PHARMIG

Verband der pharmazeutischen Industrie Österreichs

Facts & Figures 2022

Medicinal Products and Health Care in Austria

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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 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 Austrian 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 health care system and relevant policy areas. In so doing, PHARMIG demands fair, reliable and calculable framework conditions for the pharmaceutical industry which serve all stakeholders 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,


© Stefan Csaky

I am pleased to share with you this year's edition of Facts & Figures 2022. As usual, we provide you with comprehensive information about the Austrian health care system.

In this edition we have again incorporated some novelties for you.

- **Usage of health data**
  The implementation of the Austrian Micro Data Center (AMDC) and the European Health Data Space (EHDS) is intended to make health data more usable for research, innovation and evidence-based decisions in health care. At the national level, this will mean a significant improvement in scientific access to public, de-identified statistical and registry data in the future. At the European level, the EHDS will improve the pooling and cross-border use of health data. How EU citizens, scientists and policymakers will benefit from this cross-border project is summarized in the new chapter 4.7.

- **Health Technology Assessment (HTA)**
  The EU regulation on the assessment of health technologies is to be applied as of January 2025. It regulates how assessments of health technologies are to be conducted at the European level in the future. What are the detailed steps for the implementation and rollout phase up to 2030 and which improvements the regulation aims at, can be found in chapter 5.6.

Facts & Figures 2022, together with selected graphs and the German version „Daten & Fakten 2022", are available for download on our website www.pharmig.at.

I hope you have an interesting read and gain a lot of knowledge with our Facts & Figures 2022!

Kind regards,

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). This fragmentation makes an alignement between responsibilities essential. Important general conditions are 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 2021 was 8,932,664 (see also chapter 3). 99 % are covered by one of the 5 social insurance institutions (status 2021), in addition to 15 special health care institutions (see chapter 1.4).

1.2 Social expenditures

Social expenditures in total amounted to 126.5 billion Euros in 2020.
Around two thirds of social expenses are allocated to retirement and health care benefits. The increase in spending compared to 2019 (+ 11.3 %) is attributable to those social benefits that were used more intensively or for the first time to cope with the social consequences of the COVID-19 pandemic (short-time work allowances, support payment for the self-employed, one-time payments to the unemployed and families, etc.).

Social expenditures* acc. to function in 2020

	million Euros	percent
Age	53,607.00	42.4
Illness/health care	31,462.00	24.9
of which sickness benefits	855.00	2.7
of which continued payment of wages during illness	3,278.00	10.4
of which in-patient care	14,975.00	47.6
of which out-patient care	11,059.00	35.1
of which prevention of illness/rehabilitation	927.00	3.0
of which other benefits in cash/in kind**	368.00	1.2
Family/children	11,452.00	9.1
Surviving dependants	6,411.00	5.1
Invalidity/disability	7,071.00	5.6
Unemployment	14,125.00	11.2
Habitation and social exclusion	2,335.00	1.8
Total	**126,463.00**	**100**

Source: Statistics Austria

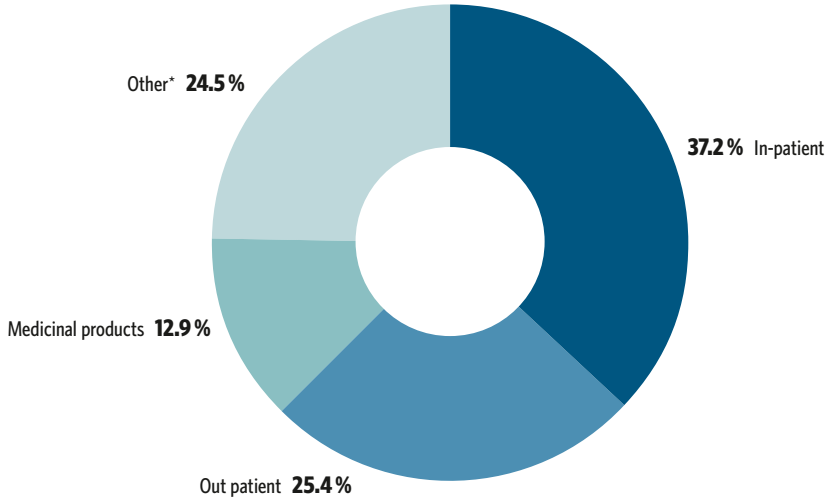
* social expenditures of functional organisation are the sum of social beneftis, without transfers between social systems (redirected social contributions and other transfers) and without other expenditures (administrative expenses, other not attributable expenditures)

** 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 health care sector.

In 2020, health care expenditures in Austria amounted to some 46.6 billion Euros, which corresponds to a share in GDP of 12.3 %.



Source: calculated by the Institute of Pharmaeconomic Research (IPF) with reference to the following data: IQVIA, Statistics Austria, SV

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

The largest proportion of 37.2 % was spent on in-patient care. At the same time, expenditure on out-patient care made up 25.4 % and expenditure on medicinal products amounted to 12.9 %.

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	2019		2020	
	million Euros	percent	million Euros	percent
Public health care financing	32,622	73.9	34,901	74.9
In-patient care*	14,052	31.8	14,894	32.0
Out-patient care	8,626	19.5	8,797	18.9
Long-term care at home**	2,393	5.4	2,518	5.4
Ambulance and emergency medical services	402	0.9	479	1.0
Pharmaceutical products, medical equipment	4,195	9.5	4,299	9.2
Prevention and public health services	632	1.4	1,320	2.8
Health care administration: State incl, social insurance	908	2.1	968	2.1
Public investments	1,413	3.2	1,625	3.5
Private health care financing	11,536	26.1	11,670	25.1
In-patient care*	2,540	5.8	2,451	5.3
Out-patient care	3,362	7.6	3,021	6.5
Pharmaceutical products, medical equipment	2,813	6.4	2,769	5.9
Health care administration private insurance	772	1.7	807	1.7
Investments (private)	1,262	2.9	1,422	3.1
Non-profit private organisations***	692	1.6	1.111	2.4
Services provided by company physicians	94	0.2	89	0.2
Total	**44,158**	**100**	**46,571**	**100**

Source: Statistics Austria

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

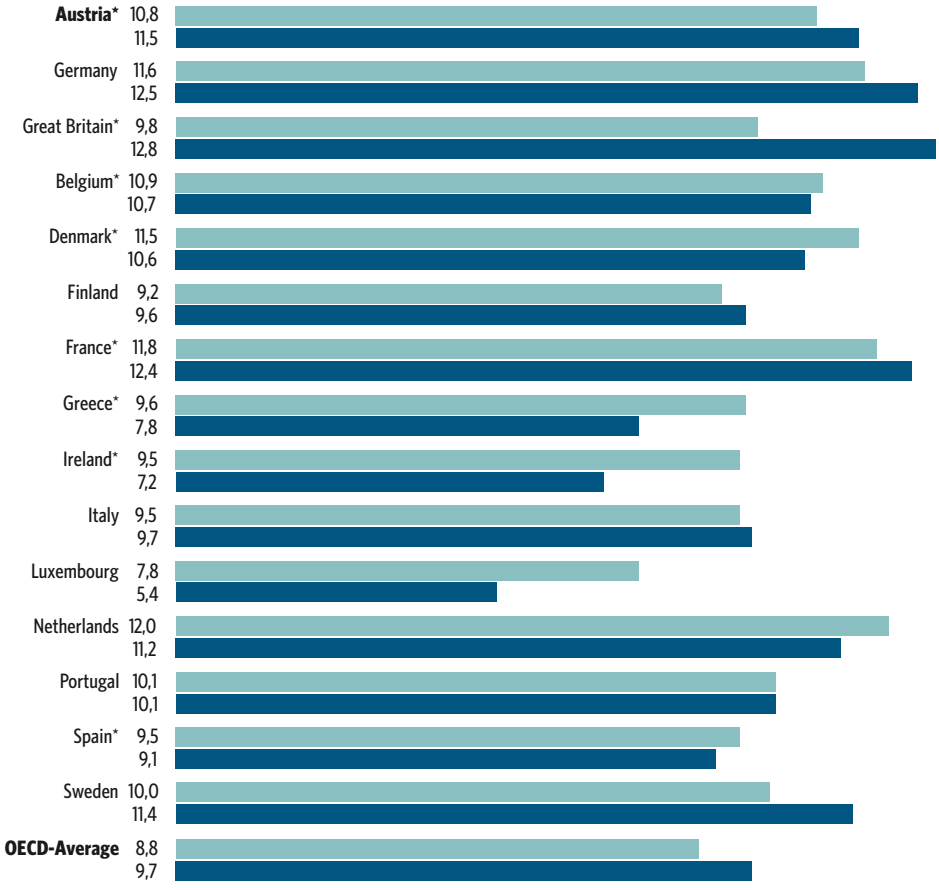
** Public spending for long-term care at home also includes federal and provincial nursing allowances.

*** 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. The increase in spending compared to 2019 is primarily due to those services that were used to overcome the COVID-19 pandemic.

Comparative health care expenditures

Health care expenditure in % of GDP[1]



[1] graphical illustration of selected OECD countries

2010 2020

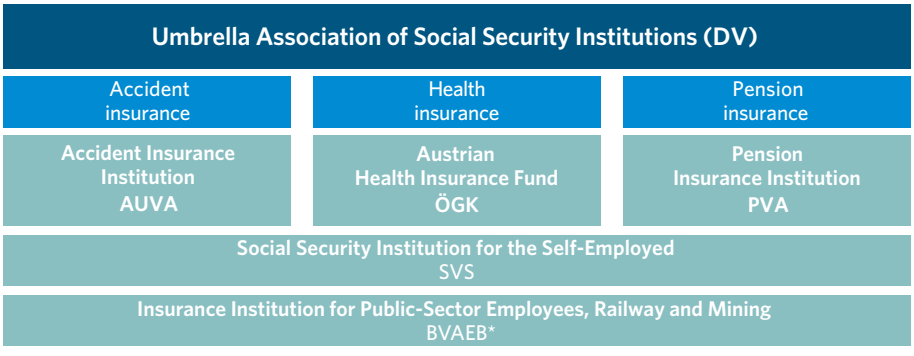
Source: Statistics Austria, OECD

* provisional 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 social security system



* incl. PV acc. Federal Pension Office Transfer Act

Graphic: PHARMIG, source: SV

With the **Social Insurance Organisation Act 2018**, the Austrian social insurance system was fundamentally reorganised through a structural reform. The previous 21 social insurance providers were reduced to 5 insurance providers and coordinated by an umbrella organisation (previously: the Main Association of Austrian Social Insurance Providers [Hauptverband der österreichischen Sozialversicherungsträger]).

The new social insurance structure exists since 1 January 2020.

The Austrian social security system protects 99 % of the resident population and rests on three pillars:

- Health insurance
- Pension insurance
- Accident insurance

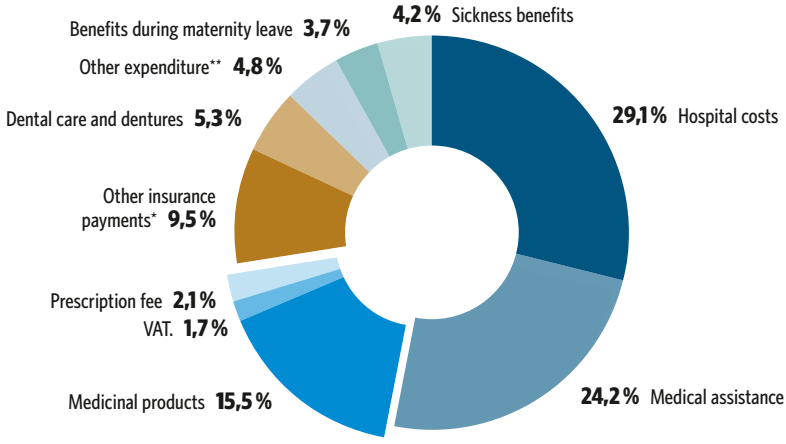
Membership is compulsory with the respective nationwide professional insurance company or the Austrian Health Insurance Fund (ÖGK [Österreichische Gesundheitskasse]). The statutory health insurance allows multiple insurances.

With 7.2 million insured persons (82 % of the people living in our country), the Austrian Health Insurance Fund is the largest social health insurance fund in Austria.

In addition to statutory health insurance, 15 health care institutions (KFA [Krankenfürsorgeanstalten]) provide health insurance for employees in various state and municipal administrations.

1.5 Budgets of health insurance institutions

Final conduct of the health insurance institutions 2020



in million Euros/percent

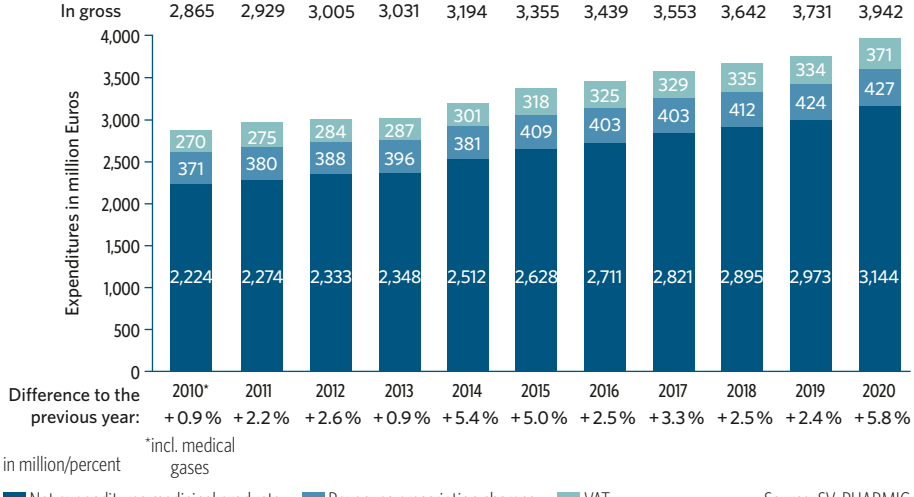
Source: SV

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

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

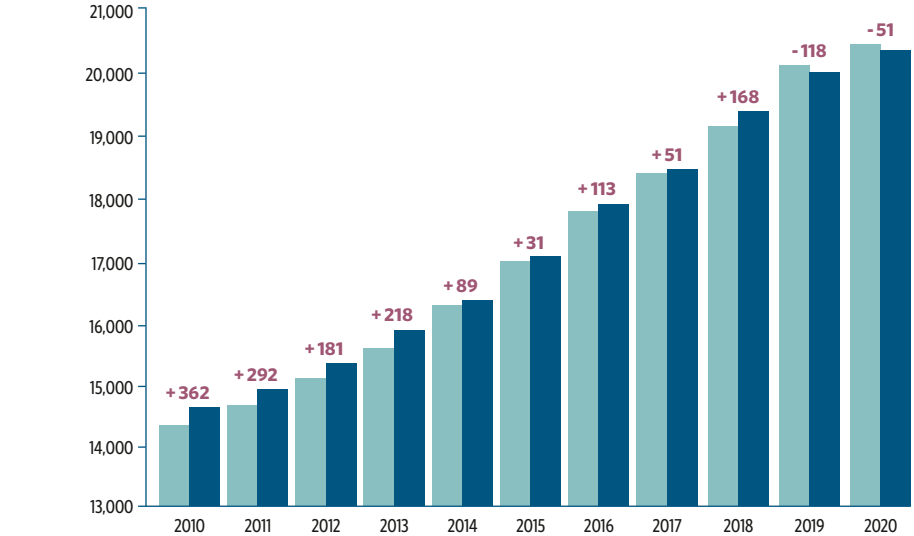
The positions for medicinal products (gross) include 10 % VAT. Prescription fees received and individual discounts are not considered, as well as solidarity fees and individual discounts by pharmaceutical companies.

