living in Austria access to important vaccinations. Herd immunity with regard to many infections could be attained through this measure. Included in the free vaccination programme are vaccinations against recurrent diseases as well as against rare diseases, if these take a difficult course. Multiple vaccinations reduce the number of administered injections to a minimum.

The financing of the free child vaccination concept breaks down as follows:



Source: ÖVIH

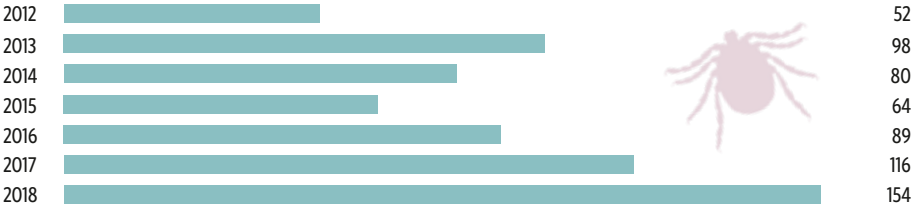
Current examples of important vaccination in Austria

The following examples show the importance of vaccines and vaccination coverage:

TBE (tick-borne encephalitis)

154 cases of TBE were recorded in Austria in 2018. There hadn't been such a high number of cases in more than 20 years. 5 people died from it. According to the Medical University of Vienna (Centre for Virology), the whole of Austria is an endemic area. A survey ("vaccination status survey" from GfK Healthcare) from 2017 showed that 82 % of the participants had been vaccinated against TBE at some point, but only 62 % indicated that they had been completely immunised and had taken the booster vaccination. A good third (34 %) of the population were not adequately protected against TBE. Allowing for the correct vaccination scheme, basic immunisation and booster vaccinations results in near complete (95–99 %) protection.

Number of diagnosed cases of TBE in Austria over the course of time



in absolute

Source: Virology MedUni Vienna

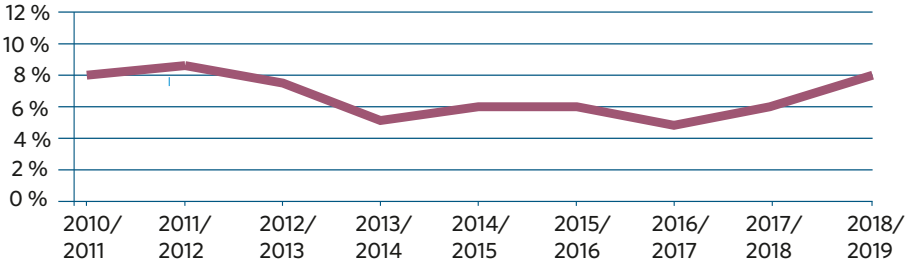
Influenza

According to AGES, there were 1,793 cases of flu and flu-like illnesses per 100,000 inhabitants in Austria at the peak of the flu season in 2018, which lasted almost three months.

- Small children (aged 0–4) fell ill particularly frequently.
- 9 children aged 3–12 died from the flu.
- At the same time, vaccination coverage was particularly low at 6,4 %.

Vaccination appeals are already showing an effect as the vaccination coverage for the 2018/19 season has grown to 7,9 % based on our initial assessment.

Vaccination coverage over time



in absolute

Source: ÖIHV

Measles

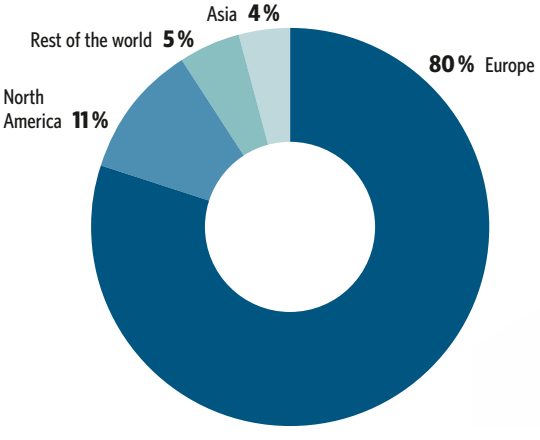
According to WHO targets, measles should be eradicated by 2020. But instead of being close to elimination, it is appearing more frequently. Nearly 60,000 cases of measles and at least 64 deaths were recorded in Europe in 2018. According to the Federal Ministry of Health, there were 77 cases of measles in Austria in 2018.

A vaccination coverage of 95 % with two doses is required for sufficient population immunity. There are vaccination gaps for children aged 2 to 5 and people aged 15 to 30.

European production and vaccine supply

Europe represents the heart of worldwide vaccine research and vaccine production: 80 % of vaccine doses produced worldwide stem from 23 European production facilities. 86 % of vaccine doses produced in Europe are distributed globally. Over 50 % of vaccine doses go to humanitarian aid programmes.

Vaccine production: Number of vaccine doses which have been produced in Europe compared to other regions in 2014



in percent

Source: FactSheet ÖVIH

Since vaccines are biological pharmaceutical products, their production is characterised by complex processes and control mechanisms. The lead time for production is up to two years.

Other challenges for producers are increased regulatory requirements, lack of coordination in the assessment of needs, strictly stipulated purchasing mechanisms (tenders) and an often unforeseeable, worldwide increased need. Due to this complexity there are very few global companies producing vaccines throughout the world. There are seven companies selling vaccines in Austria.

6 Marketing authorisation for medicinal products

6.1 Procedures

Medicinal products may only be placed on the market by the marketing authorisation holder (MAH) after they have been officially approved or registered by the authorities. The legal basis for this approval in Austria is the frequently amended law of 1983 relating to the manufacture and distribution of medicines (MPA, Medicinal Products Act).

The authorisation is granted if the applicant can demonstrate that the expected benefits of a medicine exceed the expected side effects. The proof is provided by submitting pharmaceutical, preclinical as well as clinical data.

There are three different procedures to obtain a marketing authorisation:

- **National procedure**
  The (purely) national authorisation procedure is set forth by the Medicinal Products Act and is only applicable for medicinal products which are to be authorised exclusively for Austria. The Austrian Medicines and Medical Devices Agency evaluates the application while the Federal Office for Safety in Health Care awards the marketing authorisation.

- **Mutual recognition (MRP)/decentralised procedure (DCP)**
  The authorisation procedure is applicable when the medication is to be approved in more than one EU country. This procedure is based on the principle of mutual recognition of marketing authorisations by the Member States. The mutual recognition procedure should be applied for an authorisation already existing in one of the Member States. The decentralised procedure is only applicable when there is no other corresponding authorisation in one of the Member States.
  The applicant is free to choose in which Member State the medicinal product is to be authorised. A basic prerequisite is the positive approval of the authorisation application by all Member States involved in the process. Every Member State shall issue a national marketing authorisation once the procedure has been completed.

- **Centralised procedure (EU)**
  A centralised procedure has been in place since 1995, at the completion of which a European Authorisation is awarded. In a centralised procedure, the authorisation is

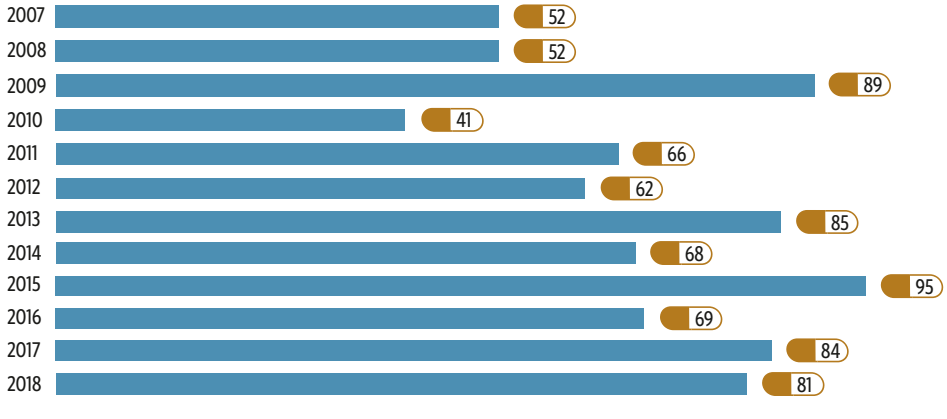
granted by the European Commission and is valid in all EU Member States. Authorisation through this procedure is mandatory for biotechnical medicinal products, medicinal products for advanced therapies, certain veterinary drugs, orphan drugs as well as new substances for the following therapeutical indications:

- acquired immunity deficiency syndrome
- cancer
- neurodegenerative diseases
- diabetes
- auto-immune diseases and other immune dysfunctions
- viral diseases

In this procedure, the evaluation is conducted not by the national authority but by the European Medicines Agency (EMA) headquartered in Amsterdam. Based on the EMA evaluation, the European Commission awards an EU authorisation for all Member States.

Until November 2005, it was differentiated between the compulsory centralised procedure (for all genetically engineered and biotechnical medicinal products) and the voluntary centralised procedure (for innovative substances). In the voluntary centralised procedure, the applicant was able to choose between the centralised and the mutual recognition procedure.
Since the new EU regulation concerning the centralised procedure has taken effect in November 2005, only one compulsory centralised procedure remains applicable for certain medicinal products.

Centralised Procedures for medicinal products in EU



Source: European Commission (per 13.3.2019)

6.2 Requirements for the marketing authorisation

In the case of innovative products or original preparations, the applicant for authorisation must submit to the authority a complete dossier (documents and study results for pre-clinical and clinical as well as medicinal product data).
For generic medicinal products (me-too products to be placed on the market after the expiry of the patent or after expiry of data exclusivity of the original preparation), the applicant for authorisation must submit only a portion of the pharmaceutical data – applicants for generics are therefore exempted from a large part of the requirements to be met by an original preparation in the authorisation procedure. Instead, the applicant for a generic medicinal product can revert to the available data of the original preparation. One therefore speaks of a "referring authorisation". This exemption markedly reduces the time until approval of the marketing authorisation.

In the approval procedure, the following is also established:

- Compulsory wording of the summary of product characteristics (for physicians, pharmacists and other specialists)
- Compulsory wording of the patient information leaflet (for patients and other laymen)
- Labelling of the outer packaging
- Prescription status (information on whether the medication requires a prescription or not)
- Distribution channel (e. g. to be sold only at pharmacies, required refrigerated transport, etc.)

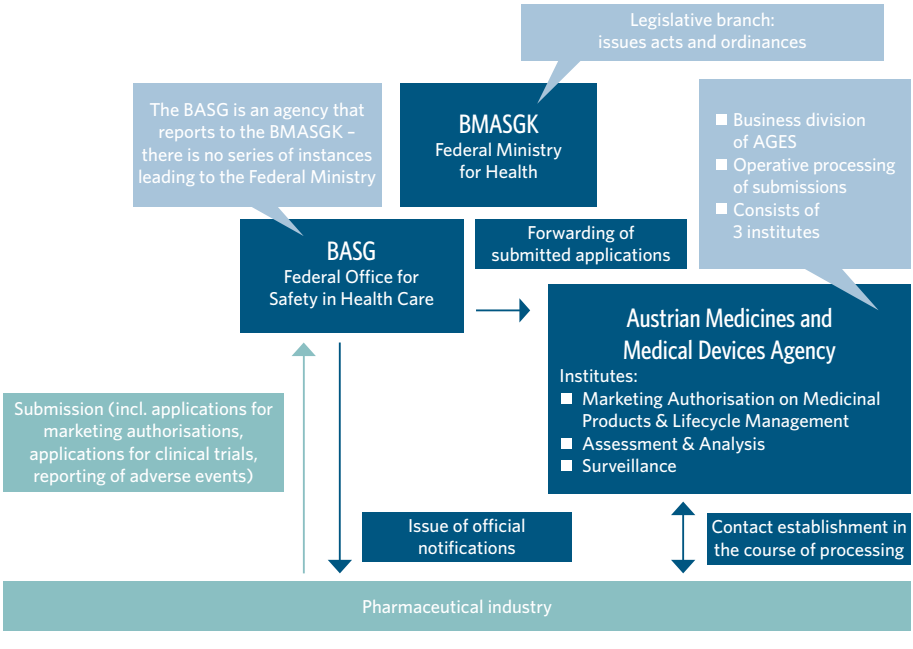
If a pharmaceutical is approved according to the MPA, it is designated as a proprietary medicinal product.