Expenditures for medicinal products



Source: SV, PHARMIG

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

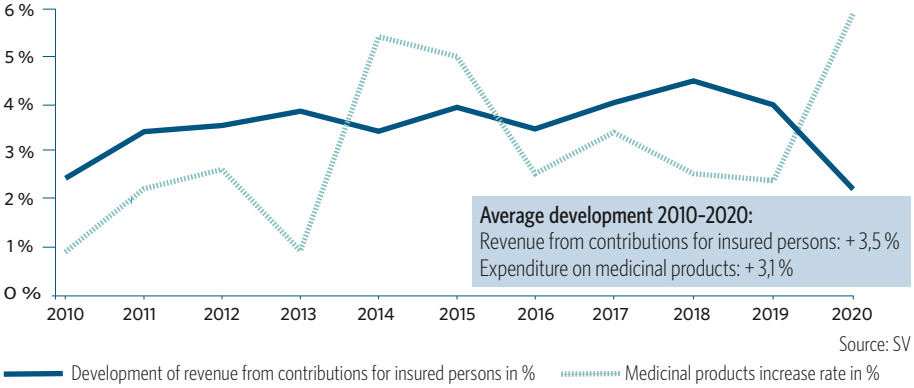


	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
total expenditures	14,278	14,657	15,189	15,676	16,275	17,088	17,776	18,440	19,192	20,115	20,405
total revenues	14,640	14,949	15,370	15,894	16,364	17,119	17,889	18,491	19,360	19,997	20,354

in million Euros Expenditures in total Revenues in total Source: SV, final conduct

The income from social health insurance funds amounted to 20.3 billion Euros according to the final conduct in 2020 (+1.8 % vs. 2019), and their expenditures amounted to 20.4 billion Euros (+1.4 %). The negative result amounted to 51 million Euros.

Development of revenue from contributions vs. expenditure on medicinal products



Source: SV

Development of revenue from contributions for insured persons in % Medicinal products increase rate in %

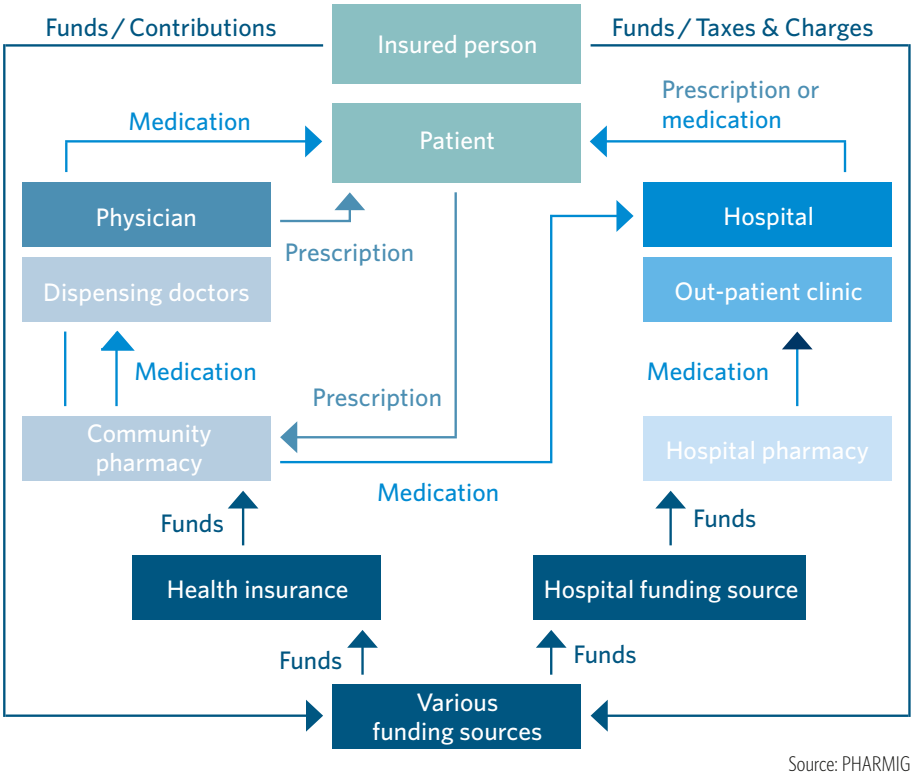
The revenue of social health insurance providers from contributions by the insured persons developed positively in the years 2010 to 2020 and increased on average by + 3.5 %. In the same period, expenditure on medicinal products increased by + 3.1 % (prescription fees, solidarity fees and individual discounts of pharmaceutical companies are not included).

1.6 Health care structure and financing

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

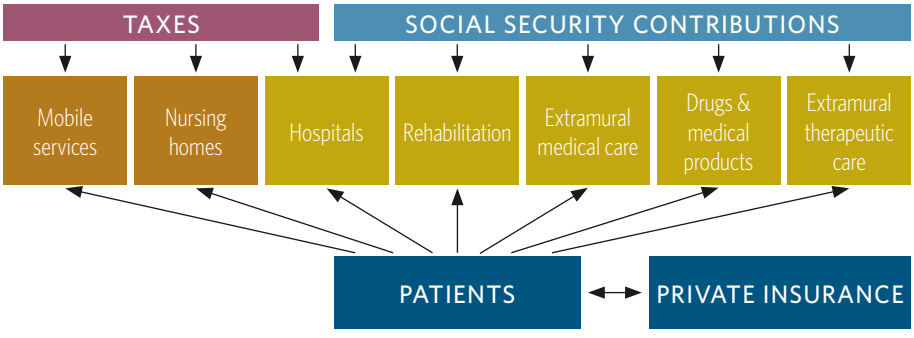
- Physicians (general practitioners and specialists), dispensing or non-dispensing as well as primary care centres (PHC "Primary Health Care")
- Hospitals and out-patient wards
- Community pharmacies
- Other medical/therapeutic services

Structure of Austria's health care system



Source: PHARMIG

Health care financing



Source: © BMSGPK

Financial equalisation

Financial equalisation regulates the financial relations between the federal government, the federal states, and the municipalities. The revenue from certain levies collected by the federal government is divided between the federal government, the federal states, and the municipalities. Financial equalisation is an agreement that must be negotiated and decided by mutual consent between the federal government, the federal states, and the municipalities. When financial equalisation is concluded, the tasks to be assumed and financed by each level are also agreed upon. In the light of the COVID-19 pandemic, the financial equalisation partners agreed to extend the financial equalisation scheme, which was supposed to run out at the end of 2021, until the end of 2023. Due to the extension of the financial equalisation several related laws were adjusted in February 2022.

Health target control

The aim of the partnership-based target control system for implementing the health care reform that has been underway since 2013 is to counteract the strong fragmentation of the health care system by joint and cross-sectoral control of the structure, organisation, and financing of health care. System partners consisting in federal government, federal states and social security conclude appropriate agreements in accordance with Article 15a B-VG [Bundes-Verfassungsgesetz, Austrian Federal Constitutional Law] on the health target control and on the organisation and financing of the health care system as well as contracts based thereon (currently 15a-VB 2017–2020). The implementing body is the federal health agency.

Role-Model "Homogeneous access throughout Austria"

In October 2020, the decision-making body of the Federal Health Agency, the Bundes-Zielsteuerungskommission, decided on the coverage of costs for an innovative therapy approved for the first time by the European Medicines Agency (EMA) by a **fund established at the federal level**. Based on an expert-supported decision, **treatment centers were defined,** that fulfill the necessary structural criteria for a qualitatively assured implementation of this therapy as well as the associated pre- and post-treatment care.

With the decision by the Bundes-Zielsteuerungskommission it was ensured that the Federal Health Care Agency would meet the costs for the implementation of a newly EMA-approved drug therapy for children with spinal muscular atrophy (SMA) under clearly defined indications and conditions and at precisely specified service centers with appropriate expertise in Austria. This means that this cost-intensive therapy is available to all insured patients, regardless of their place of residence, at all agreed service locations in Austria. A major concern of the financiers was also to link the financing of this novel therapy with a verifiable sustainable treatment success and to monitor this treatment success scientifically over several years. As of the end of 2021, it was agreed by the Bundes-Zielsteuerungskommission that the Federal Health Agency would provide nationwide funding, again under very clearly defined conditions, for another cost-intensive drug therapy (voretigene neparvovec LuxturnaTM), which has been approved in the EU for the treatment of retinal dystrophies in individuals with biallelic mutations in the RPE65 gene. These pioneering pilot projects – if they prove successful – will certainly be followed by other promising models.

Source: BMSGPK Section VII/B, Mag. Gerhard Embacher

1.7 Employees in the health care system

As per December 31, 2020, Austria's 8.9 million inhabitants were supplied by 1,397 public pharmacies (with 32 branches), 42 hospital pharmacies and 889 dispensing doctors (who dispense medicines directly to patients).

	Number
Practicing physicians	**52,880**
General practioners	13,280
Medical specialists	26,415
Dentists	5,206
Physicians in training	7,979
Pharmacy employees	**17,176**
Pharmacists, employed or self-employed	6,081
Qualified staff	7,315
Other employees	3,780
Medical experts in hospitals	**122,843**
Physicians	26,047
Nursing staff	96,796

Source: Statistics Austria, Austrian Chamber of Pharmacists

In total about 193,000 people are employed in the health care sector.

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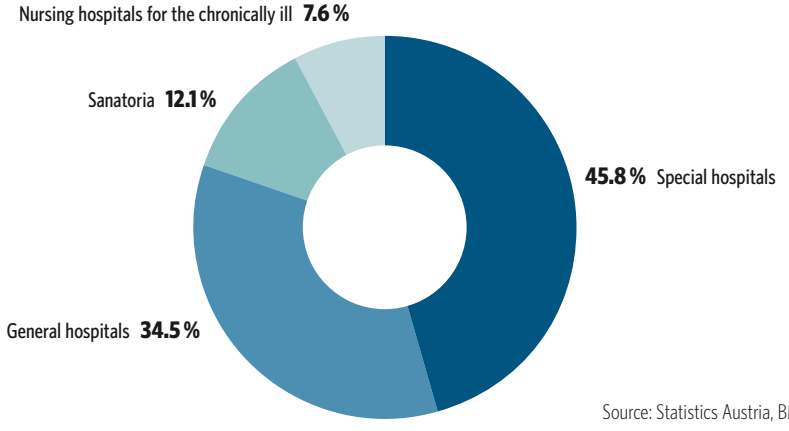
2 Hospitals in Austria

In Austria, hospitals totalled 264 at the end of 2020.
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.
Hospitals are financed from multiple sources, mainly from taxes and lump-sum contributions from social security providers of hospital financing as well as by the federal states, and the federal government. In addition, patients make small co-payments ("daily allowance"), see chapter 2.2. Hospital funding.

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) 2020

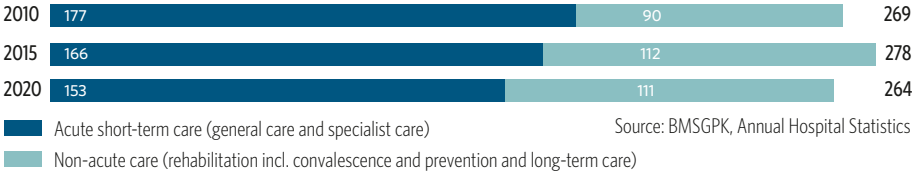


Source: Statistics Austria, BMSGPK

2.1 Structural details of hospitals

Of these 264 hospitals, 110 (42 %) are hospitals with public status and 154 (58 %) without public status. Hospitals with public status are not to be confused with hospitals of public agencies and institutions.

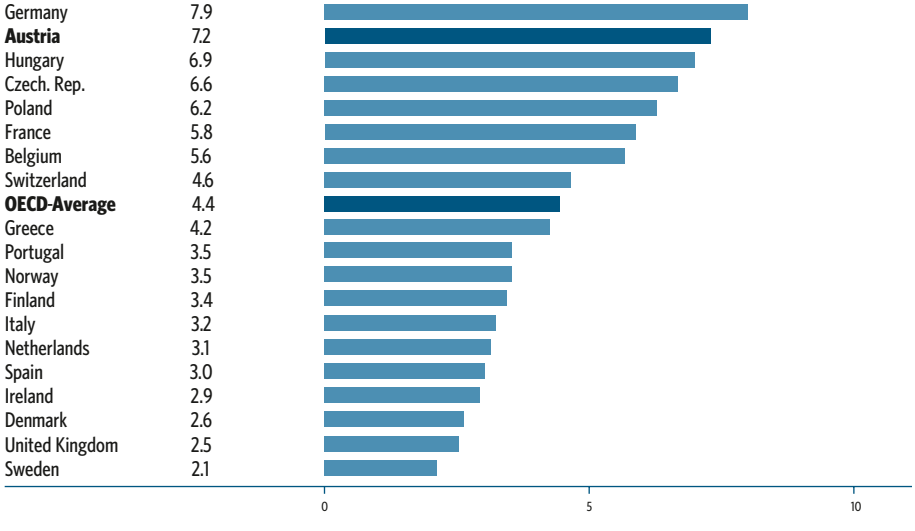
Development of hospitals according to care function



Source: BMSGPK, Annual Hospital Statistics

Throughout the years, the number of institutions in the area of acute short-term care has decreased from 177 (2010) to 153 institutions (2020). In comparison to this, the area of non-acute care has increased from 90 institutions (2010) to 111 (2020).

Hospital care in international comparison
Hospital bed capacity per 1,000 inhabitants, 2020*



* graphic representation of selected OECD countries

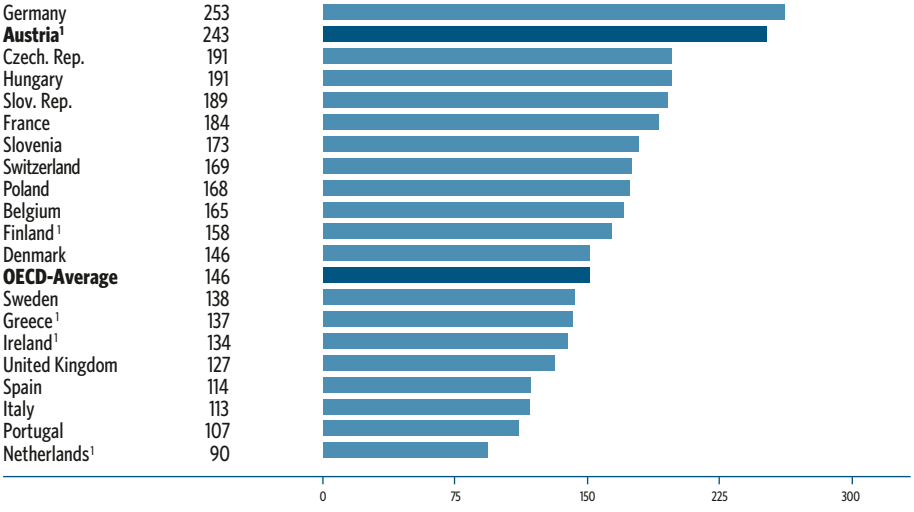
Source: OECD, Health at a Glance Europe 2021

With 7.2 beds per 1,000 inhabitants, Austria is in second place behind Germany (7.9 beds) in the 2020 OECD country comparison.

Austria has 64 % more hospital beds than the average of the OECD countries. There is a slight decline compared to 2008 (7.7 beds per 1,000 inhabitants).

Along with the large availability of hospital beds Austria also has the second highest number of hospital treatments per number of inhabitants after Germany compared to other European countries (243 vs OECD-Average: 146).

Hospital discharges per 1,000 inhabitants, 2020*



* graphic representation of selected EU countries

Source: OECD, Health at a Glance Europe 2021

[1] excluding rehabilitative care, long-term care and palliative care

Development of bed capacity in Austria

The overview also indicates the actual number of beds in Austria's hospitals in 2020 (62,873). In relation to Austria's population, the bed coverage was 7.05 beds per 1,000 inhabitants.

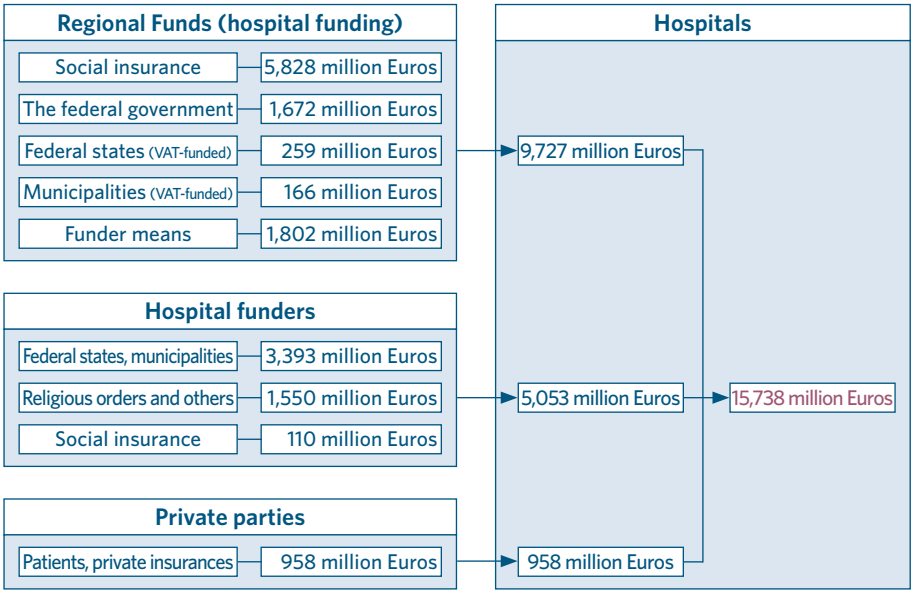
- 2.1 million hospitalisations for in-patient treatment were reported in Austrian hospitals.
- The hospitalisation frequency (= hospital stays per 100 inhabitants) amounted to 23.7 % (1991: 23.9 %, 2010: 33.4 %).
- The average stay in acute hospitals was 6.4 days (full hospital stays in acute care).

As a result of the pandemic, the number of hospital discharges from acute care hospitals has decreased by 17.2 % from 2019 to 2020.

2.2 Hospital funding

The expenditure of Austrian hospitals operating on the "LKF" basis (system of performance-oriented hospital financing) amounted to 15.7 billion Euros in 2020. 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 2020



in million Euros

Source: calculated by the Institute of Pharmaeconomic Research (IPF) with reference to the following data: SV, BMSGPK, Statistics Austria

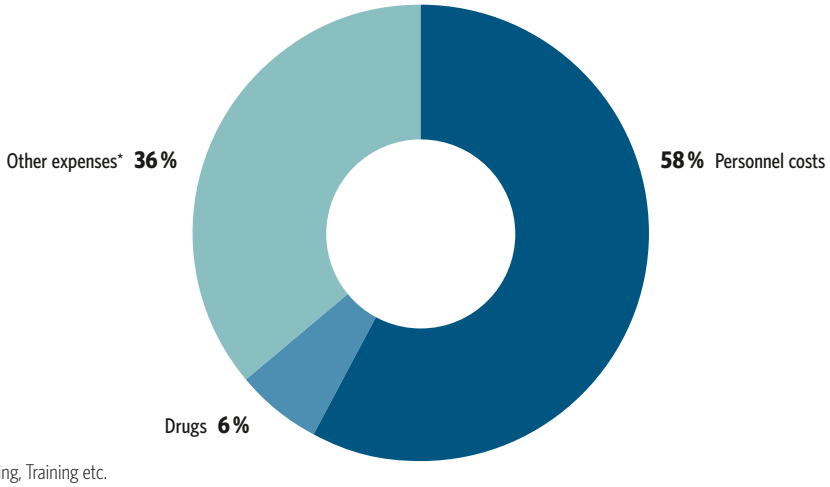
* In the Austrian social insurance system the area of hospital care incorporates the following expenses: proportionate money transfers to regional health care funds and the Federal Health Agency for Inpatient Care, payments to the remaining hospitals (funds for private hospitals, emergency hospitals, 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 9.7 billion Euros which are financed by regional health insurance funds, 60 % are covered for by the social insurance system.

Hospitals financed by regional health funds

The total costs of the hospitals financed by the regional health funds (109 hospitals with 42,251 beds) amounts to 15.7 billion Euros and concern the inpatient and outpatient sector. More than 50 % of the costs are accounted for by personnel, about 6 % by drugs and 36 % by other expenses.

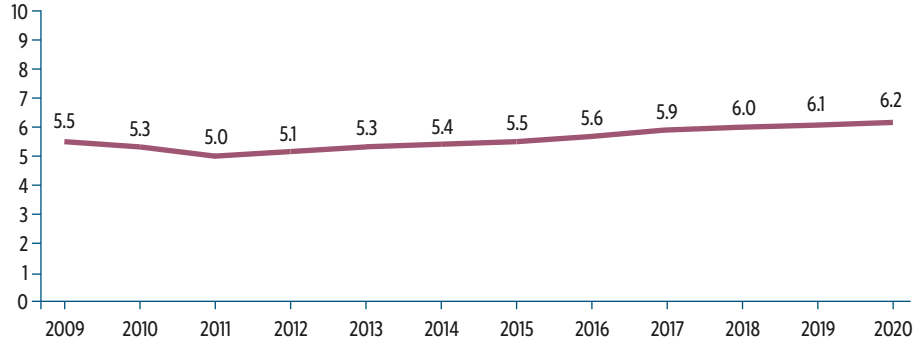
Costs in hospitals 2020



* Catering, Training etc.

The development of drug costs has remained constant at 5 to 6 % over the past 10 years.

Development of drug costs



in percent

Source: On the basis of statutory provisions (Cost Accounting Ordinance, BGBl. [Federal Law Gazette] II Nr. 638/2003 in the version of BGBl. II Nr. 18/2007), the costs of hospitals financed from public funds via the 9 state health funds are collected.

2.3 Pharmaceutical supply in hospitals

The **legal standard for the supply of pharmaceuticals** in hospitals is derived from § 8 (2) and § 19a (3) of the **Federal Hospitals Act (KAKuG)** and from the corresponding implementing regulations of the **hospital laws of the federal provinces**. According to these, the provision of medicines in accordance with the national and international state of the art in medical and pharmaceutical science is generally offered.

Not all state-of-the-art therapies have to be available in all hospitals. Rather, different requirements result from the hospital-legal supply levels (standard, focus and central hospitals*), whereby in **central hospitals a comprehensive supply of pharmaceuticals** must **take place at the international level** of medical and pharmaceutical **science**.

The supply must be based exclusively on the patient's state of health. It **must not exceed the level of medical necessity**, and inappropriate treatments must be avoided. Provided that several drugs are therapeutically equivalent in a specific case, the economically more favorable drug is to be selected (§ 19a Para. 3 and 4 KAKuG).

Medical expertise is required to determine the care required in a specific case. The answer to the question of what is to be regarded as the state of the art in medical and pharmaceutical science under the given circumstances is basically the responsibility of treating physisian. His or her assessment may also deviate from the list of medicinal products of the hospitals, if this is medically necessary in the individual case (Section 19a (5) KAKuG). Guidelines or otherwise designated technical documents from expert networks (e. g. tomour boards, medical societies) can guide the assessment in individual cases as so-called objectified expert opinions. Although they are not legally binding, they can lead to a de facto commitment of the treating physicians. However, they are not bound by the document as such, but by the standard of care correctly and currently described therein. These effects, however, presuppose that the committee is composed of physicians and pharmacists from the relevant disciplines, whose statements are based exclusively on medical and pharmaceutical criteria and not on criteria unrelated to the discipline (e. g., economic criteria). Under these conditions, documents from so-called evaluation committees can also have relevance for the assessment of the legally prescribed level of treatment.

* Standard hospitals are responsible for primary care and run departments for internal medicine, surgery as well as other bed-bearing departments; specialized hospitals run departments in several specialties and special areas as well as, among others, institutional pharmacies, laboratory diagnostics, pathology; central hospitals and university hospitals basically run departments in all specialties and thus cover the entire spectrum of medical care according to the current state of science. Source: Health portal gv.at

Rapid access to innovative therapies is particularly relevant for cancer patients. Evaluations of hospital data on the use of innovative oncological therapies, as well as expert surveys of treatment providers, reveal regional differences within Austria. Bureaucratic hurdles in the approval process can influence the course of treatment.

Further Readings:
Kopetzki, Behandlungen auf dem Stand der Wissenschaft, in: Pfeil (Hrsg), Finanzielle Grenzen des Behandlungsanspruchs, 2010
Mayrhofer, Das rechtlich gebotene Niveau der Arzneimittelversorgung in Krankenanstalten, RdM-Ö&G 2019
Mayrhofer, Sachverstand zur Bestimmung des gebotenen Niveaus der Arzneimittelversorgung in Krankenanstalten, ZTR 2020
Resch, Die Anwendung von schulmedizinisch gebotenen Arzneimitteln in Krankenanstalten, JAS 2019

Sources: GÖG Ergebnisbericht im Auftrag von BMSGPK „Verwendung innovativer onkologischer Pharmakotherapie in österreichischen Krankenanstalten", 2020
OeGHO – Mitglieder-Umfrage „Innovationszugang", 2020

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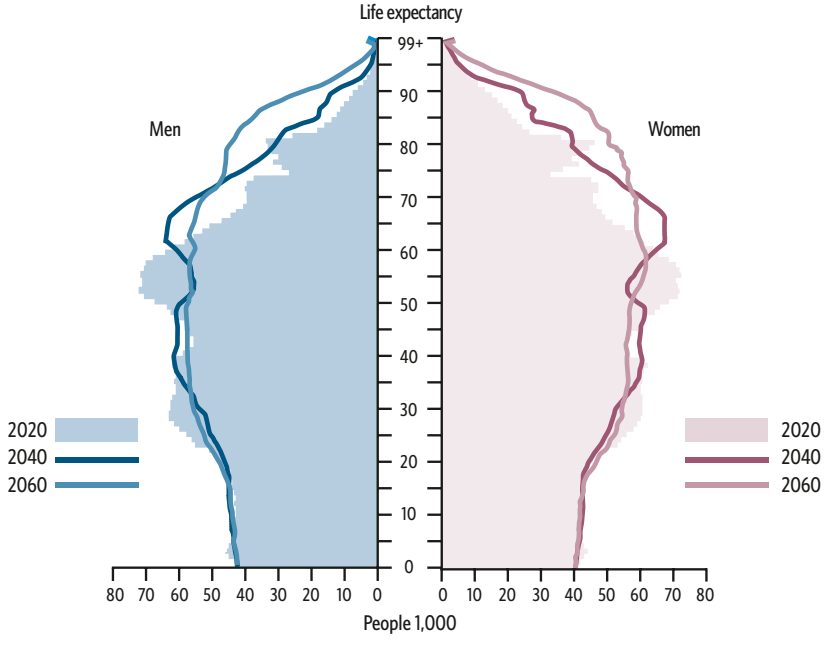
3 Population structure and demographic trends

3.1 Population structure

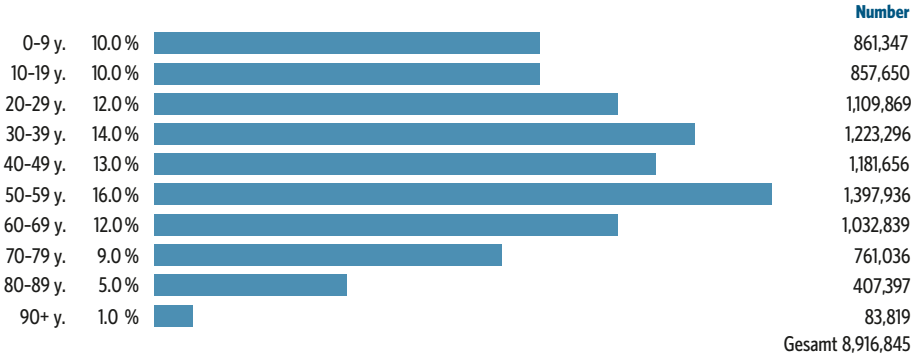
Population pyramid 2020, 2040 and 2060



Source: Statistics Austria

Statistics Austria forecasts a strong population growth until 2060 and a further shift in the age structure towards higher ages. The expected population growth is primarily attributable to migration gains. According to preliminary results from Statistics Austria, the 9-million mark was reached in April 2022 – and according to the forecast, around 9.47 million people will live in Austria by 2040. Life expectancy has increased in recent decades and is 78.9 years for men (at birth in 2020) and 83.7 years for women. However, due to COVID-19 life expectancy has decreased by 0.5 years in 2020.