Competent authorities in Austria

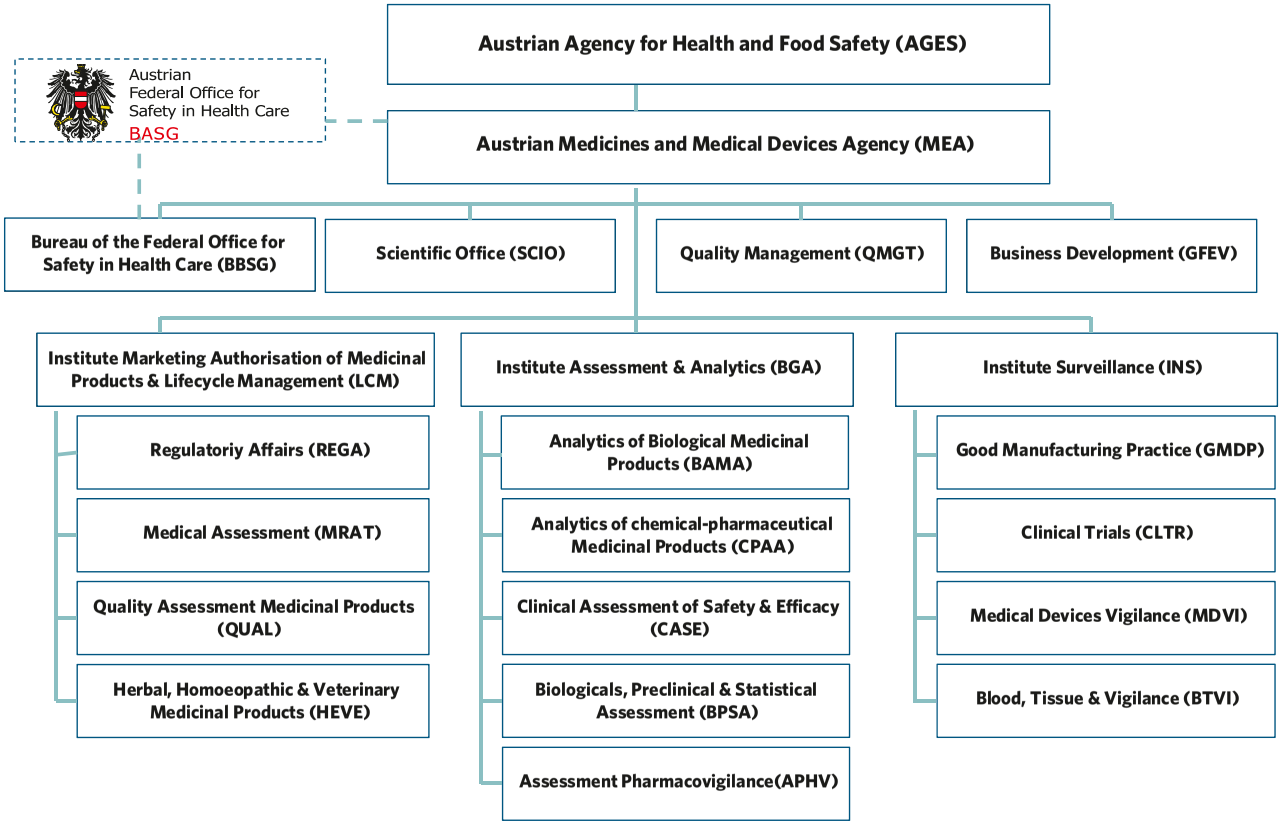
Until the end of 2005, marketing authorisations for medicinal products were granted by the Federal Ministry for Health – starting in January 2006, the Federal Office for Safety in Health Care (BASG) took on this sovereign responsibility. The operative performance of the pharmaceutical and medicinal product system (incl. authorisation, pharmacovigilance, blood safety, inspection system, clinical test) was also shifted from the responsibility of the Federal Ministry for Health and Women to the Austrian Medicines and Medical Devices Agency. The legal basis for this extensive reorganisation is the Health and Food Safety Act (GESG – Federal Law Gazette I 139/2006).

The Austrian Medicines and Medical Devices Agency is one of the 6 business divisions of AGES (Agency for Health and Food Safety) – a private services company owned by the Federal Ministry of Labour, Social Affairs, Health and Consumer Protection and the Federal Ministry of Sustainability and Tourism. The Federal Office for Safety in Health Care was set up to support the Austrian Medicines and Medical Devices Agency. The Federal Office for Safety in Health Care (BASG) is a federal office responsible for the implementation of state-conferred responsibility (e. g. issue of notification). The operational level is represented by the Austrian Medicines and Medical Devices Agency with its 3 institutes.

Drug regulatory affairs were moved to the Austrian Medicines and Medical Devices Agency of AGES to achieve, among other things, faster processing of applications with the goal of more rapid access to pharmaceuticals.



Austrian medicines and medical devices agency of AGES – organisational chart



Status: January 2019

Source: AGES

6.3 Number of medicinal products

Total number of approved medicinal products for human use 2018

Approved medicinal products for human use	9,287
Biological medicinal products	378
Homeopathic medicinal products	606
Medicinal gases	35
Herbal medicinal products	196
Radioactive pharmaceuticals	48
Chemical medicinal products	8,010
Medicinal products that represent a monography of the ÖAB/Ph.Eur*	14

* § 9c Medicinal Products Act

Source: Austrian Medicines and Medical devices Agency

Number of registered medicinal products for human use 2018

Registered medicinal products for human use	3,964
Pharmacy-proprietary medicinal products	708
Homeopathic medicinal products	2,979
Traditional use registration for herbal medicinal product application	208
Allergen manufacturing procedure	69

Source: Austrian Medicines and Medical devices Agency

6.4 Prescription status (human medicinal products)

The prescription status of the medicinal products is determined during the authorisation procedure. The Prescription Act together with the Austria's Prescription Ordinance (Rezeptpflichtverordnung) are the legal basis for this decision.

Source: Austrian Medicines and Medical devices Agency

Around 31 % of the medicinal products for human use approved in Austria are available as non-prescription medicinal products in pharmacies.

7 Pharmacovigilance

Pharmacovigilance is the science of, including the activities related to, the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem, e. g. abuse, misuse and quality defects.

Underlying objectives of the applicable EU legislation for pharmacovigilance are:

- preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure; and
- promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public.

Pharmacovigilance is therefore an activity contributing to the protection of patients' and public health.

Pharmacovigilance system

The Pharmacovigilance system is uses by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Title IX of Directive 2001/83/EC. It is designed to monitor the safety of authorised medicinal products and detect any change to their benefit-risk balance, i. e. the evaluation of the positive therapeutic effects in relation to the risks relating to the quality, safety or efficacy of the medicinal product.

7.1 Pharmacovigilance after approval

The European regulatory authorities decide on the approval of medicinal products after they have assessed the results of laboratory tests and clinical trials. Only those medicinal products whose benefits are proven to outweigh their risks reach the market. This guarantees that patients have access to the treatment they need, without being exposed to inacceptable adverse effects. In general, a limited number of patients participate in clinical trials for a defined period under controlled conditions.
Under real conditions, a larger and more heterogeneous group of patients will use the medicinal product. They may suffer from various different illnesses, and may also take other medicinal products.
Some less frequent adverse effects may occur only when a large number of persons uses a medicinal product over a long period of time.

It is therefore essential that all medicinal products placed on the market continue to be monitored for safety. Since the beginning of 2011, the additionally monitored medicinal products include newly authorised drugs as well as those for which the regulatory authorities require further studies, e. g. on long-term use or rare adverse effects that were observed during clinical trials.

The black triangle

The European Union has introduced a label for medicinal products, which will be monitored especially closely. On their package insert, these medicinal products shall carry a black triangle, standing on its apex, together with the following brief sentence:

▼ **"This medicinal product is subject to additional monitoring".**

All medicinal products are monitored carefully after their introduction to the EU market. Medicinal products labelled with the black triangle shall be monitored even more closely. This can occur if there is less information available than for other medicinal products, for example because it is a new product on the market. It does not mean that the medicinal product is unsafe.

Costs of pharmacovigilance

The industry has to make considerable efforts in order to meet legal obligations regarding pharmacovigilance. These include the installation of their own pharmacovigilance systems, the reporting of suspected adverse reactions, literature research, signal detection, and the compiling of periodic safety update reports (PSURs). In addition, there must be an ongoing technical connection and provision of information to official databases.

Amendments to the European pharmacovigilance laws in 2012 brought an increasing shift in administrative tasks in the area of drug monitoring from the member states to the European Medicines Agency (EMA). This was accompanied by a large increase in fees. As well as an annual fee for the maintenance of the EMA IT systems, additional five- to six-figure procedure-based fees are charged for PSURs, post-authorisation safety studies and pharmacovigilance-related referrals.

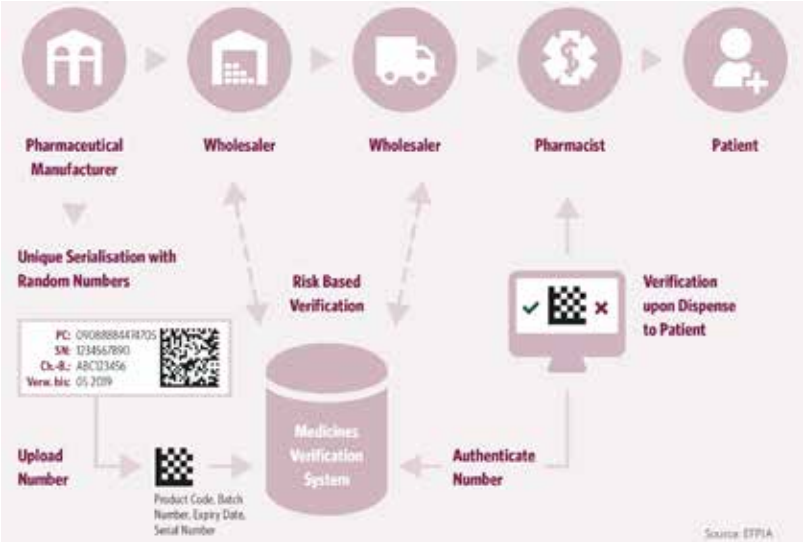
It is estimated that an average pharmaceutical company with a wide range of active ingredients could pay up to 20 million Euro annually in pharmacovigilance fees alone.* Since the monitoring of the medicinal products market is part of the general tasks of the EMA and national authorities to ensure public health, the European pharmaceutical associations believe that these authorities should be financed in part by the European Community, as is also stipulated in EU medicinal products legislation.

* Source: http://www.biopharminternational.com/extending-scope-pharmacovigilance-comes-price

7.2 Measures for protection against falsified medication

Coding and serialisation of medicinal products

The detailed legal requirements concerning the traceability of medicinal product packaging are defined at EU-level with the delegated regulation 2016/161 on "detailed rules for the safety features appearing on the packaging of medicinal products for human use". This regulation has been effective since 9 February 2019.



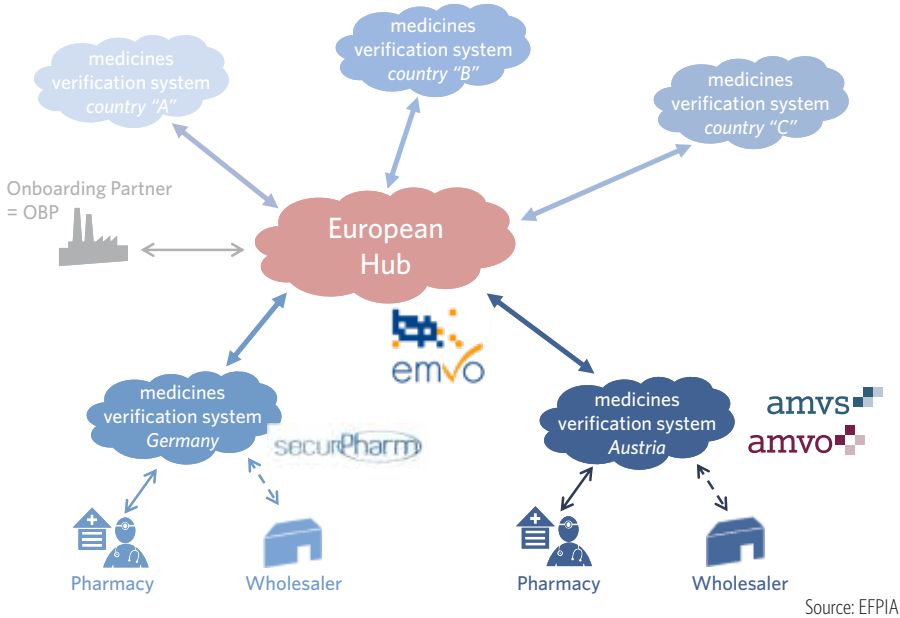
Source: EFPIA

In principle this affects all prescription drugs for human use, exceptions can be found in Annex 1 and Annex 2 of the regulation. All medicinal products must be equipped with a unique, randomised serial number, which will be encrypted in a two-dimensional barcode (Data Matrix), together with the batch number and expiry date. This shall be applied to the packaging by the pharmaceutical industry and entered into a database. While wholesalers must check the code only in certain, defined cases (e.g. when buying from another wholesaler or in the case of returned goods), the mandatory checking and deactivation of the serial number must be carried out directly when issuing to the patient (mainly in the pharmacy). When repackaging, parallel traders must replace the safety features with equivalent features and create a link to the original package data. A deactivated serial number means that the package has already been issued. If the name serial number reappears at a later time, this indicates a suspicion of falsification.