Share of age groups in total population in %

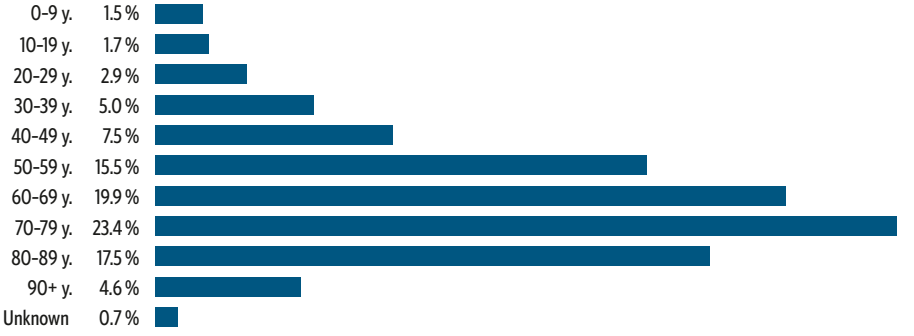


Source: Statistics Austria, 2020

In 2020, the percentage of the population over 65 years of age was 19 %.

3.2 Need for medicinal products by age group

The need for medicinal products in % (health insurance patients, by units)



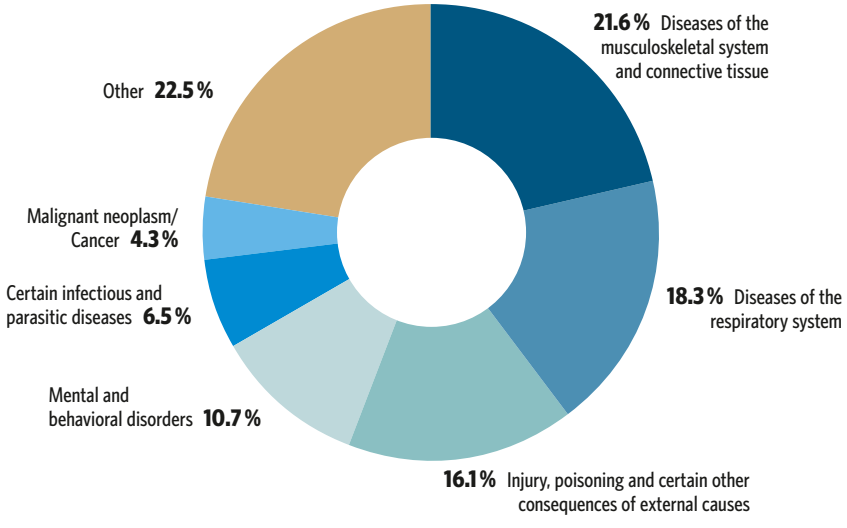
Source: Austrian Chamber of Pharmacists, 2020

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 50.

3.3 Frequent causes of illness

Illness groups as percentage of sick leave days

Survey group: blue collar and white collar



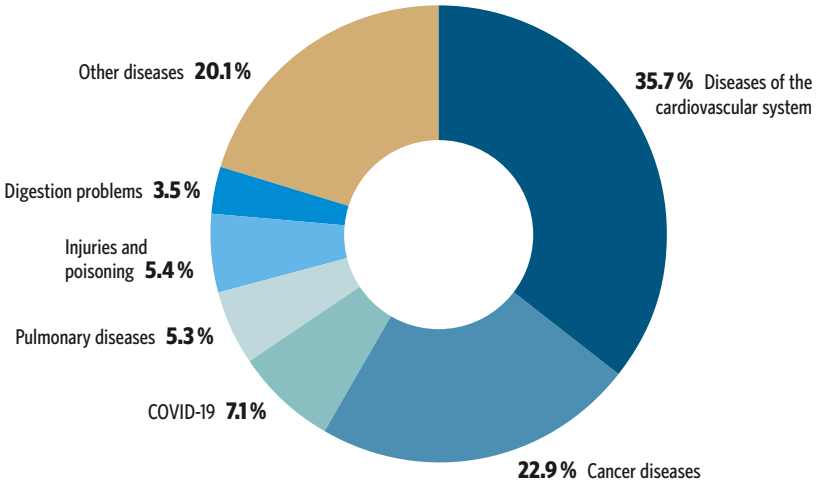
Source: SV, 2021

The 3,696,219 cases of illnesses causing absence from work and the 43,188,491 days of employee absence in 2020 show that illnesses of the musculoskeletal system and of the respiratory system are the main causes for notifications of sickness.

Diseases of the musculoskeletal system together with diseases of the respiratory system represent the cause for approximately 40 % of the notifications of illness.

3.4 Mortality

Mortality by causes of death



Source: Statistics Austria, 2021

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

In line with the increase in life expectancy (see chapter 3.1) mortality for both sexes has decreased by 8 % over the past 10 years (2019 vs. 2010), although the mortality risk for men remains significantly higher for the two most common causes of death. In 2020 nearly 10 % more deaths were recorded than in 2019; the increase was primarily due to the COVID-19 pandemic.

Classification of ICD 10:

- diseases of the cardiovascular system: heart attack, stroke, hypertension etc.
- malignant neoplasm: 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 in Europe

Cancer is a challenge for society:

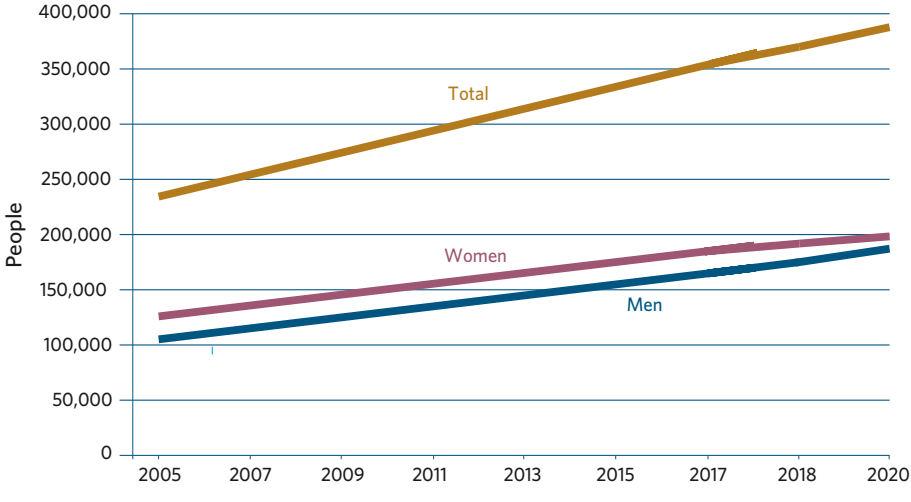
- In Europe, cancer is the leading cause of death after cardiovascular diseases (26 % in 2018),
- 3 out of 5 new cases and 4 out of 5 deaths concern older people (65 years and older),
- In the period 1995–2018, the incidence has increased by 50 % (new cancer cases are approx. 3 million), while mortality has "only" increased by about 20 % (mortality is approx. 1.5 million)
- Approx. 40 % of all new cases would be avoidable; lifestyle factors such as smoking, overweight, alcohol consumption, physical inactivity, poor diet, but also UV-radiation or infections with HPV, hepatitis or HIV have a particular negative effect.

Source: Comparator Report, IHE 2019

Cancer in Austria

- There were 375,749 people living with cancer (of which 52 % were women, 48 % were men) at the beginning of 2020.
- This represents a significant increase compared to 2007 (270,000 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 2020, 41,775 new cancer diagnosis had been documented:

  ➔ **The risks 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 the cancer mortality rate in Austria has declined significantly: according to the latest calculations from the 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

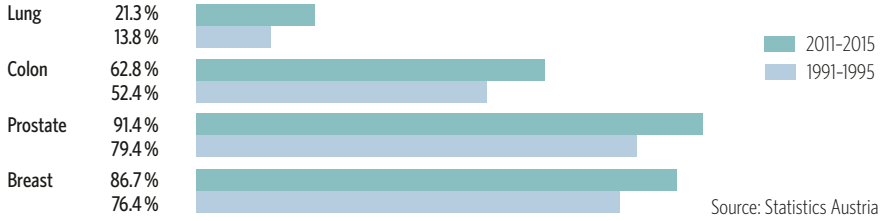
According to the latest calculations by Statistics Austria (for the period 2013–2017), the comparative 3-year survival rate has increased to an average of 65 % in recent years, however tomour stage and type of cancer at diagnosis influences survival rate.

Source: OEGHO Österreichischer Krebs Report 2022

In Austria, survival for cancer patients has improved significantly:

- Relative 5-year-survival for women increased from 56.5 % (diagnosis period 1991–1995) to 63.3 % (period 2011–2015) and for men from 49.4 % to 58.3 %.
- For "younger" cancer patients (up to 44 years), the relative 5-year survival in the period 2011–2015 was as high as 83.4 %. This represents a significant improvement over the comparable period 1991–1995, when this value was 73.1 %.
- The tomour stage at diagnosis is an important parameter for assessing the chances of survival: the later a tomour is detected, the poorer its prognosis. In the period 2011–2015, the relative survival rate after five years is 59.5 % for regionalized stage (i. e. cancer affected) vs. 87.8 % for localized stage (not yet breached).

5-year-survival rate for each type of cancer:



Source: Statistics Austria 2021

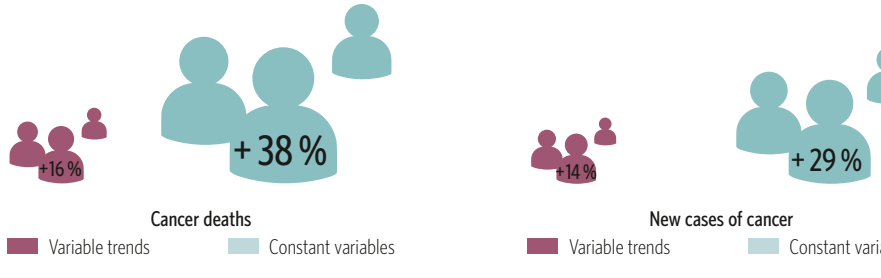
Patients can take part in clinical trials early on and therefore gain access to innovative active substances which increase the chances of curing the disease. About a third of all clinical trials are conducted in the field of oncology. Therefore oncology is the field which is most intensively researched 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 4.2 and 7.3).

Projection for Austria

According to projections, the number of illnesses with malignant neoplasm 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

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4 Pharmaceutical research, development and production

Research location Austria

In the comparative assessment of research and innovation performance of the EU member states, Austria ranks – as in the previous year – 8th in 2020 and in the "European Innovation Scoreboard", which is published annually by the European Union, Austria is classified again as a "Strong Innovator". Compared to 2014, this represents a significant improvement of +11 %. Austria thus ranks behind Luxembourg, Germany, the Netherlands and other strong innovators with its innovation performance above the EU average. The innovation leaders are Sweden, Finland, Denmark and Belgium, whose innovation performance is far above the EU average.

The share of expenditure on research and development (R&D) in gross domestic product (GDP), expressed as a percentage is referred to as the research ratio. This was 3.21 % in 2021, which was above the European target of 3 %, and has grown steadily over the last 10 years (2012: 2.91 %).

For 2022, a research ratio of 3.26 % is expected, which represents a further increase compared to previous years (as of April 2022)*.

- With 50 % the largest share of total spending (in the amount of almost 13 billion Euros in 2021) was borne by companies;
- 33 % was borne by the public sector and
- 16 % by foreign countries.

With research contracts the domestic pharmaceutical industry in Austria in particular contributes to the value added. In 2019, 283 million Euros were invested by the pharmaceutical industry in Austria for research and development (Statistics Austria 2019).

In the life science sector, Austria has, in addition to very good universities, other excellent and internationally recognized research institutes such as the Research Institute of Molecular Pathology (IMP), the Institute of Molecular Biotechnology (IMBA) and the Research Center for Molecular Medicine (CeMM). Since 2008, Graz has been home to Europe's first Research Center Pharmaceutical Engineering (RCPE)

* latest global estimate by Statistics Austria includes COVID-related slumps in economic performance for 2020 and 2021.

to optimise product and process development in the pharmaceutical sector. Austria is also home to the European biobank research infrastructure, which aims to connect existing and new biobanks in Europe, and thus to improve access to biological samples for research. In 2014, the Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC), also based in Graz, began operations.

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 molar 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 9.5) 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 molar 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, etc.). 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 9.6).

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 Health care 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, uniform administrative rules for clinical trials have been established since Jan. 31, 2022, under EU Regulation 536/2014 on clinical trials of medicinal products for human use. Clinical trials still running under Regulation 2001/20/EC have a three-year transition period. Within this transition period, clinical trials must be completed or converted to the requirements of Regulation EU 536/2014. It is still possible to submit clinical trials until Jan. 31, 2023, under the requirements of Directive 2001/20/EC, but these trials must be completed or converted to the regulation within the three-year transition period.
An overview of the legal requirements and processes can be found on the following BASG page: https://www.basg.gv.at/gesundheitsberufe/klinische-studien/klinische-pruefung-arzneimittel

Divergent approaches among the various member states in implementing this directive have resulted an insufficient harmonization across the EU. This has made it particularly difficult to conduct multinational clinical trials in Europe. With the new EU Regulation 536/2014 on clinical trials on medicinal products for human use, this has now been changed. A central approval procedure with uniform applications submitted via a central portal will harmonize and simplify the conduct of clinical trials in Europe.

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. 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

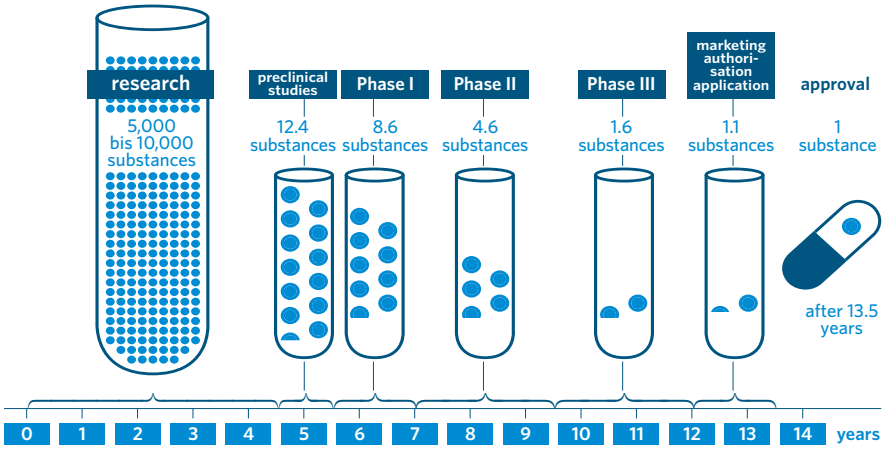
application can be submitted to the appropriate authorities for authorisation of the medicine.