The European system of serialising medicinal products

A data storage system was set up for this process. The delegated regulation foresees that system will be set up by the pharmaceutical manufacturers and authorisation holders, with the involvement of the other stakeholders (e. g. wholesalers, parallel traders and pharmacists).

The authorities must be given the opportunity to check and monitor the system. This system, the European Stakeholder Model (ESM), developed by the European associations, foresees that all medicinal products shall be entered by the industry into the so-called "European hub". There, they are then allocated to each national system. If a package cannot be found in a national system (e. g. in the case of individual imports), the hub serves as a data router and forwards the request to the relevant national system in which the number was stored. In this country the serial number is finally deactivated, i. e. the package is booked out of the system. In this manner, all packaging that can be issued in a number of countries (so-called "multi-country packs") can be deactivated in all national systems. The EU hub is operated by EMVO (European Medicines Verification Organisation).



Source: EFPIA

When setting up the national databases, the member states had the opportunity to develop their own national systems or to revert to a prefabricated system (blueprint system). An example for a national system is the SecurPharm model in Germany. This started as a pilot in 2013 and continued running until full operation in 2019.

Implementation in Austria

Pharmig, the Austrian Generics Medicines Association, PHAGO (Austrian Association of Full-Line Pharmaceutical Wholesalers) and the Austrian Chamber of Pharmacists together founded the AMVO, the Austrian Medicines Verification Organisation, in Austria. AMVO was officially registered in the Austrian association register in December 2016 and is responsible for the governance of the medicinal product verification system. In August 2017 the Austrian Medical Chamber joined AMVO. At the same time, the members of the AMVO committed themselves to work together to clear up and handle any cases of suspected fraud. The competent authorities are integrated through the supervisory and control advisory board and can therefore fulfill their sovereign supervising tasks.

AMVO formed its own operating company, AMVS GmbH (Austrian Medicines Verification System) for the technical operation of the Austrian repositories system. AMVS GmbH has to guarantee the perfect functioning of the national system. All affected stakeholders are connected to the system operated by AMVS GmbH in order to fulfil their legal obligations. AMVS GmbH commenced operations in July 2017.

The EU-wide verification system was implemented in all member states on 09/02/2019 as planned. To ensure a smooth start and a high level of care, a six-month stabilisation was introduced between February and August 2019.

8 Pharmaceutical industry as an economic factor

8.1 Pharmaceutical production in Europe

Pharmaceutical production in selected European countries

	Euro million	Euro per inhabitant	estimated population beginning 2016
Switzerland	46,280	5,558	8,327,126
Italy	30,010	495	60,665,551
Germany	29,197	355	82,175,684
Great Britain	22,445	343	65,382,556
Ireland	19,305	4,085	4,726,286
France*	19,040	285	66,730,453
Spain	15,144	326	46,440,099
Belgium	12,812	1,133	11,311,117
Sweden	7,302	741	9,851,017
Netherlands	6,180	364	16,979,120
Hungary	3,050	310	9,830,485
Austria	2,737	315	8,700,471
Finland	1,721	314	5,487,308
Portugal	1,686	163	10,341,330
Greece	895	83	10,783,748
Norway	745	143	5,210,721

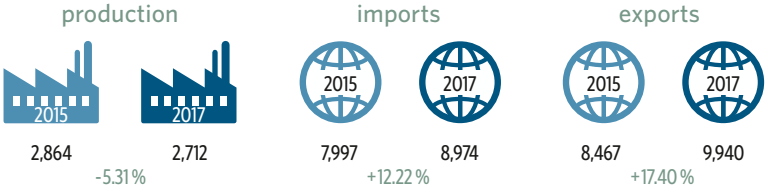
* Estimates

Source: EFPIA, Statistics Austria, Eurostat 2019

In 2016, Switzerland, Germany, Italy and the United Kingdom produced the majority of pharmaceuticals in Europe. Switzerland reported the highest production value per capita and also continued to increase the per capita output in comparison to 2015.

8.2 Pharmaceutical production in Austria

Pharmaceutical production in Austria, imports and exports



in Euro million

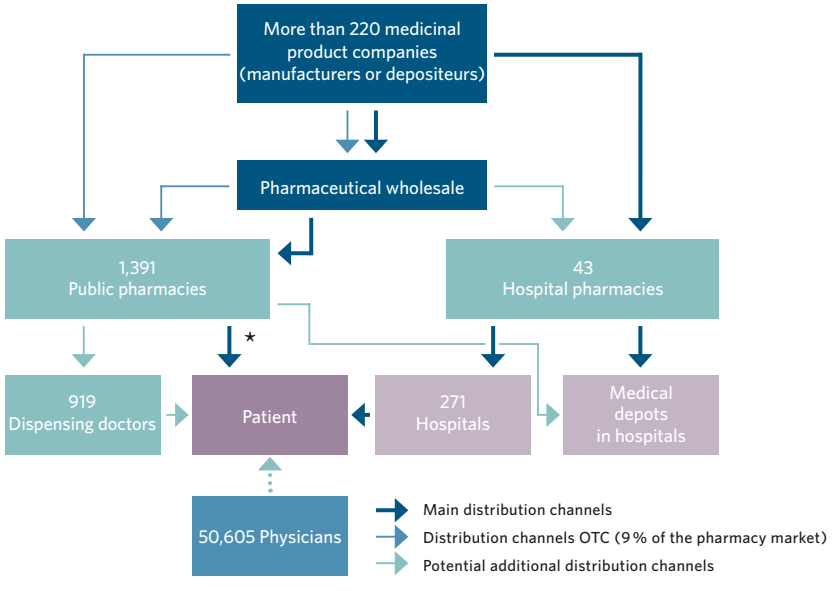
Source: Statistics Austria

In the pharmaceutical industry Austria is among the exporting countries. Despite declining production, more pharmaceuticals were exported abroad than imported in 2017.

8.3 Pharmaceutical distribution

The Austrian medicinal product distribution system

In Austria the medicinal product distribution is covered by the following distribution chain: pharmaceutical companies – pharmaceutical wholesalers – pharmacies – patient



Source: Pharmig, Statistics Austria, IQVIA, HV, BMGF/BMASGK, Austrian Chamber of Pharmacists, 2018

* as of 25 June 2015 also distance-selling for OTC products

About one third of the medicinal products were sold to hospitals, and two thirds to public pharmacies, i. e. the out-patient sector (based on value).

Parallel trade

If a medicinal product is not imported or exported by the manufacturer or marketing authorisation holder, respecitvely, but by a third party which parallel imports/exports the medicinal product by a distribution channel which is not defined by the manufacturer or marketing authorisation holder, we call this parallel trade.
In many EU member states medicinal product prices are directly or indirectly regulated by the respective national government. Therefore it is possible that the prices for a particular medicinal product are different in various countries which makes it attractive for parallel traders to purchase medicinal products in low-price countries and to import them into high-price countries. Due to the EU principle of free movement of goods this parallel trade is legal, however it involves some risks. Manufacturers are not able to calculate the flows of goods, therefore shortages of supply could occur. The law requires that labelling is adapted to the respective national standards, therefore medicinal products are repackaged and a patient information leaflet in the respective national language is inserted. It is not unusual that medicinal products are resold via several intermediaries until they are accessible for the patient on the domestic market. These measures increase the potential that falsified medicinal products enter the legal distribution chain.
For healthcare organisations which resort to these imports cost savings are usually very slight, because the parallel trader benefits from the major part of the price difference.

Distance selling

Distance selling, as defined by the Medicinal Products Act (MPA), is the selling of medicinal products that do not require prescription by a public pharmacy through means of distance communication, e. g. via internet trade.

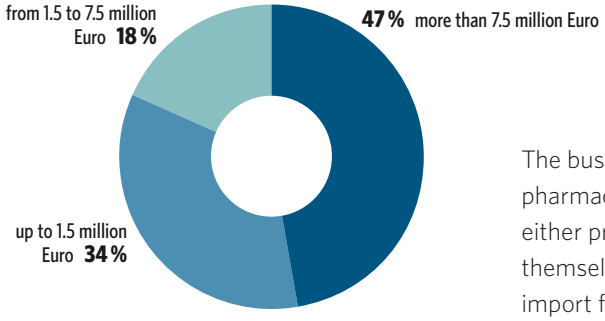
The implementation of the "falsification directive" (2011/62/EU) created a standardised logo for all member states to designate authorised internet pharmacies, leading to the introduction of distance selling, also in Austria.

In the case of orders from an Austrian internet pharmacy, there must be an Austrian flag symbol. Internet pharmacies that operate from other EU countries can also be recognised by their respective flag symbol. Legal internet pharmacies may only sell medicinal products in or to Austria that do not require prescription.

Since 25 June 2015 domestic distance selling is also possible for Austrian pharmacies. The list by the AGES MEA – Austrian Medicines and Medical Devices Agency contains information in all distance selling pharmacies registered in Austria:
https://versandapotheken.basg.gv.at/
Legal provisions are set out in the Ordinance on Distance Selling.

8.4 Company structure

Size of pharmaceutical companies, by turnover



Source: Pharmig, 2018 according to yearly sales of Pharmig members in percent

The business volume of the Austrian pharmaceutical companies that either produce medicinal products themselves (manufacturers) or import finished medicinal products (distributors) to Austria varies greatly.

8.5 Pharmaceuticals sector in Austria

18,000
employees in companies in the Austrian pharmaceuticals industry (63,000 indirect employees)

Euro 9.6 billion
is the pharmaceuticals industry's share in value added (= 2.8 % of the GDP)*

Euro 2.6 billion
invested by pharmaceuticals companies in Austria (2013–2018)

Sources: Haber, G (2016): Life Sciences und Pharma: Ökonomische Impact Analyse; internal publications 2013–2018)

* includes companies involved in the following fields: research and development, sales, supply, production

Every individual company makes a significant contribution to the Austrian economy and provides the best possible healthcare. The interactive map under www.pharmastandort.at visualizes the performance of the industry and shows what companies are constantly working for Austria.

9 The pharmaceutical market

9.1 Pricing for medicinal products

Pricing for medicinal products is regulated by law in Austria. The 1992 Price Act (for all human medicines) and the ASVG (for inclusion in the Code of Reimbursement) form the relevant basis for this. The Pricing Committee of the Federal Ministry of Labour, Social Affairs, Health and Consumer Protection (BMASGK) is responsible for the prices of medicinal products.
The manufacturer's price or depot selling price (MP/DSP) form the price basis of a medicine. The respective mark-ups (wholesaler & pharmacy mark-up – legally regulated by staggered maximum mark-ups) and value added tax are added to this price. The MP/DSP can be freely defined by authorised pharmaceutical company, whereby the BMASGK is informed about this price.

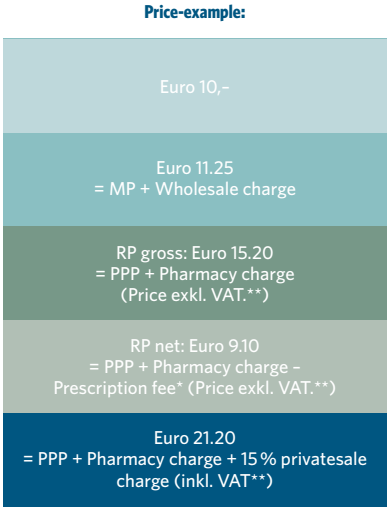
Prices of medicines

- Price ex works (MP/DAP):
  Manufacturer/Depositeur –› Wholesale

- Pharmacy purchase price (PPP):
  Wholesale –› Pharmacy

if reimbursed:
- Reimbursement price (RP):
  Pharmacy –› health insurance

if a private purchase:
- Pharmacy selling price:
  Pharmacy –› Customer

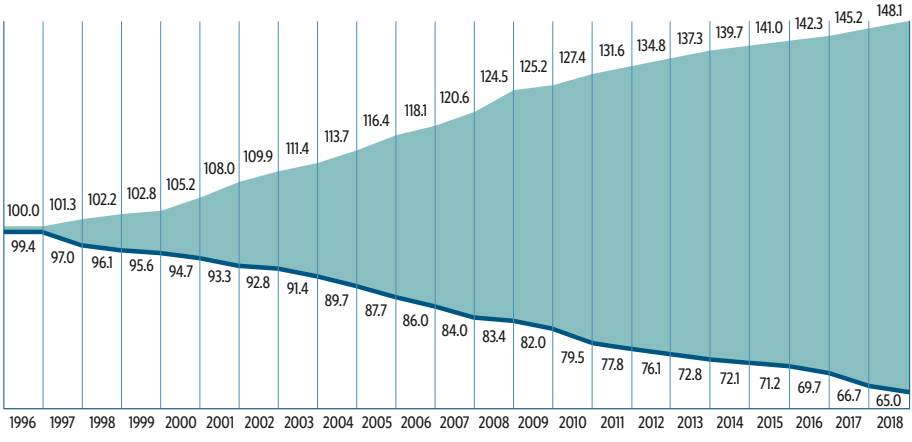


* Prescription fee since 1.1.2019: Euro 6.10; ** VAT. since 1.1.2009: 10 %

Source: Pharmig

- Price ex works: this is a price that a wholesaler pays for a medicine (excl. VAT)
- Pharmacy purchase price: this is a price which a pharmacy pays for a medicine, (excl. VAT)
- Pharmacy selling price: this is a price which a customer pays for a medicine
- Reimbursement price: this is a price which a health insurance pays for medicines, that are reimbursable.

Price trends (based on wholesale purchasing price)



in percent

Source: Statistics Austria, IQVIA

Consumer price index* (annual average). CPI 96 (1996=100)

Pharmaceutical price index** (based on wholesale purchasing price)

* The consumer price index (CPI) is the standard index for general pricing trends and inflation in Austria.

** The pharmaceutical price index (based on wholesale purchasing price) is based on IQVIA calculations and is an element of growth. The pharmaceutical price index incorporates changes in pricing (in per cent) of products which have already been placed on the market in comparison with the previous period. (see chapter 9.2 Elements of growth)

Prices for medicinal products already on the Austrian market have decreased annually since 1996. A fictional pack of medicine costing Euro 10 in 1996 now only costs Euro 6.65 in 2018.

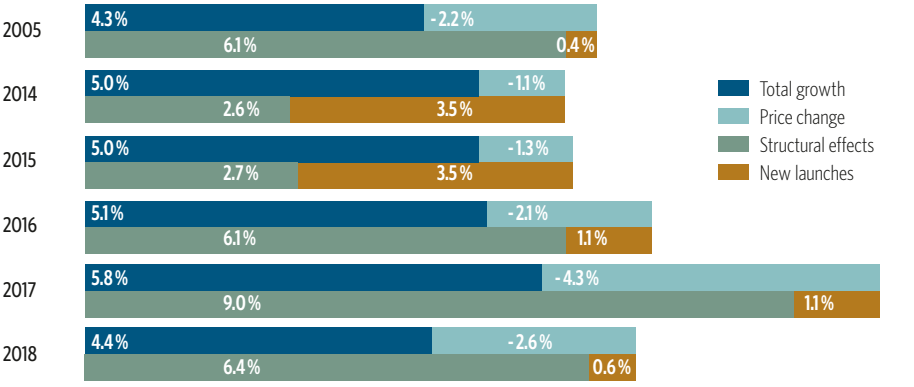
The CPI (consumer price index), however, underwent the exact opposite development.

The divergence between consumer price index and pharmaceutical price index continues year to year. The pharmaceutical price index decreases continuously.

9.2 Elements of growth

The growth of the medicinal product market – amounting to + 4.4 % in 2018 – is influenced by a number of factors:

Elements of growth (based on manufacturer price, MP)



Source: IQVIA

- **Price changes** are changes in the price of a certain product already introduced in the market. **In 2018, this amounts to –2,6 %, thus price drops are lower than in 2017** (- 4,3 % as it was the first time that the price band kicked in – see page 91, chapter 10.3 of the ASVG [General Social Insurance Act] 2017 amendment; section 351c, para. 11)

- **New product launches** include new products containing new active substances in the first year after being put on the market. These products replace previous forms of treatment or make new medicinal treatment possible for the first time.
  In 2018, the influence of new product launches on market growth was + 0,6 % – this is lower then in 2017 when it amounted to + 1,1 %.

- Factors like changes to prescription practices, replacing and expanding previous forms of treatment, new forms of delivery and increases in volume, etc. are merged together under **structural effects**. **In 2018, the structural effects amounted to + 6,4 %** – and were significantly lower compared to 2017 when it amounted to + 9 %.

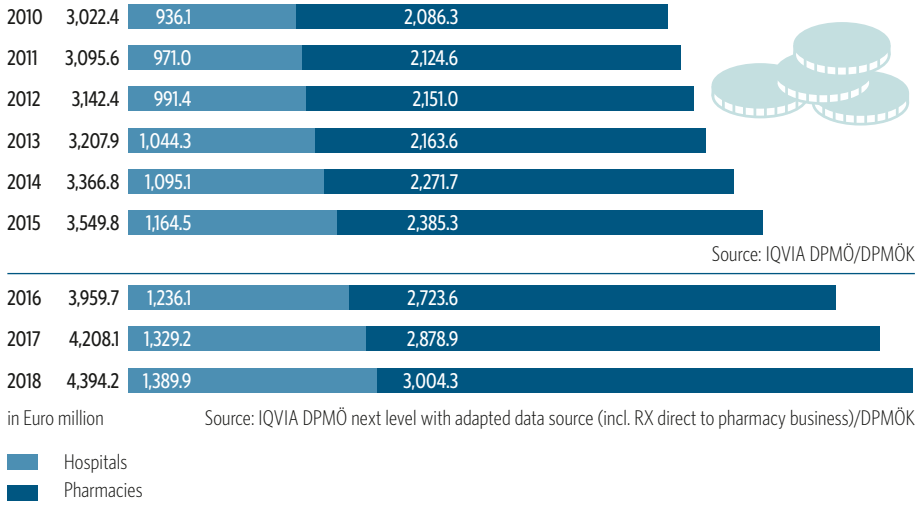
9.3 Hospital and pharmacy market

In 2018, the Austrian medicinal product market reported sales of 4.4 billion Euro and a sales volume of 234 million packages. This represents a growth rate of 4.3 % in value and a growth rate of 0.9 % in volume.

From the perspective of the manufacturers and distributors the medicinal product market is divided into two segments:

- Hospital market (intramural sector)
- Public pharmacies and dispensing doctors (extramural sector)

Pharmaceutical sales (based on manufacturer price, MP*)



Source: IQVIA DPMÖ/DPMÖK

in Euro million

Source: IQVIA DPMÖ next level with adapted data source (incl. RX direct to pharmacy business)/DPMÖK

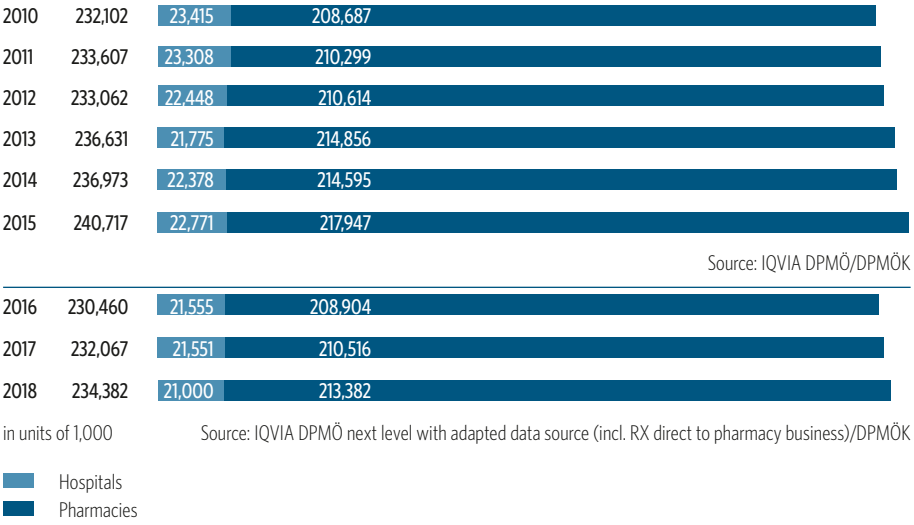
* Not taking discounts and pricing models into consideration

In 2018, compared to 2017, both the pharmacy and hospital market have grown in terms of value, while in terms of quantity the pharmacy market has stayed the same and the hospital market has declined.

- Pharmacy market: + 4.4 % regarding value according to Euro in turnover or + 1.3 % regarding quantity according to packages
- Hospital market: + 4.3 % regarding value according to Euro in turnover or - 2.9 % regarding quantity according to packages

In 2018, 234.4 million packages were sold in Austria. Around 9 % of these went to hospitals (hospital pharmacies) and around 91 % to pharmacies in the extramural sector.

Sold packages



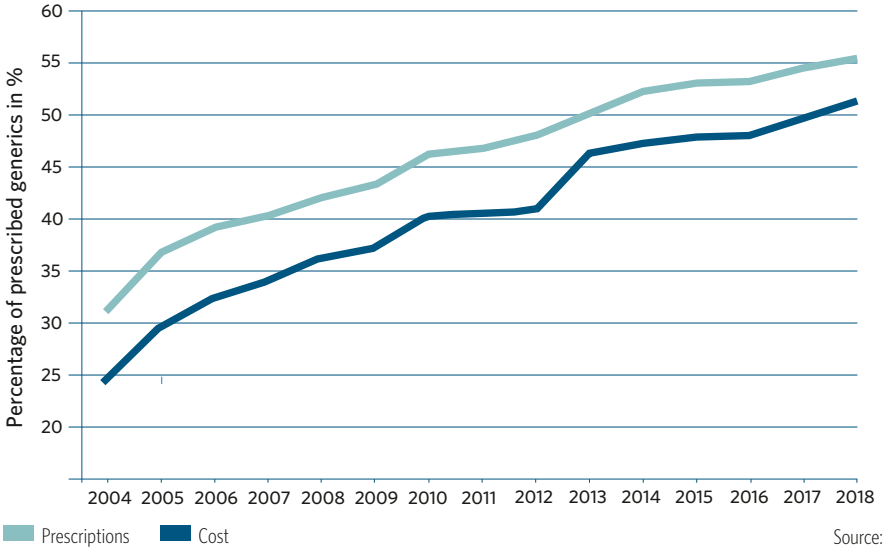
Source: IQVIA DPMÖ/DPMÖK

Source: IQVIA DPMÖ next level with adapted data source (incl. RX direct to pharmacy business)/DPMÖK

In 2018 vs. 2017 the number of sold packages increased by 0.9 %.

9.4 Generics in the reimbursement market

Prescribed generic products in the reimbursement* market



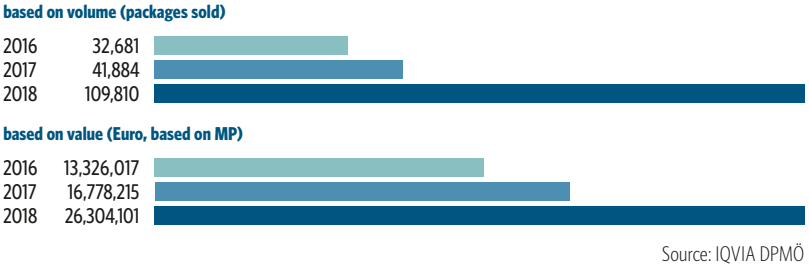
Source: HV

* When calculating the percentage of generics, only the product first added to the reimbursement system (initial supplier) and the products added at a later time (generics) are differentiated.

The percentage of generics in the reimbursement market is about 56 % (according to billing records of the health insurance funds for 2018), this means more than every second prescription is accounted by a successor product and about 51 % of the costs are accounted by successor products on the reimbursable market.