- **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 recent years. Both commercial and academic applications are on the rise again.

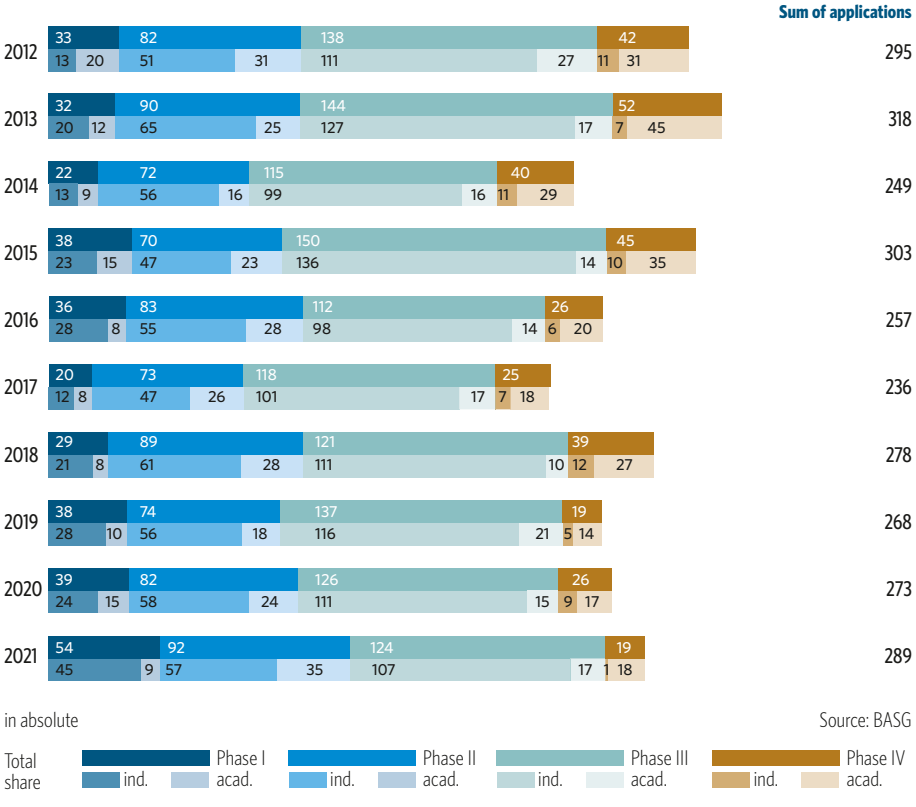
On average in the EU, about 80 % of clinical trials are conducted by the pharmaceutical industry (industry-sponsored); 20 % by academic scientists (academically sponsored). With a share of 27.3 %, Austria is above this value. Compared to last year, especially phase I and phase II studies have increased. It should be noted, however, that integrated designs (phase I/II or II/III) are counted as the lower phase. Of the 54 phase I studies submitted, 21 were declared by the sponsors as first-in-human studies. This is almost double the number of the previous year (12).

The focus of the studies differs between commercial and academic sponsors. For commercial studies, Phase I is mainly first-in-human applications and new developments. This may also explain the strong increase in “Phase I studies” (including “Phase I/II”). Academic studies, on the other hand, are mainly aimed at the kinetics of approved drugs in humans and indication extensions. The proportion of “pilot studies” is usually very high. This is reflected in the increase in "phase II" studies.

Confirmatory clinical trials (phase III) in preparation for approval are mainly conducted in the commercial sector. In contrast, far more phase IV studies are carried out in the academic sector, i.e. further research on approved drugs within the terms of approval.

Phase IV also includes observational studies that require additional measures (e. g., the additional collection of biomarkers).

Distribution of clinical trial applications in Austria according the phases



Pandemic-related activities:

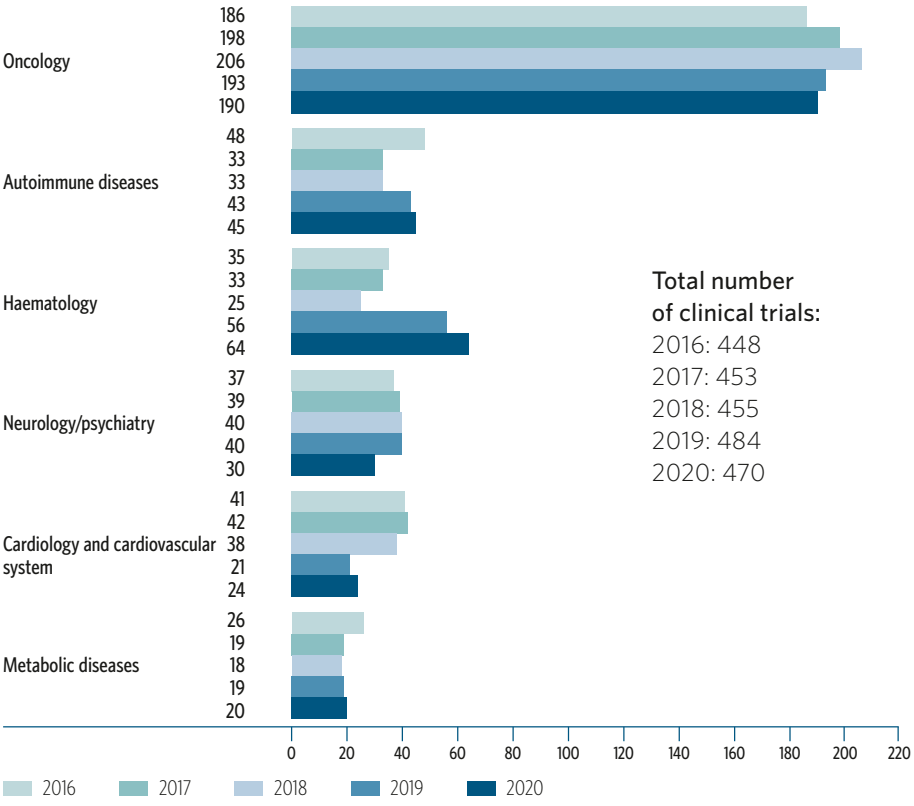
The pandemic continued to have a major impact on clinical trials in 2021. 24 clinical trial applications with COVID-19 relevance were processed, of which two were withdrawn early. About half of these were new therapeutic approaches. The remainder were optimizations of the use of approved vaccines as well as reviews for vaccine response and safety in subgroups with potentially compromised immune responses.

Industry-sponsored clinical research in Austria

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 participated 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 33 companies participated in the survey** during the past five years retrospectively. **This corresponds to a market coverage of approximately 79 %** (in rerms of revenues as of of all PHARMIG member companies).

Ongoing industry-sponsored clinical trials according to indication groups

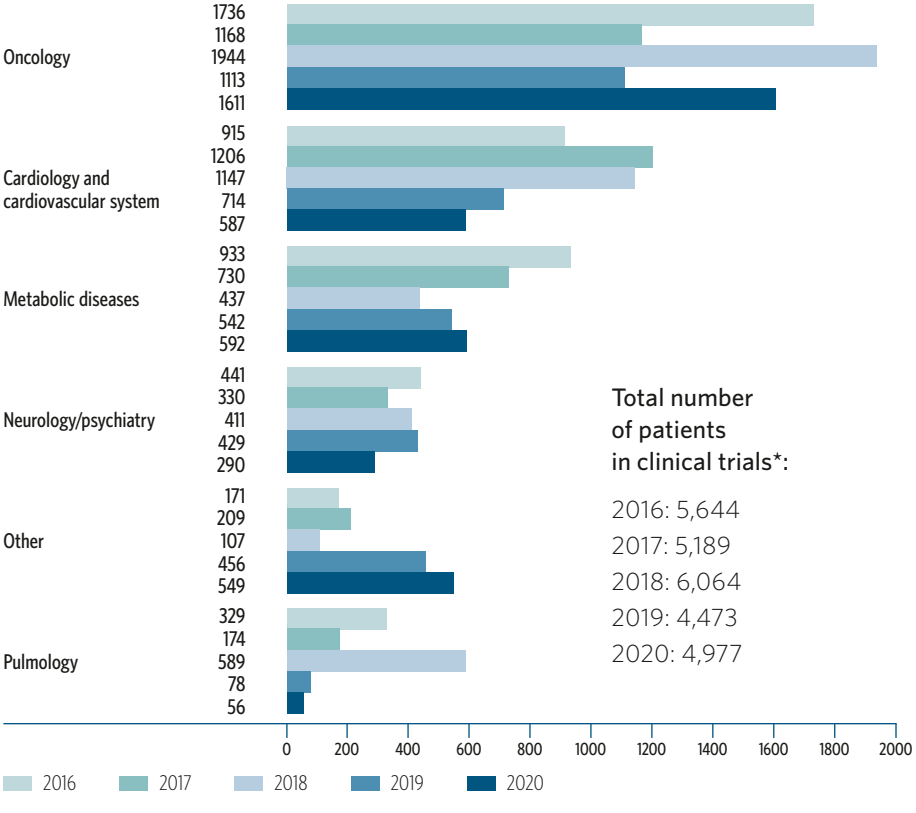


in absolute

Source: Survey of industry-sponsored clinical research in Austria, PHARMIG 2016–2020

The average **total** of approximately **462** clinical trials per year over the last 5 years includes ongoing, initiated and terminated clinical trials.

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



in absolute

Source: Survey on industry-sponsored clinical research in Austria, PHARMIG 2016–2020

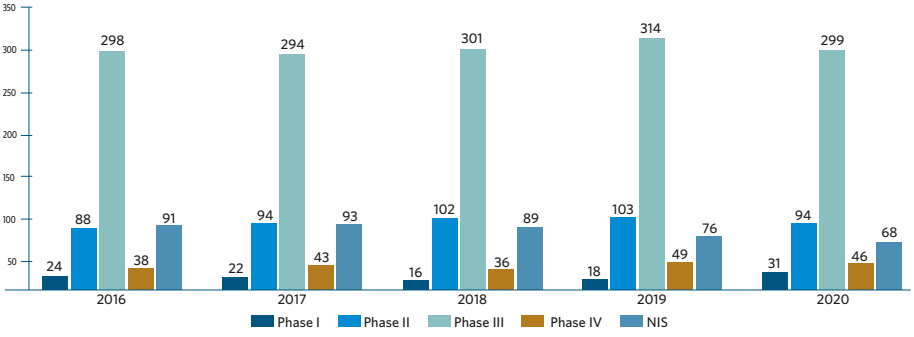
Around 5,269 patients participated annually in ongoing, initiated and terminated clinical trials in Austria*.

* Information on the number of patients is available for an average of 86 % of clinical trials

Number of running clinical trials according to phases and Non-interventional studies (NIS) in AT 2016 to 2020

The average total number of clinical trials:

2016: 448 2018: 455 2020: 470
2017: 453 2019: 484



in absolute

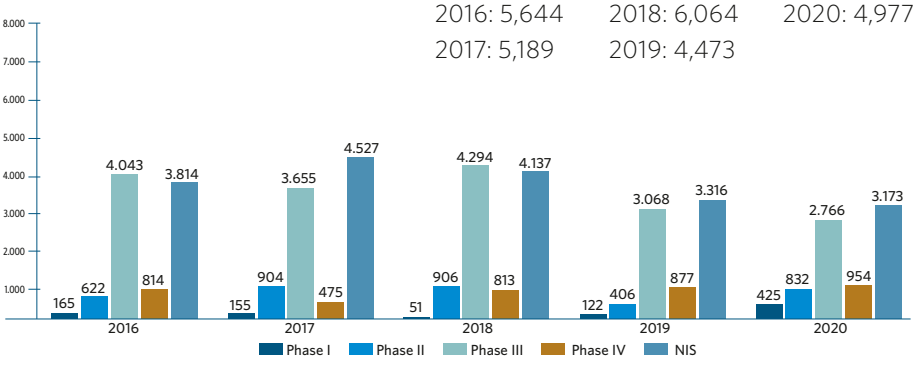
Source: Survey on industry-sponsored clinical research in Austria, PHARMIG 2016–2020

Furthermore, through the support of the pharmaceutical industry, on average **124 "investigator initiated trials"** were made possible per year in the years 2016–2020.

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

The average total number of patients in clinical trials*:

2016: 5,644 2018: 6,064 2020: 4,977
2017: 5,189 2019: 4,473



in absolute

Source: Survey on industry-sponsored clinical research in Austria, PHARMIG 2016–2020

* Information on the number of patients is available for an average of 86 % of clinical trials

Pediatric pharmaceutical research

50–90 % of medicinal products conventionally used in pediatrics are not authorised for children because pediatric 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 Pediatric 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 (pharmaceutical industry, university medical centers, clinical trial coordination centers, specialty departments, etc.). Together with the Federal Ministry of Health and funds from the "joint health care objectives from the pharmaceutical framework agreement", 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 24 companies, including PHARMIG, and further funding for the OKIDS network from the "joint health care objectives" (2019–2022), which will, among other things, facilitate an expansion of the facilities in Linz, (more information: http://okids-net.at/unternehmen.html). As of the 3rd funding period (since June 2020), the contracting is done directly between funding companies incl. PHARMIG and OKIDS. Additional funding was acquired through participation in EU projects. Recently, OKIDS has also received funding through a private foundation.

Since its foundation in May 2013, OKIDS has conducted 142 feasibilities from CROs, pharmaceutical companies and through Enpr-EMA and c4c (Collaborative Network for European Clinical Trials for Children). 272 trials and registries have been conducted with OKIDS support since OKIDS' foundation. The number of participating patients is well over 1000 children and adolescents.

After the successful inclusion in the European pediatric research network Enpr-EMA (European Network of Paediatric Research at the European Medicines Agency) and as a project partner of PedCRIN (Paediatric Clinical Research Infrastructure Network –

project has been completed) and c4c (Connect for Children), OKIDS has taken on important tasks in European structural planning and is, thus, gaining increasing visibility in the European study landscape for pediatric medicines. OKIDS was part of the Enpr-EMA working group on "Trial Preparedness" with a focus on establishing early synergies and cooperation between industry and academic partners in drug development.