9.5 Biosimilars in the reimbursable market*

Development of biosimilars 2016–2018



Source: IQVIA DPMÖ next level 2018

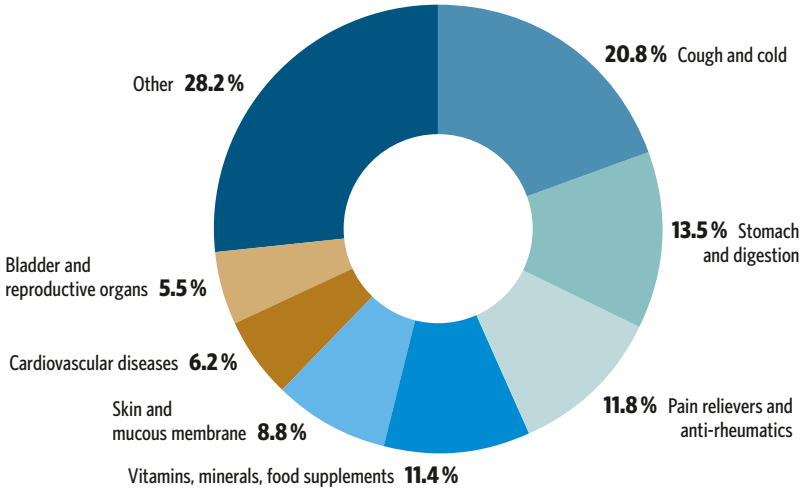
In 2018, the use of biosimilars in the reimbursable market increased by 57 % according to turnover. In terms of quantity – based on volume (packages sold) – the market grew by 162 %.

* Refundable market: IQVIA DPMÖ next level with adapted data collection (incl. direct prescription sales) without selected non-refundable ATC 3 classes G03Am G40E, J07B/D/E, V01A, with non-prescription refundable products

9.6 Self-medication market

The OTC market grew in value in 2018 compared to 2017 by 2.8 % to Euro 878.9 million on the basis of the pharmacy sales price and consists to 53 % of registered and 47 % of non-registered products.

Indication groups in self-medication (based on pharmacy sales price)

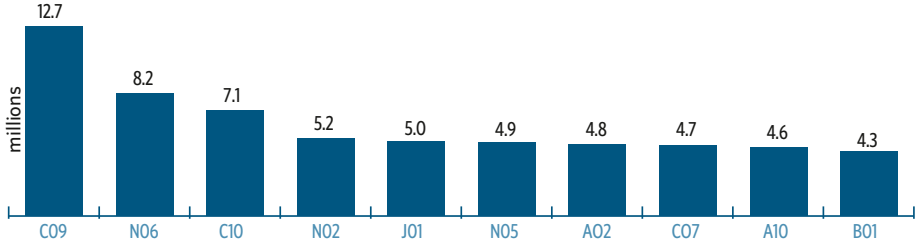


Source: IGEPHA/IQVIA

The Top 3 cough/cold, stomach/digestion and pain relievers/anti-rheumatics, jointly cover 46 % of the self-medication market.

9.7 Pharmaceutical consumption by indication groups

The indications group with the highest prescription share was treatment subgroup ATC level 2*, 2017



C09 Medicine for treating the renin-angiotensin system (e. g. with high blood pressure, chronic cardiac insufficancy)
N06 Psychoanaleptics (treatment of psychological illnesses such as depression, dementia, ADHD)
C10 Lipid lowering medicine (to counter metabolic disorders, e. g. with high cholesterol levels)
N02 Analgetics (pain medication)
J01 Antibiotics for systemic use (e. g. penicillin)
N05 Psycholeptics (for treatment of psychotic illnesses such as psychosis, schizophrenia. Medication for the treatment of sleep and anxiety problems)
A02 Medicine for the treatment of acid complaints (for neutralising stomach acid, e. g. with heartburn, acid indigestion)
C07 Beta-adrenoreceptor antagonist medication (e. g. for high blood pressure, cardiac insufficiency, angina pectoris)
A10 anti-diabetics (medicine against diabetes)
B01 Antithrombotic agents (inhibits clotting)

in packs

Source: HV

* ATC Code: Anatomical Therapeutic Chemical Classifikation System of the WHO

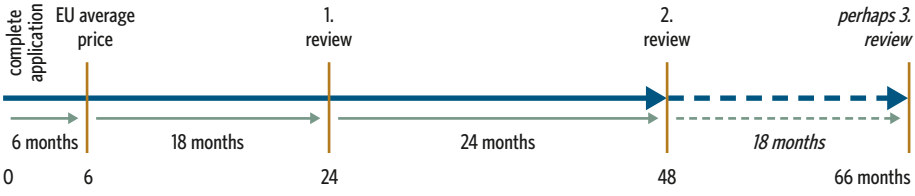
The most frequently prescribed medications according to the ATC system are: Medicines for the treatment of the renin-angiotensin system (e. g. with high blood pressure), medicine for the treatment of acid complaints (e. g. heartburn), psycho-analeptics (for the treatment of psychological illnesses, e. g. depression) as well as agents which influence lipid metabolism.

10 Pharmaceuticals reimbursement through health insurance

The principle of benefits in kind prevails with regard to the overwhelming number of benefits provided by health insurance institutions. The scope of medical treatment at the expense of social health insurance is defined by law as follows: "It must be sufficient and purposeful, but shall not go beyond what is necessary." (§ 133 ASVG) Effective 1 January 2005, the Code of Reimbursement (EKO) replaced the Register of Medicinal Products (Heilmittelverzeichnis) which was used until then.

EU average price

The EU average price as a maximum limit for reimbursement prices was newly regulated in the course of the 61st amendment of the General Social Insurance Act (ASVG). The Pricing Committee determines the EU average price from the prices reported by companies based in EU Member States. As long as the EU average price cannot be determined (the EU average price is determinable if the MP/DSP is available in at least 2 Member States of the EU, excluding Austria), the price reported by the authorised pharmaceutical company applies provisionally. The EU average price is to be determined by the Pricing Committee within 6 months after application. The health institution known as Gesundheit Österreich GmbH (GÖG) can be consulted. After the first price determination, the Pricing Committee has to once again determine an EU average price after 18 months and after another 24 months. A further determination is possible after another 18 months.



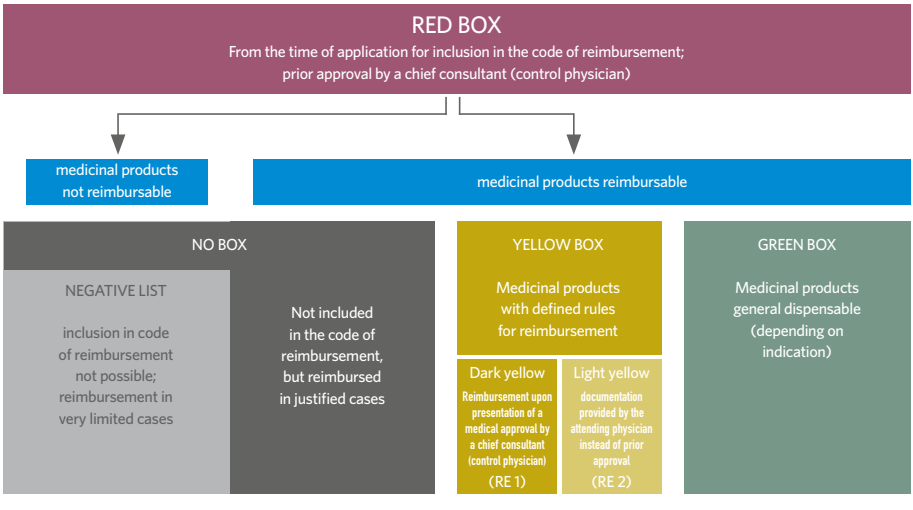
Source: Pharmig

10.1 Code of reimbursement (EKO)

The ASVG governs access to medicinal products for all insured persons in Austria in accordance with authorisation by social insurance. The Code of Reimbursement (EKO) represents a "positive list" and thereby enables either the "freely ability to prescribe" (without prior approval by the chief & control physician service = Green Box) or defines rules (specific use - "regulatory text") for approval by chief & control physicians (Yellow Box of the EKO). The products listed in the EKO undergo a pharmacological, a medical-therapeutic and health economic evaluation (see chapter 10.2 concerning this) – they convince by means of their benefits as well as with regard to the costs.

The EKO consists of three groups (also called boxes):

The box system – simplified presentation



- The **Green Box** comprises medicinal products which are either general dispensable or under specific circumstances in specified amounts. The authorisation of a chief consultant (control physician) belonging to the health insurance is not required if the rules of the Code of Reimbursement are complied with. The comparator products listed in this box are relevant for price determination. If a higher price is targeted for the requested proprietary medicinal product, an added therapeutic value must be proven.

- The **Yellow Box** includes all those medicinal products which exhibit an essential additional therapeutic benefit for the patient and which are not included in the green area for medical and/or reasons of health economy. At most the determined EU average price may be offset for a proprietary medicinal product in this box. The costs

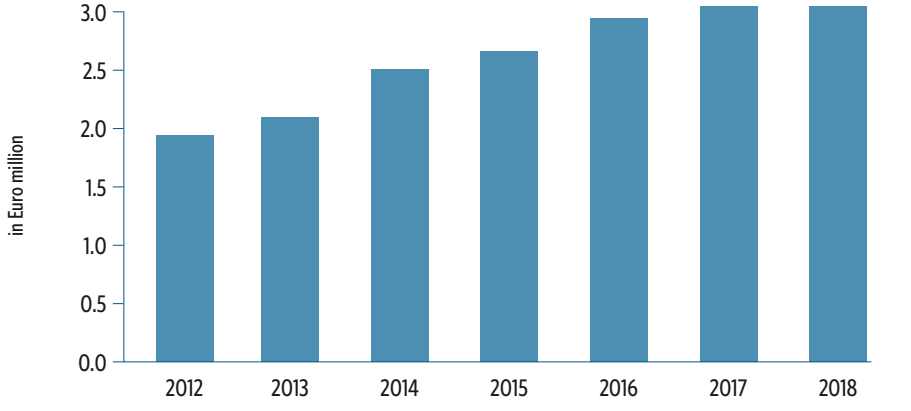
are only reimbursed by the health insurance upon presentation of a medical approval by a chief consultant (control physician) of the insurance fund (RE1 = dark yellow box). For specific medicinal products in this box, whose inclusion relates to a specific application, the Main Association provides for a follow-up verification of compliance with the specified application (using the documentation provided by the attending physician) instead of the approval by a chief consultant (control physician; RE2 = light yellow box).

- The **Red Box** temporarily comprises all medicinal products for which an application for inclusion in the Code of Reimbursement was submitted. The price of the proprietary medicinal product may not exceed the EU average price. The costs are assumed by the health insurance only upon presentation of a medical approval by a chief consultant (control physician) of the insurance fund.

All other medicinal products not included in the Code of Reimbursement are only reimbursed in justified cases and upon presentation of the medical approval by a chief consultant (control physician). Authorisation has to occur via the Pharmaceuticals Authorisation Service (ABS). Before a contracted physician is allowed to prescribe medicinal products which are subject to authorisation to his patients, they must submit an electronic request to the chief & control physician service of the health insurance institution.

In 2017, 113 million medicinal product prescriptions were invoiced. The number of applications for authorisation has steadily increased in recent years.

Development of ABS-approval applications

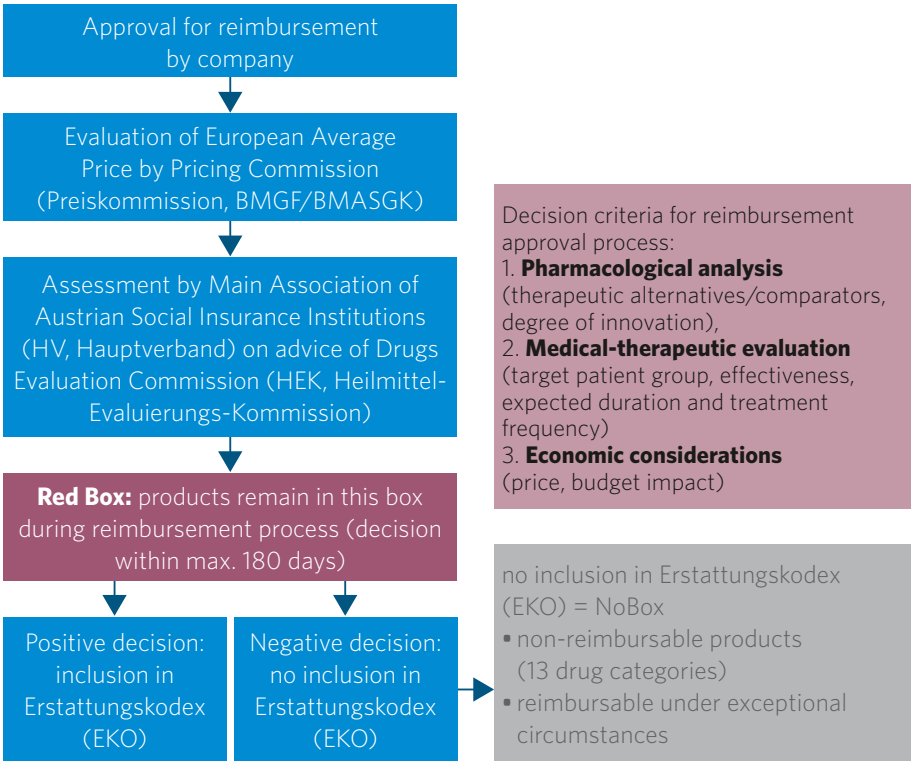


Source: HV

In 2018 there were 3.1 million applications for approval by a "chief physician".