Transparency of study data

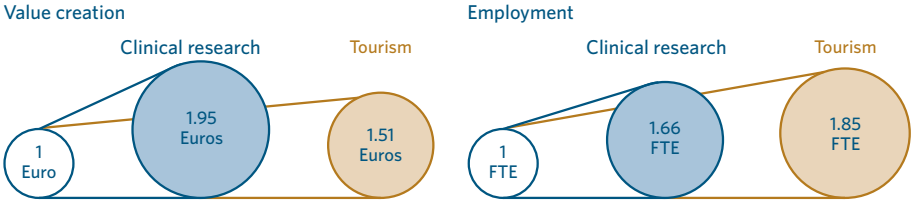
- The U.S. National Institutes of Health keep the largest public register since 1997. They publish study data from all 50 federal US states and from a further 180 countries:
  https://www.clinicaltrials.gov
- The European Clinical Trials Register (EudraCT) by the European Medicines Agency (EMA) has made 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://www.basg.gv.at/gesundheitsberufe/klinische-studien/nicht-interventionelle-studien-nis

The value creation of industry-sponsored clinical trials

The value creation generated by conducting industry-sponsored clinical trials in Austria amounts to 144.2 million Euros annually. Each year, a medical treatment value of 100 million Euros was financed through 463 industry-sponsored clinical trials with an average medical treatment value of 37,068 Euros per recruited patient. This treatment value includes free trial medication, the assumption of costs for diagnostics, therapy as well as administrative services and documentation. This corresponds to a significant share of 0.3 % of the current annual health expenditure.

Every Euro invested in clinical trials by the pharmaceutical industry generates 1.95 Euros for the Austrian economy. Jobs in the order of 2,021 full-time equivalents are created and secured, which leads to an employment multiplier of 1.66 (see chapter 8.5)**.**

Industry-sponsored clinical trials



The overall economic benefit of 144.2 million Euros annually is divided into direct (gross production value), indirect (advance performance relationship of the suppliers of clinical trials) and secondary (consumption and investment effect in other economic areas) effects.

Effects	Value creation	Employment
Direct effects	74.13 million Euros	1,215 FTEs
Indirect effects	38.47 million Euros	475 FTEs
Secondary effects	31.60 million Euros	331 FTEs
Sum	**144.19 million Euros**	**2,021 FTEs**
Multiplier	1.95	1.66

The performance of clinical trials by the pharmaceutical industry leads – in addition to the benefit for patients – to positive macroeconomic effects (contributions to the Austrian health care system, but also location and industrial policy).

Source: Study of the Institute for Pharmaeconomic Research (IPF) in cooperation with PHARMIG from 2019, published in the Journal of Medical Economics: https://www.ncbi.nlm.nih.gov/pubmed/32046538

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 Health care (BASG) is the responsible enforcement authority for Austria together with the Austrian Medicines and Medical Devices Agency (Medizinmarktaufsicht) of the Austrian Agency for Health and Food Safety (AGES).

Measures against falsified medication

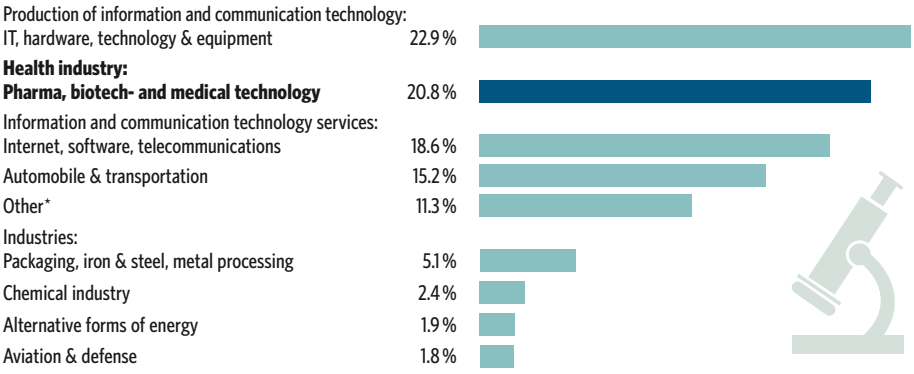
Security features on every pack of medication should make any tampering immediately apparent and ensure the medication is fully traceable from the manufacturer to the pharmacy.

see also chapter 6.2

4.4 Research and development – investments

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

Research rate, by industry (Europe)



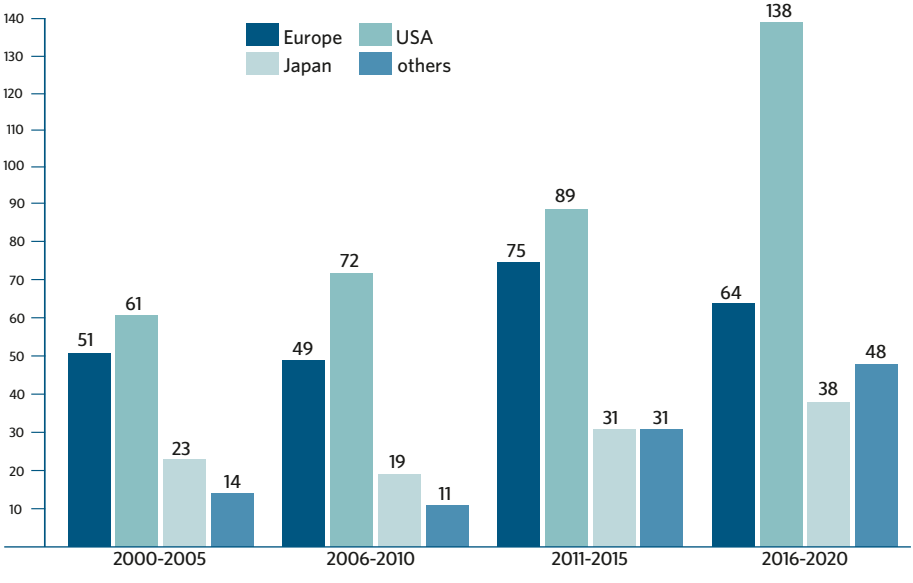
Source: The 2021 EU Industrial R&D Investment Scoreboard

* financial and banking, electricity, paper industry, recreational goods, and many more

In the area of research & development, the "health care industry" (pharmaceutical, biotech and medical device industry) ranks second behind the information and communications technology industry: 188.7 billion Euros were invested in research & development in 2020; this corresponds to approx. 20.8 % of sales.

4.5 Medicinal product innovations

New molecular entities by region



in absolute

Source: SCRIP/EFPIA, 2021

- In 2021, 92 new medicines for human use were approved in Europe (EMA)
- 53 of these contain a new active substance
- New approvals are for the treatment of cancer, infectious diseases, diseases of the central nervous system, cardiovascular system, inflammatory diseases, etc.
- In 2022, new products are also expected to be launched for the treatment of cancer (almost one third of the new drugs), for the treatment of infectious and inflammatory diseases, and many more.

Source: EMA, VfA, IQVIA, EFPIA

Number of innovations in Austria

in absolute

Source: AGES, 04/2022

In the last ten years, a total of 378 drugs with a new active substance have been approved in Austria. On average, 38 new treatment options are available each year.

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)

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)
2019	First vaccine against ebola
2019	First anti-cancer drug whose use is not restricted to certain tumours but is instead dependent on the presence of a certain gene mutation (so-called "tumour diagnostic cancer drug")
2020	First vaccines against COVID-19, along with a development time with less than a year, the all time fastest developed vaccines ever
2020	First drug against the viral disease hepatitis D
2020	Causally effective drug against cystic fibrosis, potentially applicable to around 60 % of patients (instead of just a small percentage)
2020/ 2021	First selectively immunosuppressive drugs against atopic dermatitis (= neurodermatitis)
2021	First antiviral antibodies against COVID-19; with less than two years development time, the fastest developed therapeutic drugs with new agents since the introduction of drug approval.

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 Patent law

The value of a medicinal product is based on the research and development achievement, which receives special protection as intellectual property. The term "Intellectual Property" (IP for short) includes copyright and related trademark rights, trade secrets and industrial property rights (patents and utility models, brands and designs). This protection of intellectual property 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 12 years (see chapter 4.2). Due to the high investment and 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 invention is protected from imitation for a legally defined period of time (in favor of the patent holder, who finances and carries out the research and development), which results in the exclusive economic use for the patent holder for this period of time.

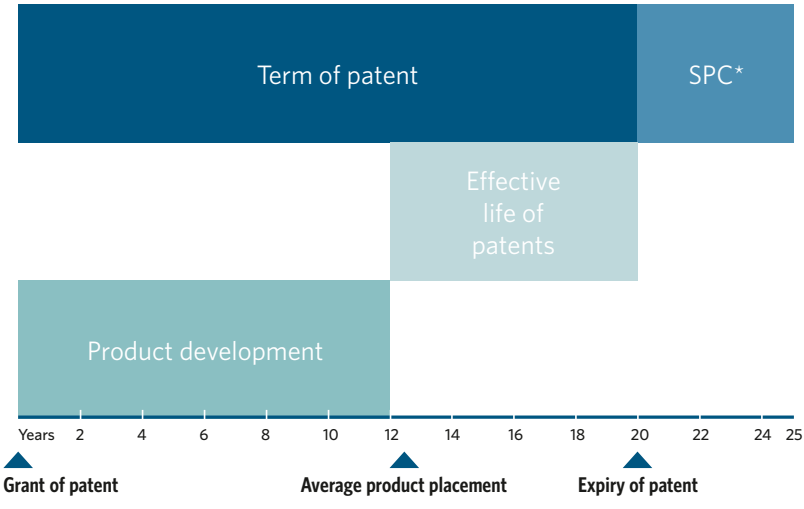
They are therefore an important driver of innovation.

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 its 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.

SPC Waiver

In 2019, the EU Commission created an exemption of the supplementary protection certificate (SPC Waiver) for the production of generic drugs for the purpose of export as well as for generic drug production and storage for the first placing on the market in the EU (6 months before the expiration of the SPC). National patent offices must be informed about the production. A new EU export logo (http://patentblog.kluweriplaw.com/wp-content/uploads/sites/52/2019/04/EU_export.gif) must be displayed on the outer packaging for exports to third countries.

The SPC waiver is intended – according to the argument of the proponent – to strengthen the production of generic drugs and biosimilars in Europe. On the part of the innovative industry, this regulation is viewed critically as an intervention in patent protection.

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 (pediatric medicinal products), may assert an additional 6 months of patent protection after submission of a Pediatric Investigation Plan (PIP). Any medicinal products whose patent protection has already expired, may apply for an additional year of data exclusivity – upon submission of new pediatric 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.

4.7 Usage of health data

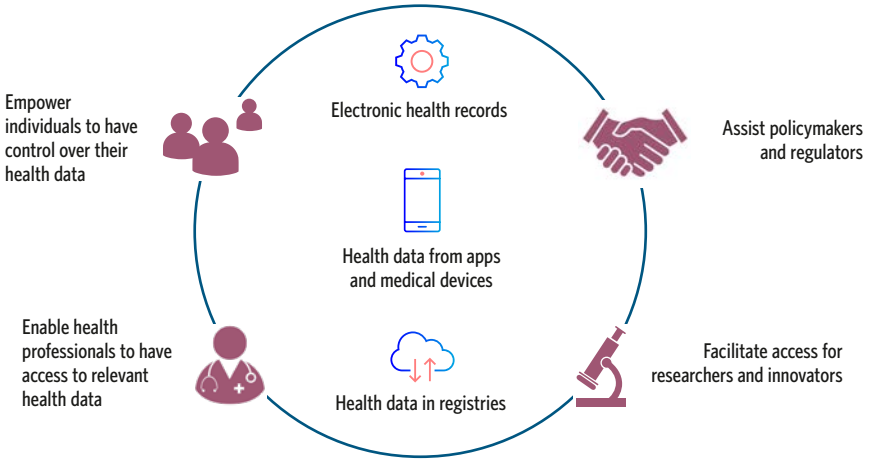
The amendment to the Federal Act amending the Federal Statistics Act (BStatG) 2000 and the Research Organization Act (FOG) (400/BNR), was passed in November 2021. It represents a significant milestone in improving scientific access to public, de-identified statistical and registry data while respecting data confidentiality provisions.

For the purpose of scientific research, access to microdata from Statistics Austria and to data from registries (access standardized by FOG) should be made accessible. Statistics Austria was commissioned to set up a technical platform **"Austrian Micro Data Center"** (AMDC), in order to provide researchers access to anonymized data remotely. The implementation of the AMDC is planned for July 2022.

At the European level, the implementation of the **"European Health Data Space"** (EHDS) – one of the priorities of the European Commission – is scheduled. The central element is the orientation towards the common good: structured collection, connection and careful use of health data enables evidence-based decisions for optimized planning, quality care and future-oriented research. In addition to citizens of the European Union, regulatory authorities and policymakers will benefit from secure and transparently accessible data.

Individuals – EU citizens – will benefit from **primary data use**, such as cross-border exchange also of health data, i.e. information on diagnosis, treatment, care and reimbursement of insurance benefits. **Secondary data use** is the anonymized reuse of existing information for the purpose of scientific research (for further development of therapies and medicines). Patients subsequently benefit from this. It goes without saying that data protection has top priority in any form of data use. European regulations, directives and laws provide the legal basis*.

* Data Protection Regulation (GDPR), Data Governance Act, Data Act and Directive "on measures to ensure a high common level of security of network and information systems in the Union" (NIS Directive).



Source: European Commission

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5 Marketing authorisation for medicinal products

5.1 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)**
  This 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.

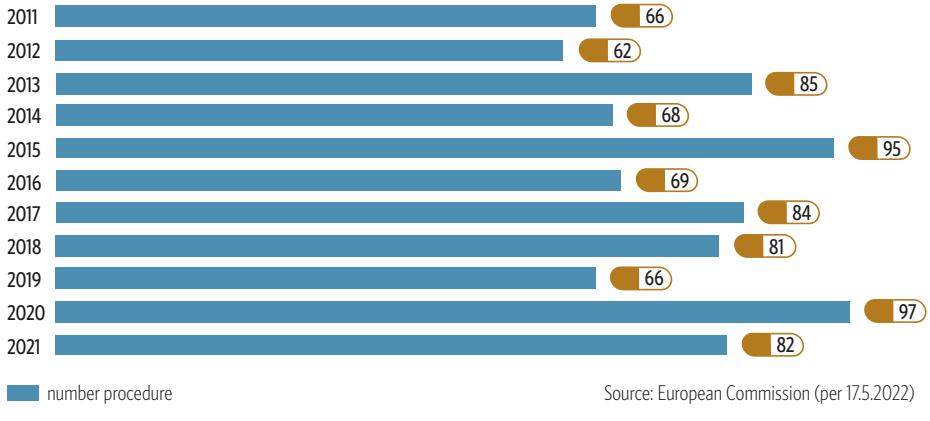
- **Centralised procedure (EU)**
  A centralised procedure has been in place since 1995, at the completion of which a European Authorisation is awarded. In a centralised procedure, the authorisation is

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.

Centralised Procedures for medicinal products in EU



Source: European Commission (per 17.5.2022)

5.2 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.)

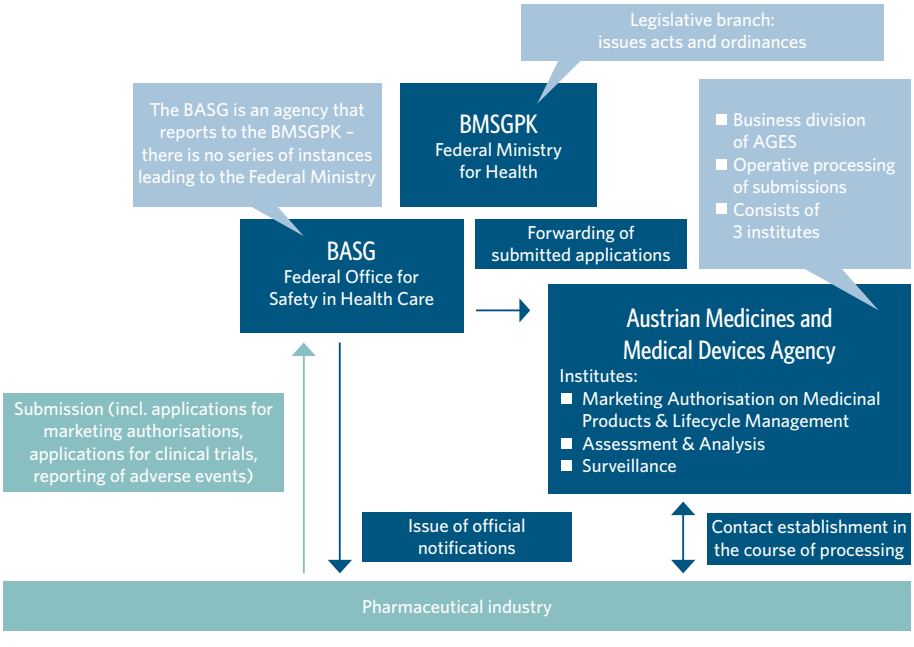
If a pharmaceutical is approved according to the MPA, it is designated as a proprietary medicinal product.

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 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 Social Affairs, Health, Care and Consumer Protection and the Federal Ministry for Agriculture, Regions 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 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 – Organigram

Download here:
https://www.basg.gv.at/fileadmin/redakteure/01_Formulare_Listen/A/L_A03_Organigramm_MEA_Deutsch.pdf

5.3 Authorised and registered human medicine specialities

Total number of approved medicinal products for human use 2021

Approved medicinal products for human use	9,149
Biological medicinal products	383
Homeopathic medicinal products	542
Medicinal gases	37
Herbal medicinal products	178
Radioactive pharmaceuticals	47
Chemical medicinal products	7,948
Medicinal products that represent a monography of the ÖAB/Ph.Eur*	14

* § 9c Medicinal Products Act

Source: Austrian Medicines and Medical devices Agency

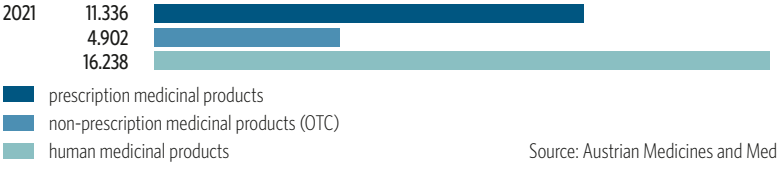
Number of registered medicinal products for human use 2021

Registered medicinal products for human use	3,987
Pharmacy-proprietary medicinal products	677
Homeopathic medicinal products	3,011
Traditional use registration for herbal medicinal product application	213
Allergen manufacturing procedure	86

Source: Austrian Medicines and Medical devices Agency

5.4 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 30 % of the medicinal products for human use approved in Austria are available as non-prescription medicinal products in pharmacies.

5.5 Regulatory characteristics

Conditional approval

The European Medicines Agency (EMA) supports the development of medicines that address unmet medical needs. In the interest of public health, applicants may be granted conditional marketing authorization for such medicines. This requires less comprehensive clinical data than would normally be required.

Conditional approval is granted when the following **criteria** are met:

- the benefit-risk ratio of the drug is positive;
- it is likely that the applicant will be able to provide comprehensive post-authorization data;
- the drug meets an unmet medical need;
- the benefit of the drug's immediate availability to patients outweighs the risk that additional data will still be needed.

Conditional marketing authorizations are valid for one year and are renewable annually. Once a conditional marketing authorization is granted, the marketing authorization holder must meet certain obligations within specified timeframes, such as completing ongoing or new studies or collecting additional data to confirm that the benefit-risk balance of the drug remains positive. The conditions are published in the EMA's Assessment Report. The conditional approval can be converted to a standard approval once the obligations imposed are met and the completed data confirms that the benefits of the drug continue to outweigh the risks.

Rolling Review

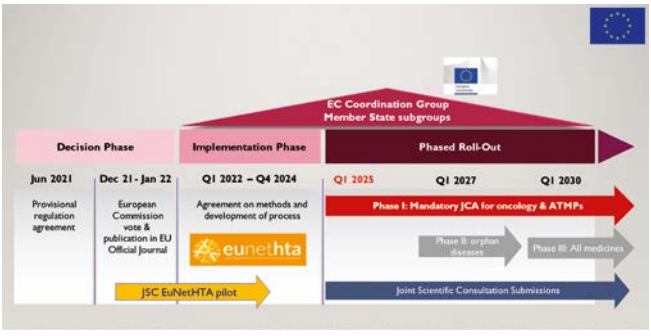
Normally, as part of the approval process, a complete application with all required data must be available before the evaluation begins. In the rolling review-procedure, however, the lead reviewers (rapporteur and co-rapporteur from two EU member states) of the Committee for Medicinal Products for Human Use (CHMP) evaluate individual successively submitted data packages as soon as they have been submitted and are available. The rolling review of successively submitted data packages, thus, serves to accelerate the evaluation.

The rolling review-process continues until the data provide sufficient evidence to allow a formal regulatory submission and benefit-risk assessment. It will also be considered at what point sufficient data are available to allow a final benefit-risk assessment.

Despite acceleration, the requirements for quality, safety and efficacy of the drugs in question remain high. The rolling review-procedure was used for the approval of COVID-19 vaccines by the EMA (see chapter 7.8)**.**

5.6 Health Technology Assessment (HTA)

Health technology assessment (HTA) is the **systematic evaluation of medical procedures and technologies** (a large proportion of which relate to drugs and medical devices) in health care. For this purpose, all available data are presented and evaluated under a specific question. HTA reports are often the basis for decisions by physicians, health authorities, health insurers and other payers on the medical and economic value, as well as the social and ethical framework of the respective issue. Following a legislative proposal from 2018, the European Commission issued the "Regulation on Health Technology Assessment" (Regulation (EU) 2021/2282) on January 12, 2022. It will apply from January 2025. It regulates how health technology assessments are to be carried out at European level in the future. How the findings of the joint clinical evaluations are handled remains a matter for the individual EU member states. The implementation and rollout phase is set until 2030. https://www.sozialministerium.at/Themen/Gesundheit/Gesundheitssystem/Health-Technology-Assessment-(HTA)/Health-Technology-Assessment-in-der-EU.html



Source: EK, EFPIA

The regulation aims to
- efficiently use resources and improve the quality of HTA across the EU,
- avoid duplication of work between national HTA bodies and industries,
- prove certainty to companies and
- provide long-term sustainability of HTA cooperation in the EU,
- and thus to give patients better and faster access to innovative medicines and medical devices in the EU.

The administration of health services, including pricing and reimbursement for pharmaceuticals, remains the responsibility of member states.
https://ec.europa.eu/commission/presscorner/detail/de/IP_21_6771

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6 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, health care professionals and the public.

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

Pharmacovigilance system

The Pharmacovigilance system is used 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.

6.1 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. 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.

Reporting of side effects and evaluation

After marketing authorization manufacturers and drug authorities systematically search for additional, still unknown side effects. The most important source of information for this is spontaneous reporting: in this process, health care professionals such as physicians and pharmacists report suspected cases of side effects that have occurred in patients under their care. Since 2012 patients themselves have also been able to voluntarily report side effects. For them, there is an online adverse reaction reporting form on the BASG website https://nebenwirkung.basg.gv.at/. Physicians, pharmacists and other health care professionals are required by law to report side effects.
The BASG records all suspected adverse reactions to medicines and vaccines that have occurred in Austria. After processing and assessment, the data are forwarded to the EMA in accordance with the applicable European regulations. This makes the data available to all national drug authorities for ongoing safety monitoring.
The risk-benefit balance of medicinal products is continuously monitored in close cooperation between the EU authorities. The Pharmacovigilance Risk Assessment Committee (PRAC) at the EMA analyzes all aspects relevant to the safety and efficacy of a drug. If necessary, new side effects are included in the specialization and usage information or other measures are taken in order to ensure safe and effective use.

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.

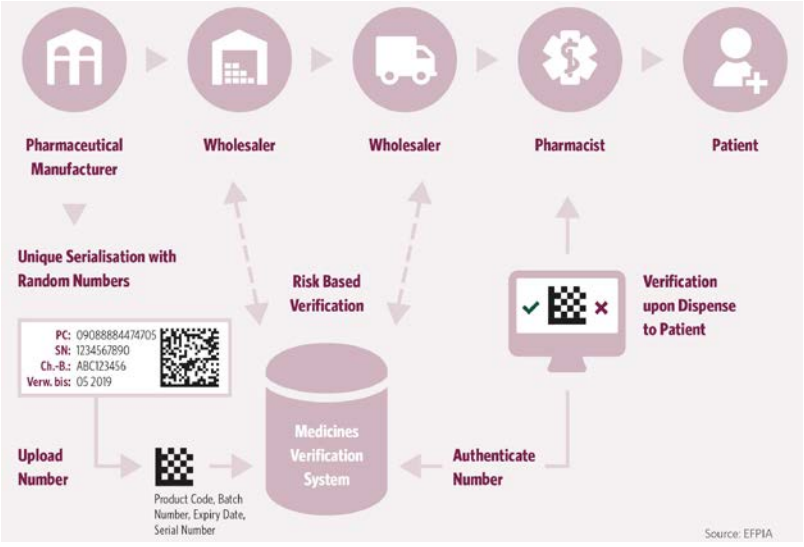
It is estimated that an average pharmaceutical company with a wide range of active ingredients could pay up to 20 million Euros annually in pharmacovigilance fees alone.*

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

6.2 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.



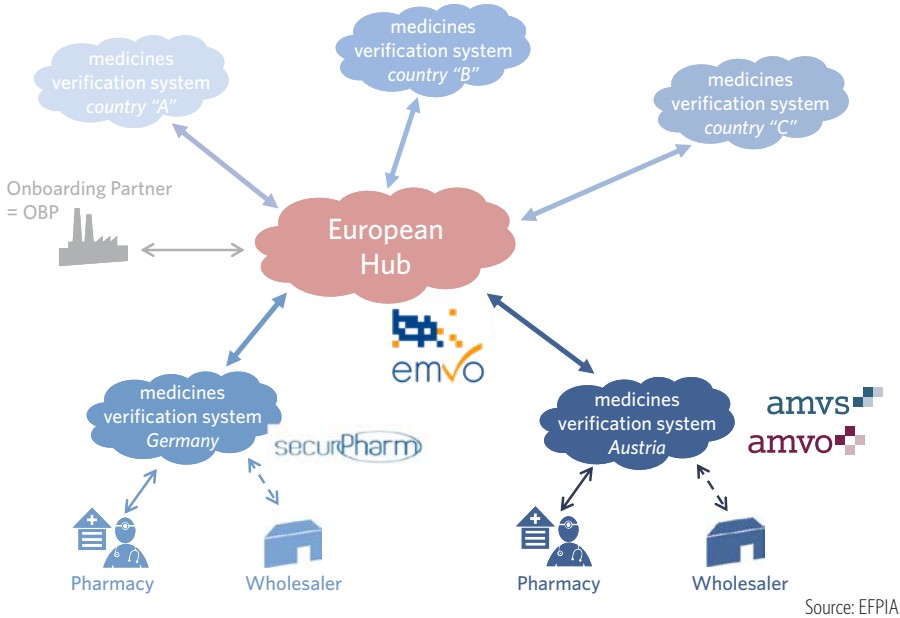
Source: EFPIA

In principle this affects all prescription drugs for human use, exceptions can be found in Annex 1 and Annex 2 of the delegated 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 is 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). A deactivated serial number means that the package has already been issued. If the same serial number reappears at a later time, it indicates a suspicion of falsification.

The European system of serialising medicinal products

For this process, in accordance with the Delegated Regulation, a data storage and retrieval system was set up by the pharmaceutical manufacturers and marketing authorization 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 (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.

The EU-wide verification system was implemented in all member states on 9 February 2019 as planned.

For further information, please visit https://www.amvs-medicines.at/ or https://www.amvo-medicines.at/.

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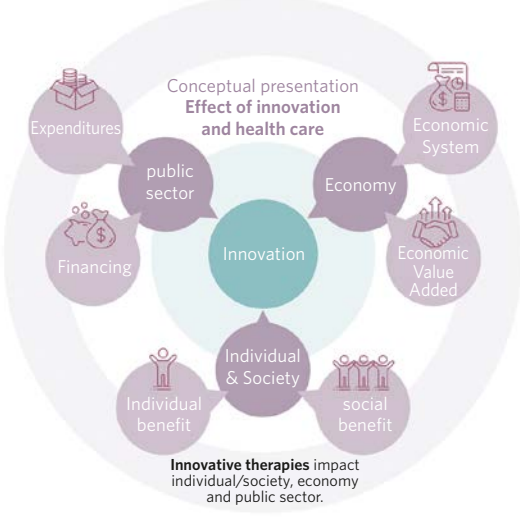
7 Benefits of innovative therapies

Medicinal products make an important contribution to our society: they help heal, relieve or protect against diseases. Based on new scientific findings – about fundamental biological processes or specific diseases – novel drugs are developed with which patients can be treated (even) better or for the first time.
Pharmaceuticals and medical progress make a significant contribution to longer life expectancy. A study conducted in Germany shows the link between pharmaceutical innovation and life expectancy: in the period from 2007 to 2011, life expectancy increased by 1.4 years, with one-third of this improvement attributed to newer drugs (Liechtenberg 2012). The effects of medical innovations extend far beyond **direct benefits to patients**. They can **reduce health care spending**, for example by shortening or avoiding hospital stays, as well as the amount of care needed by family members. Sick leave can also be reduced or even avoided and the health care system as a whole can be improved at the process level as a recent study by the IHS shows.