10.2 Approval for inclusion in the reimbursement process (VO-EKO in accordance with § 351 ASVG)

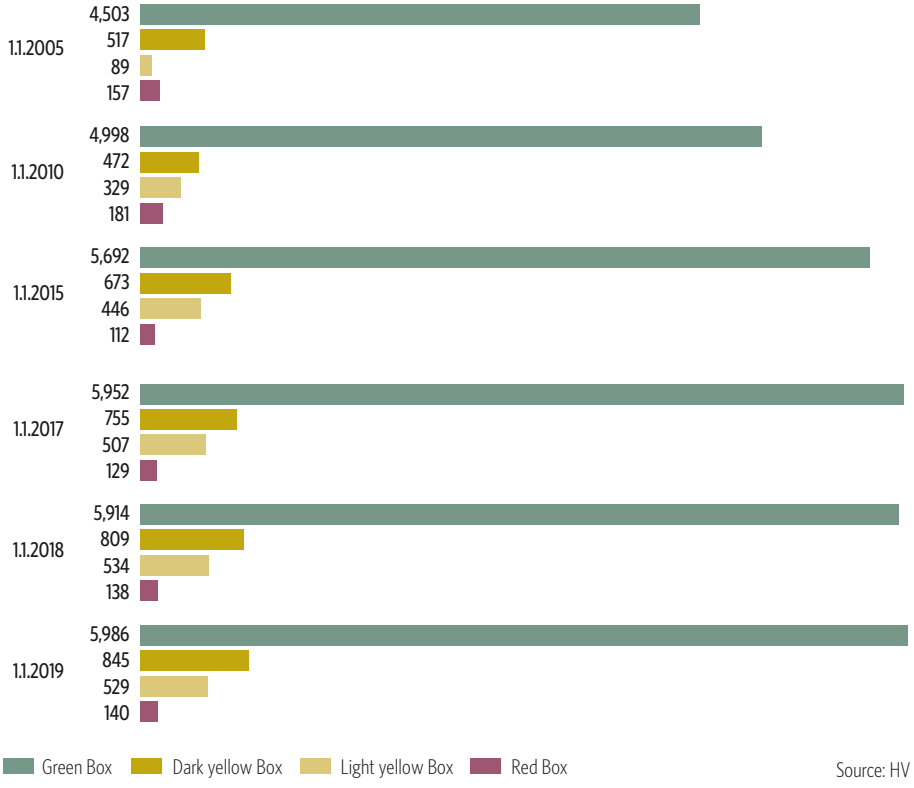
Based on ASVG (§ 351c ff.), the rules of procedure out of the publication of the Code of Reimbursement (VO-EKO) govern in detail the process, the prerequisite and the deadlines for inclusion of medicinal products in the Code of Reimbursement. The inclusion procedure is an administrative procedure and occurs via electronic application. The publication of the medicinal products included in the Code of Reimbursement is always available in printed form at the beginning of the year. The monthly changes are published on the Internet at https://www.ris.bka.gv.at/SVRecht/.



Source: Pharmig

Specific groups of medicinal products are fundamentally excluded from inclusion in the EKO (Official Bulletin No. 34/2004: List of non-reimbursable medicinal product categories pursuant to § 351c Para.2 ASVG) and as a rule must be paid by patients themselves, unless the absorption of costs is authorised in advance by the chief physician (e. g. medicinal products which are mainly dispensed in a hospital, contraceptives).

Number of medicinal products in the EKO (acc. to national drug code)



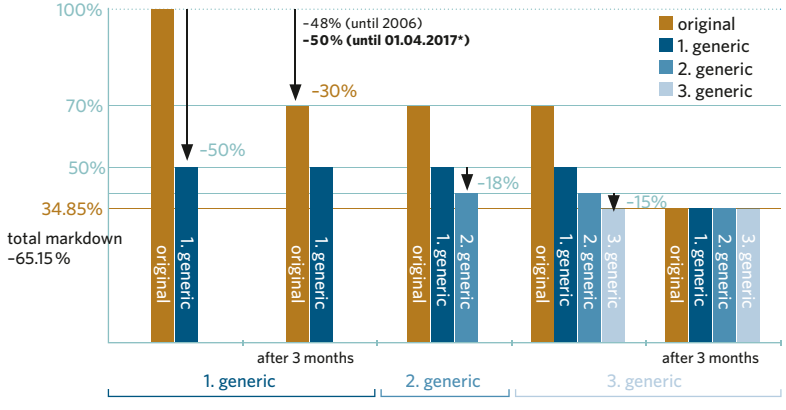
Source: HV

As of 1 January 2019, a total of 7,500 packages were listed in the EKO. There were 5,266 packages upon its introduction in 2015.

10.3 Special price regulations through social insurance

Generics

The previous price regulation was adapted with the 2017 amendment of the ASVG (Federal Law Gazette [BGBl.] I 49/2017; § 351c Para. 10 Z1 ASVG , see also chapter 4.1 p. 29 with regard to generics) for the inclusion or the continuance of interchangeable products with identical active substances (original and successor products):

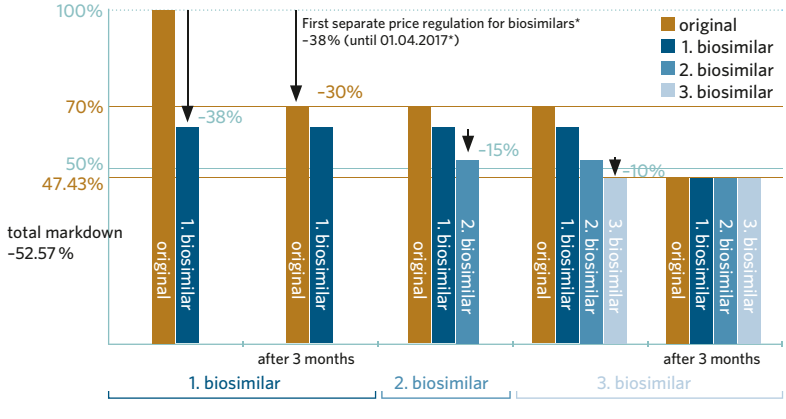


* ASVG amendment from BGBl. No. I, 49/2017 § 351c Para. 10 in force as of 1 April 2017, limited until 31 December 2021

Source: ASVG/VOEKO/Economic Evaluation Criteria of the Medicinal Products Evaluation Commission (HEK)

Biosimilars

A separate price regulation for biosimilars was specified in the ASVG with the 2017 amendment of the ASVG (§351c Para. 10 Z2 ASVG, see also chapter 4.1 p. 30 with regard to biosimilars), with which the predictability of the market entry is facilitated:



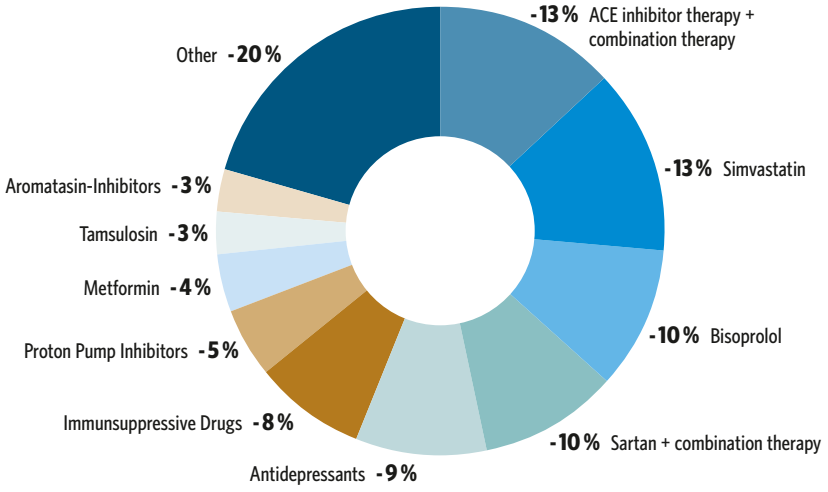
* ASVG amendment from BGBl. No. I, 49/2017 § 351c Para. 10 in force as of 1 April 2017, limited until 31 December 2021

Source: ASVG/VOEKO/Economic Evaluation Criteria of the Medicinal Products Evaluation Commission (HEK)

"Price range" (the so called "Preisband")

Due to price variations of individual active substances within the Green Box, a price range was specified for the purpose of an approximation. The price of the affected interchangeable proprietary medicinal product with identical active substance (see statement of the Main Association of Social Insurance Institutions) in the Green Box may be a maximum of 30 % above the proprietary medicinal product with the lowest price within the same active substance (amendment of the ASVG in 2017, § 351c Para. 11). The prices were first determined with effective date 1 February 2017, and the regulation was applied for the first time on 1 October 2017. This procedure will be repeated with the same effective dates in 2019. Conversely, until 1 October 2020 the Main Association of Social Insurance Institutions cannot initiate any cancellation procedure due to economic reasons for those products which are within the price range.

Impact on sales due to the application of the price band according to ATC class



Source: IQVIA

Based on a one-year extrapolation, the application of the price band in 2017 led to a drop in turnover of about Euro 34 million (FAP).

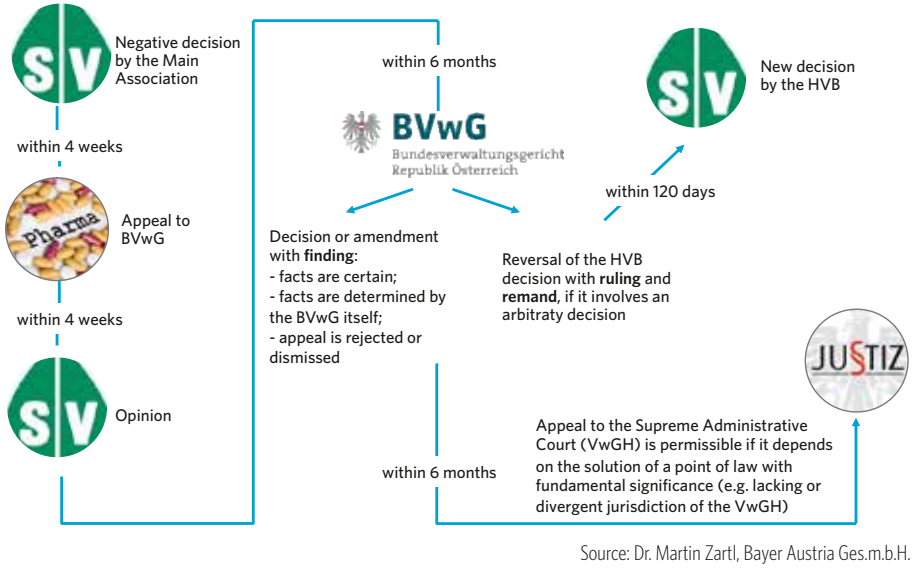
Special provisions for proprietary medicinal products outside of the EKO ("No Box")

Proprietary medicinal products which are not listed in the EKO (see chapter 10.1), but are nevertheless reimbursed in certain exceptional cases, were introduced with special provisions in the amendment of the ASVG in 2017 (§ 351c Para. 9a ASVG). If the annual turnover exceeds Euro 750,000, these proprietary medicinal products will only be reimbursed at the EU average price. The Pricing Committee determines the EU average price for these products. If the manufacturer price offset by the social insurance institutions should exceed the determined EU average price, a repayment obligation arises for this portion.

10.4 Federal administrative court

Due to the administrative jurisdiction amendment of 2012, since 01 January, 2014, the Federal Administrative Court has been responsible for reviewing decisions of the Main Association of Social Insurance Institutions in accordance with § 351 h ff ASVG (before: the Independent Drug Commission "UHK"). Appeals against decisions of the Main Association of Austrian Social Insurance Institutions must be filed within four weeks of the decision on the website www.sozialversicherung.at. The appeal postpones the implementation of the decision. The decision shall be made by the Senate of 5 (discussion and voting of the Senate is not open to the public). The findings of the Federal Administrative Court (BVwG) will be published in the Legal Information System (RIS) of the Austrian federal government at https://www.ris.bka.gv.at/Bvwg/.

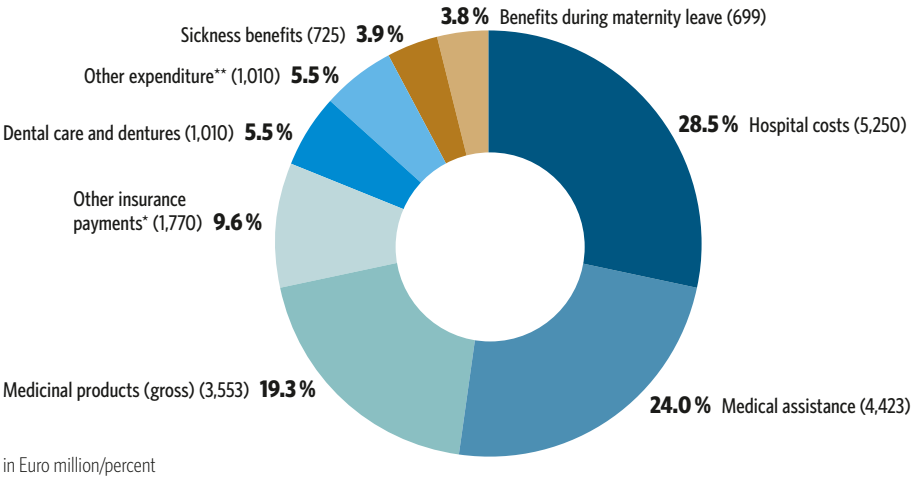
Process flow



Source: Dr. Martin Zartl, Bayer Austria Ges.m.b.H.

10.5 Budgets of health insurance institutions

Final conduct of the health insurance institutions 2017



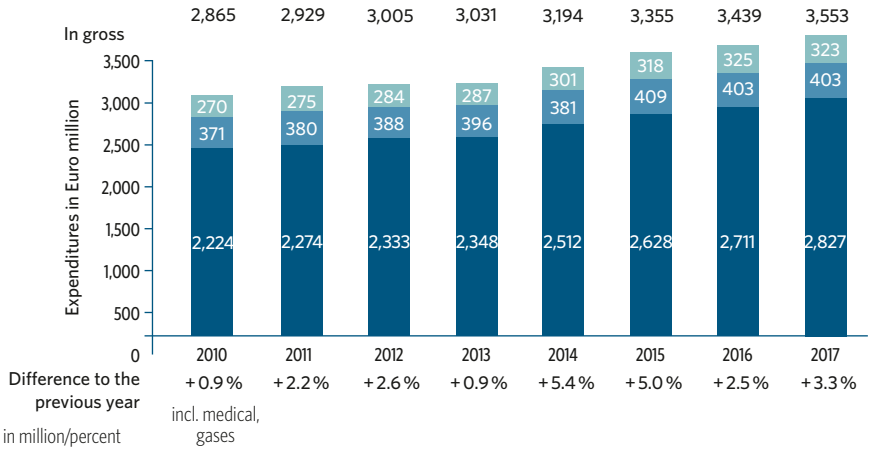
in Euro million/percent

* Rehabilitation, Medical Aids, Transport Costs, Desease Prevention, Early Diagnosis, Home Nursing, etc.

** Administration, Remittance of equalisation funds, Capital Consumption, others

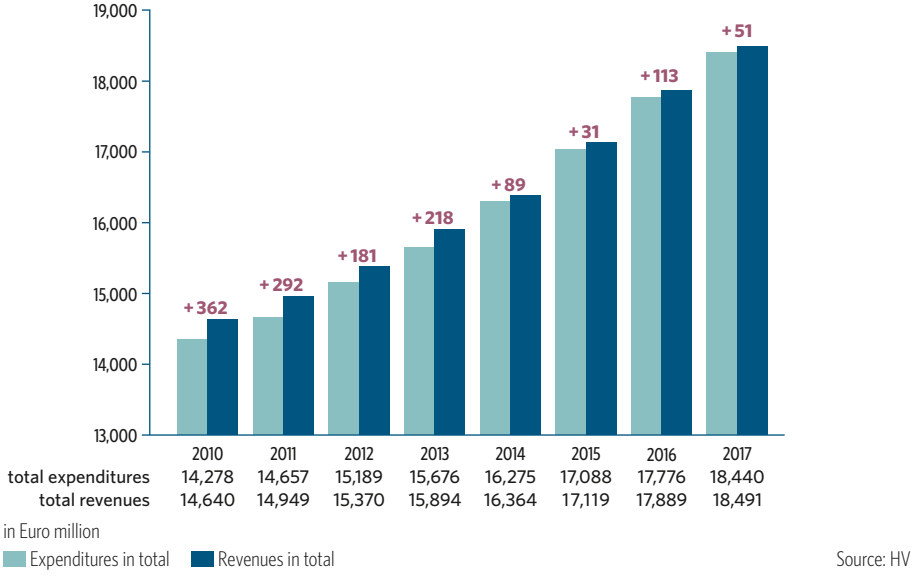
The positions for medicinal products (gross) include 10 % VAT. Prescription fees received and individual discounts are not considered, solidarity fees as well as individual discounts for pharmaceutical companies.

Expenditures for medicinal products



Source: HV, Pharmig

Development of the total expenditures/total revenues of the health insurance funds



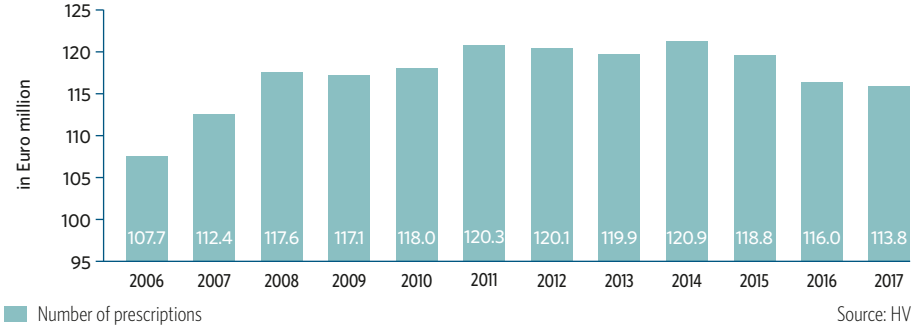
Source: HV

The income from social health insurance funds amounted to 18.5 billion Euro according to the final conduct in 2017 (+ 3.4 % vs. 2016), and their expenditures amounted to 18.4 billion Euro (+ 3.7 %). The earnings therefore amounted to 51 million Euro.

10.6 Prescription trends

The number of prescriptions has declined since 2017. Compared to 2014, it is down by just under 6 %.

Number of reimbursed prescriptions

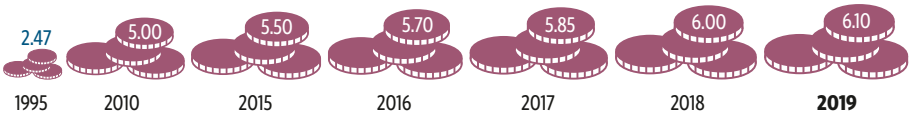


Source: HV

10.7 Co-payment: Prescription fee

There exist numerous co-payments and additional fees which have, as of yet, not been harmonised. All together, in 2017, the health insurance institutions collected approx. 403 million Euro in prescription fees only. The prescription fee per package of a medicine amounts to 6.10 Euro in 2019. Besides a general exemption of the prescription fee granted to persons based on social reasons there is an annual ceiling on prescription fees since January 2008. This ceiling is 2 % of the annual net income (excluding special payments such as holiday or Christmas allowance) of the person insured. As soon as this amount is exceeded, the person insured and his co-insured dependants do not have to pay the prescription fees for the rest of the respective calendar year.

Development of prescription charge



in Euro

Source: Austrian Pharmacist Chamber

Since 1995 the prescription fee has more than doubled.

When setting the net expenditures of health insurance funds for medicinal products (2017 2,821 million Euro) off against the prescription charge revenue (403 million Euro), a deductible of 14.25 % remains which is to be paid for the medicinal product by the patient.

Deductible for medicinal products

Source: HV

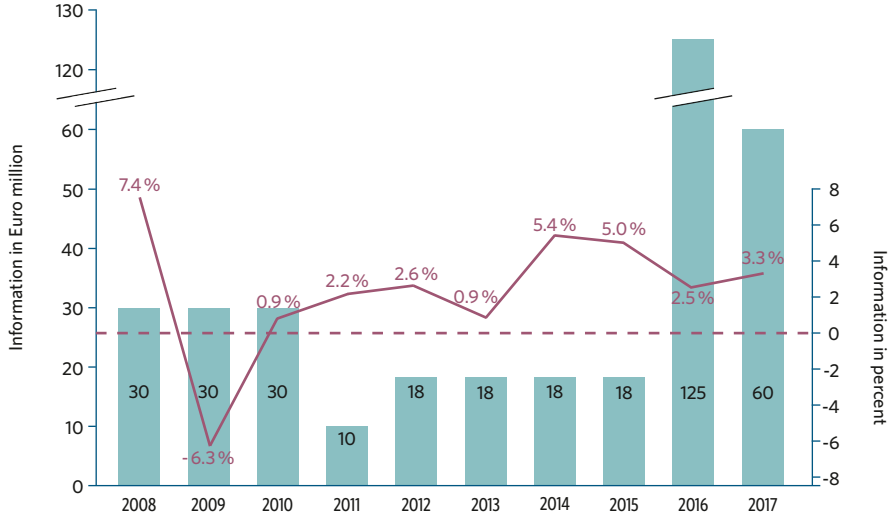
Medicinal products with prices under the prescription fee are not considered. Patients pay for these medicinal products themselves. Just under a quarter of the medicines in the refundable market* cost less than the prescription fee in 2018 which amounted to Euro 6.00.

* Refundable market: IQVIA DPMÖ next level with adapted data collection (incl. direct prescription sales) without selected non-refundable ATC 3 classes G03A, G40E, J07B/D/E, V01A, with non-prescription refundable products

10.8 Pharma master agreement

Pharma master agreement 2018

The framework pharmaceutical contract is a unique prime example of successful work in Europe. Since 2008, the pharmaceutical industry and social health insurance have been working together on a contractual basis in order to support the efficiency of the legal health insurance companies, in particular with patients. The pharmaceutical industry is committed to further strengthening the health care industry.
104 pharmaceutical companies and 7 medicinal product wholesalers contribute with the Pharma Master Agreement 2018 (term 1.1.2016–31.12.2018), shall further make social contributions totalling several millions to the domestic health insurance institutions: 125 million Euro in 2016, and a total of up to 160 million Euro in 2017 and 2018 (depending on the actual increase in spending on medicinal products).



During the three-year term, the common healthcare objective will also be continued. An earmarked amount of 6.4 million Euro in total is thus available for projects relating to child health and prevention.

Health objectives committee – funding focus & projects

Over the past seven years (2011–2018) around Euro 2 million have been made available for children and youth healthcare projects in the joint healthcare objectives from the pharma master agreement. The donor is the "healthcare objectives committee" staffed by representatives from social insurance funds, Pharmig and PHAGO.

In the time it has existed, about 92 projects have been funded with about Euro 12.5 million, which is an average of about Euro 135,000 per project. Some of the model projects have been able to stay anchored in the Austrian healthcare system.

Joint healthcare objectives – 92 projects funded

Source: Joint healthcare objectives – cooperation between social insurance and the pharmaceutical industry

Further information under www.pharmig.at and https://www.pharmig.at/media/1622/gemeinsame-gesundheitsziele_broschu-re-2019.pdf

Projects funded in 2018: medication for children and health skills

No.	Project title	Applicant	Scope
1	Information platform for medication for children in A.	Österr. Ges. für Kinder- und Jugendheilkunde (ÖGKJ)	Nationwide
2	OKIDS expansion and innovations in the network	OKIDS GmbH	Nationwide
3	Easy-peasy! Large families.	OÖ Gebietskrankenkasse	Linz and Vöcklabruck plus their catchment areas
4	Food under the microscope 2.0	AGES	Nationwide
5	Health skills of children in the hospital	Gesundheit Ö Forschungs- u. Planungs GmbH	Nationwide
6	Measuring health skills of children	Tiroler Gebietskrankenkasse (TGKK)	Tyrol
7	GeKo health skills theatre for children	PROGES – Wir schaffen Gesundheit	Burgenland
8	Healthy nurseries	Steiermärkische Gebietskrankenkasse (STGKK)	Styria
9	Child-friendly information with JIA	Medizinische Universität Wien, Päd. Rheumatologie	Vienna
10	Grow together – dads project	Grow Together – Für einen guten Start ins Leben	Vienna
11	aRAREness – Raising awareness for rare diseases through patient involvement within the clinical environment of health care professionals	Pro Rare Austria, Allianz für seltene Erkrankungen	Nationwide
12	GET – making healthy decisions	Styria Vitalis	Styria, Upper A.
13	Psychosocial care for intersex children	UNTERWEGS zwischen den Geschlechtern e. V.	Eastern Austria

PP = Practice-based project RP = Research project

11 Pharmig Code of Conduct

Pharmaceutical companies develop, produce and sell medical products. They are also responsible for updating doctors, pharmacists, patients and the general public about their medicines, and so to contribute to the safety of the medicine and to the products being used correctly.
The Pharmig Code of Conduct (CoC) codifies, in addition to the basic principles, binding rules for information about medication and advertising tactics. It comprehensively regulates the collaboration between pharmaceutical companies and doctors, institutions and patient organisations, with the target of making this collaboration fair and transparent.

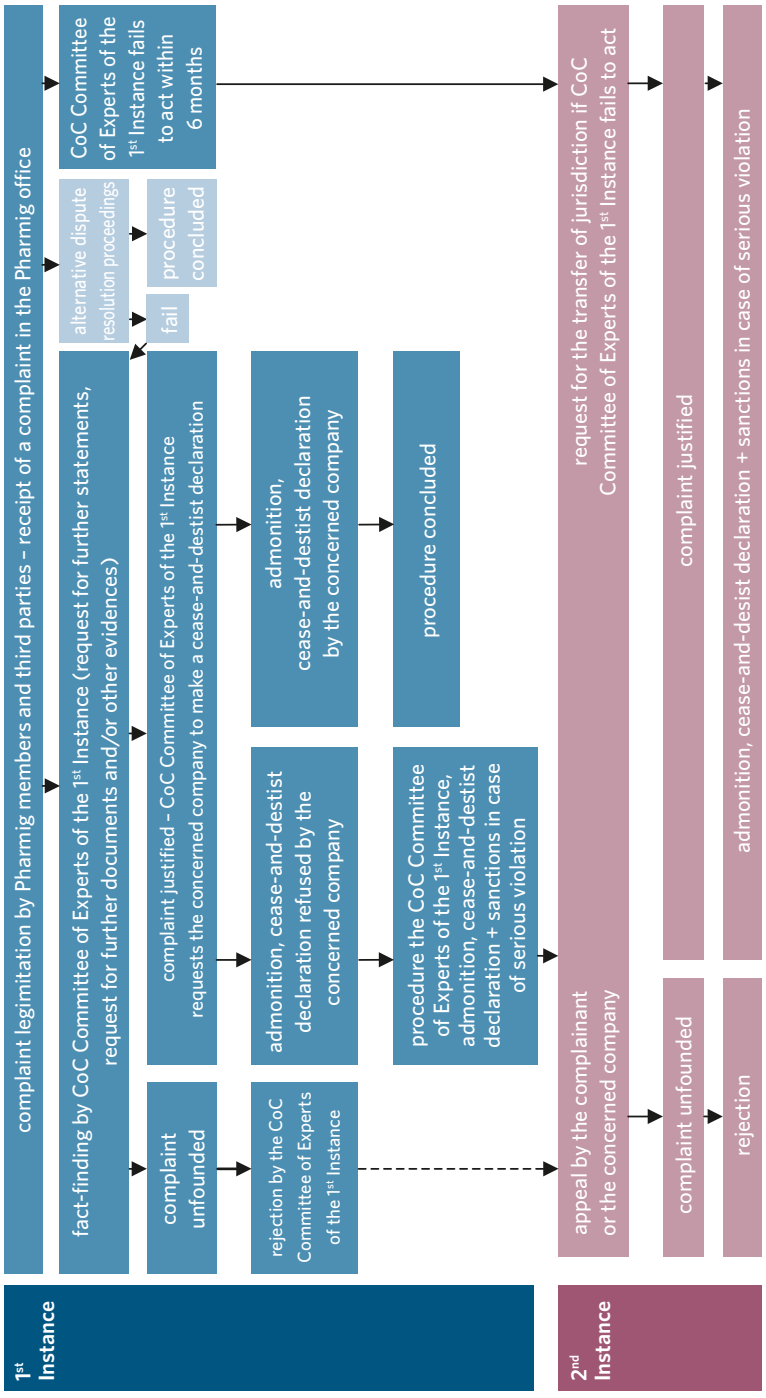
Transparency creates trust

Since 2014, the Code of Conduct has also contained regulations on how pharmaceutical companies disclose payments in kind if they work with doctors or university hospitals, or if they support the work of patient organisations.
In principle individual disclosure of transfers of value which result from these cooperations should be aimed at. For individual disclosure it is necessary to seek consent. All applying data protection provisions must be complied with. In the case that there is no consent, disclosure must be made in aggregated form. The data has to be disclosed annually (as per 30.6.) on a publicly accessible homepage.
You can find more information on the transparency creates trust:
www.transparenz-schafft-vertrauen.at.

Ethical standards of the pharmaceutical branch

This voluntary self-regulation through the Pharmig Code of Conduct bears witness to a keen sense of responsibility and the express will of our members to embrace the high ethical standards of our branch. The Code of Conduct was introduced in 1970 and was last updated in 2015.
The rules of procedure for the technical committees of the CoC I and II determine the procedural framework for the handling of complaints filed. A streamlined and simplified procedure, which quickly leads to the clarification of contentious cases and allows for the filing of a cease-and-desist order, has been available since 2015.
Non-members and third parties also have the possibility to file complaints about alleged violations of the CoC, whereby a written agreement for the relevant procedure is to be drawn up regarding this. This ensures that the parties are subject to the same rules. Under certain circumstances, the complaints can also be filed anonymously. Five complaints were dealt with in 2018. In the interest of legal security, the results of the CoC procedures are published in an anonymised format on our webpage, www.pharmig.at.

Flowchart – procedure of the CoC committees of experts of the 1st and 2nd instance



12 Laws and regulations

The table below lists the major laws relating to the development, production, evaluation, marketing authorisation and the distribution of medicinal products. Further information can be downloaded under www.pharmig.at

Law	Scope of applicability
Medicinal Products Act	definitions, clinical trials, marketing authorisation, manufacture, distribution, advertising, pharmacovigilance, approval of plant and equipment
Austrian Medicine Import Act	Import and distribution of medicinal products
Prescription Act	Prescription status
narcotic Substance Act	narcotics status, charges and placing on the market
Act Against Unfair Competition (UwG)	Advertisement with regard to consumers and competitors
Industrial Code	Right to run a pharmaceutical company
Pharmacopoeia Act	Quality and testing of medicinal products
Price Act	Pricing and (by ordinances) maximum mark-ups (margins)
Health and Food Safety Act	Spin-off of responsibilities and procedures reg. the medicinal product system from the Federal Ministry for Health to the Austrian Medicines and Medical devices Agency
Patent Protection Act	Patent protection also of medicinal products
Federal Hospitals Act (KAKuG)	Forms the legal basis for all hospitals and the foundations for the 9 provincial laws, which represent implementation statutes
General Social Insurance Act (ASVG)	Governs the General Social Insurance for persons employed in Austria, incl. the self-employed persons who have an equal standing and the health insurance of retirees from the General Social Insurance. The General Social Insurance comprises health insurance, accident and pension insurance with the exception of specific special insurances.
EU "Human Medicines Community Code" (dir. 2001/83/EC)	definitions, marketing authorisation and procedures, manufacturer and importation, labelling and package leaflet, wholesaling, advertising and information, pharmacovigilance
EU Transparency directive (dir. 89/105/EEC)	procedural provisions, timelines and transparency rules for national decisions regarding reimbursement and prices
Federal Administrative Court Act (BVwGG)	Governs the organisation of the Federal Administrative Court
Administrative Court Procedural Act (VwGVG)	Governs the procedures at the Federal Administrative Court
EU-delegated regulation on safety features (Reg 2016/161)	Governs the technical specifications, modalities of the verification, characteristics of the repository system and derogations for the safety features appearing on the packaging of medicinal products for human use
Federal Procurement Act	governs the procedure for procurement of services (procurement procedure) in the public sector

National regulation	Scope of applicability
Ordinance on the Retail of Medicinal Products	Definition of pharmacies and drug stores as distribution channels
Narcotic Substances ordinance	Distribution of narcotic-containing medicinal products
Summary of Product Characteristics Ordinance	Structure of the summary of product characteristics
Patient Information Leaflet Ordinance	Structure of the patient information leaflet
Ordinance on the Labelling of Products	Structure of labelling/outer packaging
Pharmacovigilance Ordinance	PV responsibilities of the marketing authorisation holder, notification of side effects and incidents
Ordinance on pharmaceutical representatives	Authorisation and testing of pharmaceutical representative
Ordinance for Companies Producing Medicinal	Products Corporate requirements for pharmaceutical companies
Fee Tariff Ordinance	Governs the tariffs for activities of the BASG (e. g. marketing authorisations, inspections)
Ordinance on the Authorisation and Control of Medicinal Products	ordinance setting forth the principles of approval of medicinal products by chief consultants and control physicians, follow-up control of prescriptions and documentation principles
Rules of procedure for the publication of the Code of Reimbursement acc. to § 351g ASVG (VO-EKO)	Rules of procedure published by the Main Association of Austrian Social Insurance Institutions
Procedural Cost ordinance pursuant to § 351g Abs. 4 ASVG (VK-VO)	Governs the amount of flat-fee cost rates for applications for a procedure in connection with the EKO
Ordinance on NIS	compulsory registration of nIS before implementing (since 01.09.2010) contains planning, inspection, authorization of non interventional studies; relevant for pharmaceutical companies who plan, implement, inspect/or finance a NIS
Ordinance on Distance Selling	Sales of medicinal products via distance selling

Other legal regulations		Scope of applicability
Good Clinical Practices	GCP	Guidelines on clinical trials
Good Manufacturing Practices	GMP	Guidelines on the manufacture of medicinal products
Good Laboratory Practices	GLP	Guidelines on the evaluation of medicinal products
Good Distribution Practices	GDP	Guidelines on logistics for medicinal products
Declaration of Helsinki		duties of the physician (e. g. in clinical trials)
Code of Conduct	CoC	Rules for the information and advertisement policy of pharmaceutical companies, cooperation with members among experts, institutions and patientorganisations
EU average prices acc. to ASVG		Governs the procedure of the price commission when determining the EU average price pursuant to § 351c (6) ASVG
Guidelines for the economic prescription of medicinal products and curing aids	RöV	Cost guidelines of the health insurance
Principles of the HEK (Medicinal Product Evaluation Commission)	HEK	Includes information on HEK relating to economic evaluation criteria, package sizes, follow-up controls and principles for the verification of deliverability in the red box of the EKO

13 Abbreviations

AGES	Agency for Health and Food Safety
ASVG	General Social Insurance Act
AMVO	Austrian Medicines Verification Organisation
AMVS	Austrian Medicines Verfication System
BASG	Federal Office for Safety in Health Care
BMGF	Federal Ministry for Health and Women until 7.1.2018
BMASGK	Federal Ministry of Labour, Social Affairs, Health and Consumer Protection, as of 8 January 2018
BVG	Austrian Constitutional Law
CPI	Consumer Price Index
DCP	Decentralised Procedure
EFPIA	European Federation of Pharmaceutical Industries and Associations
EKO	Code of Reimbursement
EMA	European Medicines agency
FAC	Federal Administrative Court
GDP	Gross Domestic Product
GESG	Health and Food Safety Act
GMP	Good Manufacturing Practice
HEK	Medicinal Products Evaluation Commission
HV	Main Association of Austrian Social Insurance Institutions
ICD10	International Classification of Deseases and Related Health Problems
IGEPHA	The Austrian Self-Medication Industry
IPF	Institute of Pharmaco-economic Research
IQVIA	IQVIA Marktforschung GmbH
IKF	Performance-oriented Hospital Financing
MAH	Marketing Authorisation Holder
MRP	Mutual Recognition
MP	Manufacturer Price
MPA	Medicinal Product Act
NIS	Non-Interventional Study
OECD	Organisation for Economic Cooperation and Development
OeGV	Austrian Generics Medicines Association
OTC	Over The Counter
ÖVIH	Austrian Vaccine Manufacturer Association
PHAGO	Austrian Association of Full-Line Pharmaceutical Wholesalers
PV	Pharmacovigilance
R&D	Research & Development
SHA	System of Health Accounts
SPC	Supplementary Protection Certificate
UHK	Independent Medicinal Products Commission
VAT	Value-Added Tax
VHC	Pharmig Code of Conduct
WKÖ	Austrian Federal Economic Chamber

PHARMIG

Verband der pharmazeutischen
Industrie Österreichs