Source: Wert von Innovation im Gesundheitswesen, IHS 2021

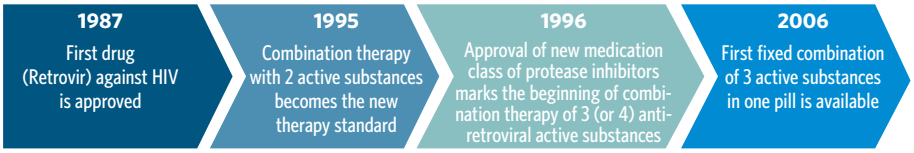
The following examples illustrate how innovations in drug development can change the entire health care system and the opportunities they offer – first and foremost to save lives and giving people suffering from diseases a better quality of life again.

7.1 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.

According to current expert calculations (such as Österreichische AIDS Gesellschaft, AIDS Hilfen et al), it can be assumed that there are about 9,000 HIV-infected persons in Austria, which corresponds to about 0.1 % of the population. In 2021, according to the Center for Virology of the Medical University of Vienna, 376 people were newly infected, in 2019 there were 430. The observed decrease may also be due to a low number of tests.

Important milestones in the treatment of HIV:



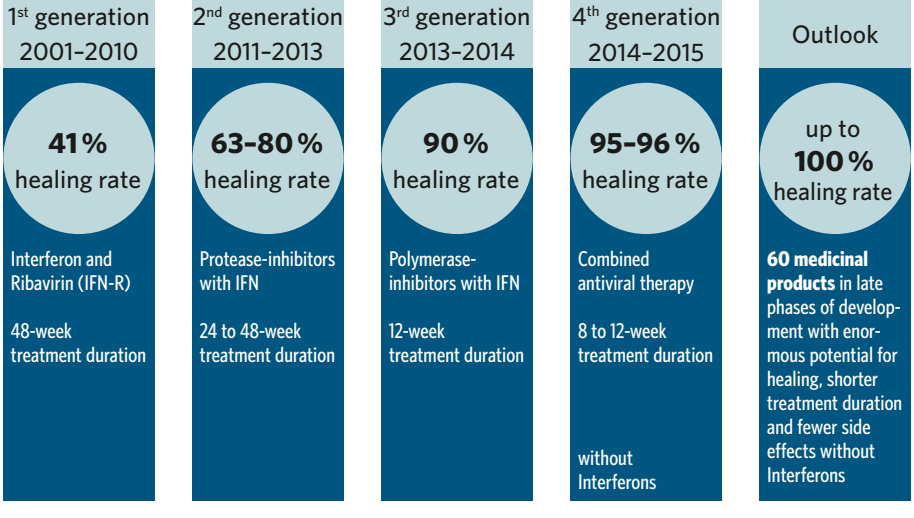
Now there are more than 35 medications available as individual active substances or fixed combinations of up to 4 active substances for HIV therapy.

Source: Aidshilfen Styria, Austria, Germany

7.2 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 (HCV) 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: IFPMA, 2021

7.3 Cancer

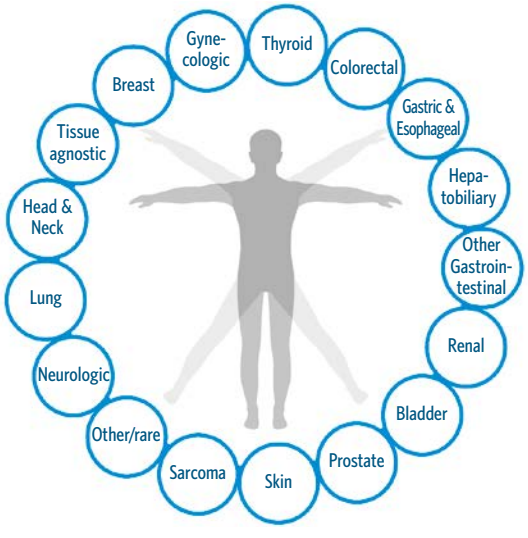
In the past 10 years modern cancer treatments have helped patients to increase quality of life and gain valuable time of life. Cancer is increasingly turning into a chronic illness and can now often be healed in some areas. With new diagnostic and therapeutic possibilities the treatment of cancer also 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 in Austria from 2018 vs. 1995 by approximately 21 % – Europe wide by 15 %.
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.
In addition to common forms of treatment – surgery, radiotherapy, and chemotherapy – patients have access to biopharmaceutical therapies such as targeted and immuno-oncological therapies.

- In the period 1995–2020, **145** new drugs were approved in oncology.
- **20 new cancer medicines** came onto the market in Europe in **2021 – 12 of them with a new active substance**.
- Numerous new medicines are in development at the moment
  Also in Austria **oncology** (approx. 50 % of all studies in Austria) is the **most researched therapeutic area** (see chapter 4.2 Clinical research).

Number of cancer drugs and indications approved by the EMA

Source: EMA

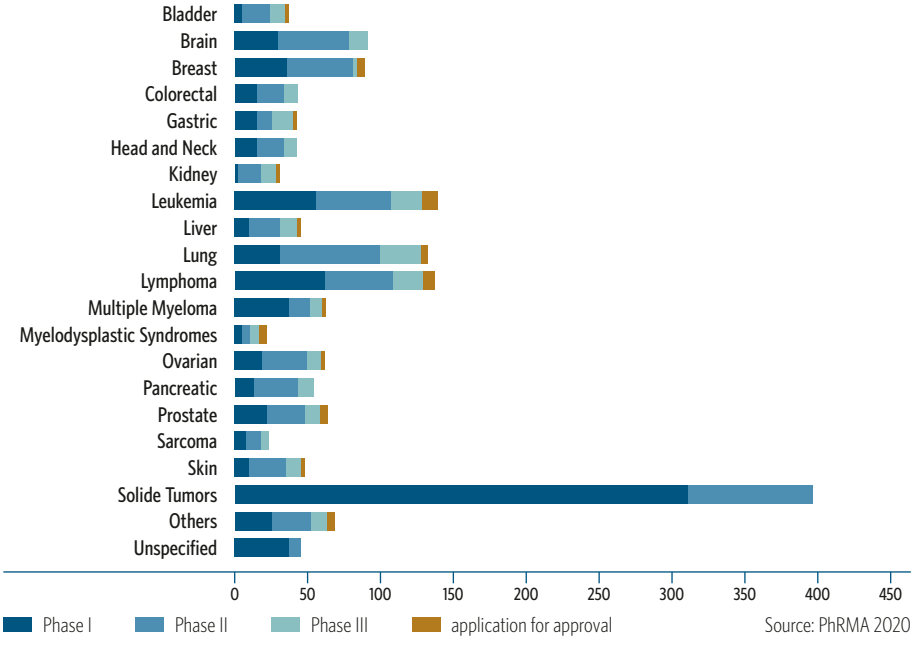
Novel active substances in oncology by indications:



Source: IQVIA

Outlook: according to IFPMA, more than 2,740 drugs are in development for the treatment of more than 20 tomour types using novel approaches (gene analysis, viral therapy (mRNA), immunotherapies, antibody-drug conjugates)

Medicines and vaccines in development against cancer



Source: PhRMA 2020

The cost of cancer treatment in Austria, measured as a proportion of total health care expenditure, remains constant at around 6.4 %, despite significantly higher incidence rates and longer treatment periods (see 2014: 6.5 %). There is a clear correlation between the level of expenditure on cancer care and treatment outcomes or survival rates: The higher the investment in innovation-oriented cancer care, the better the prognosis for cancer patients.

Source: IHE Comparator Report 2019, EMA 2019

7.4 Personalised medicine in oncology

Personalised medicine in oncology means the interaction of state-of-the-art diagnostic solutions and precise cancer therapies to enable patients to achieve better treatment success and a better quality of life. Personalised medicine begins with precise diagnostics. This requires high-quality, certified, and validated diagnostic tests (molecular tumour profile analyses) using state-of-the-art technology.

The first targeted cancer drugs were already approved more than 20 years ago. Technological developments and a high research intensity have further advanced the possibilities of precise cancer treatment. Today, more than 70 targeted therapies are available in Europe. In recent years, approximately 10 new cancer therapies have been approved annually. A milestone in this process is a novel precision therapy for the treatment of a specific gene fusion in the tumour, regardless of where the cancer is located in the body. Until now, cancer therapies have been targeted to a specific type of cancer or organ (e. g. breast cancer or lung cancer). Personalised medicine is increasingly looking at the genetic fingerprint of the cancer.

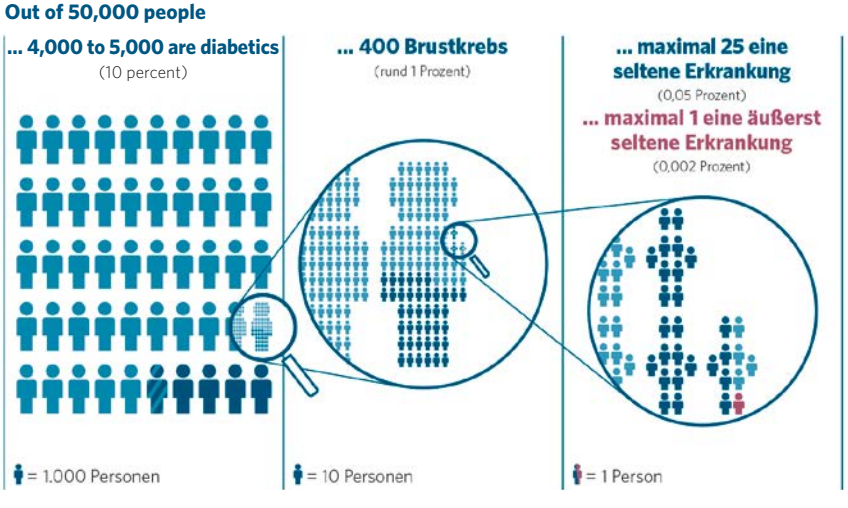
In addition, the field of regenerative medicine and gene and cell therapies opens up further possibilities not only to fight complex diseases but even to cure them. Current examples are the two gene therapies with so-called CAR-T cells, which have been approved in the USA and Europe in 2018. These are active ingredients from genetically modified cells.

Source: vfa, BPI

7.5 Medicinal products for the treatment of rare diseases

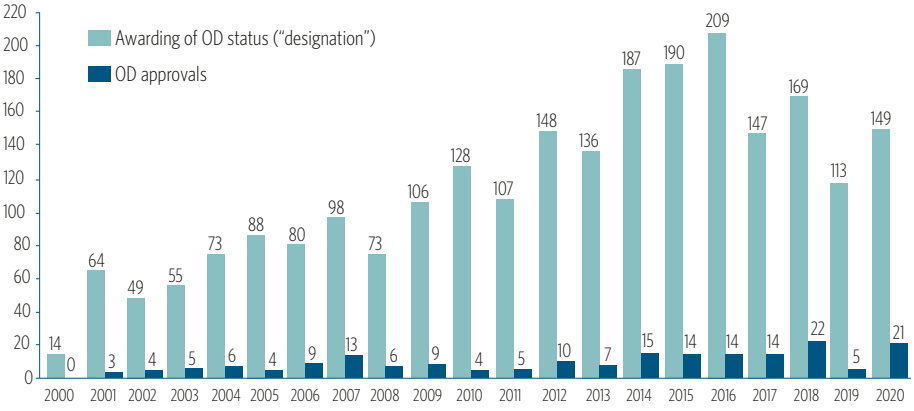
Rare diseases are disorders which are life-threatening or chronically debilitating and which affect less than 5 in 10,000 people (in relation to the European average). Of around 30,000 diseases known to this day, 6,000 to 8,000 count as rare diseases and over 50 % of these affect children. In Austria 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:



3,678 applications for orphan drug status were filed from 2000 to 2020. In 2,382 cases orphan drug status was awarded but, so far, only in 190 of these cases marketing authorisation has been granted. The great number of applications (3,678) 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 (190 approvals) demonstrates the high entrepreneurial risks for companies.
In 2021, 19 orphan drugs could once again be approved, 4 of which are entirely new therapies for the treatment of rare childhood diseases.

Awarding of orphan drug status vs. approval of orphan drugs (2000–2020)



in absolute

Source: EMA Orphan Medicines Figures 2000–2020

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 of 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 health care objective, the health care reform or the children and youth health care strategy.

The NAP.se combines plan and strategy, and defines 9 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, as well as the evaluation of the reports, and information on the NKSE can be found here: https://www.sozialministerium.at/Themen/Gesundheit/Seltene-Krankheiten.html

The NAP.se evaluation report provides, among other things, more clarity regarding further implementation and recommends ongoing monitoring the implementation of the measures.

7.6 Plasma donation in Austria / products made from blood plasma

The medicinal products derived from human blood plasma (more than 60 authorised medicinal products) have numerous applications, such as

- the treatment of congenital and acquired immune defects,
- haematology including haemophilia,
- for serious injuries and burns (for haemostasis and for wound closure),
- for liver diseases,
- for severe infections (such as COVID-19; plasma-based therapy was injected for treatment),
- for neurological diseases and
- in oncological pathologies.

The cooperation of local research and development facilities with hospitals, universities and local industrial manufacturers forms the basis for the development and the worldwide launch of new products.

Blood plasma has been donated and processed in Austria for about 55 years, the longest tradition in Europe.

Plasma donation and processing in Austria:

- 22 plasma centres
- about 40,000 donations and about 510,000 litres of plasma in 2018
- 58 litres of plasma per 1,000 inhabitants: Austria is part of the world's top plasma collection country and leading in Europe
- 1.5 to 5 million Euros each year, each plasma centre contributes to the local economic performance
- over 400 employees in the Austrian plasma centres
- 2 plasma processing companies with a capacity of approx. 4 million litres of plasma per year (about 15 % of the worldwide capacity)
- extraction of plasma components, fully integrated production of high-quality pharmaceuticals and export to over 100 countries
- more than 5,000 jobs

7.7 Vaccination

Not only can 2 to 3 million lives be saved every year (exclusive COVID-19), but many disabilities can also be avoided through the widespread use of vaccinations, as well as prevention of another 1,5 million deaths. 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 health care 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 by vaccination programs.

A calculation by the Institute of Pharmaeconomic Research (IPF) from 2019 shows that vaccination against influenza, pneumococcus and HPV and from 2021 against COVID-19 also pays off for society and the health system.

Vaccines – just like all medical products on the market – are monitored for their safety (see chapter 6 Pharmacovigilance).

The vaccination system in Austria

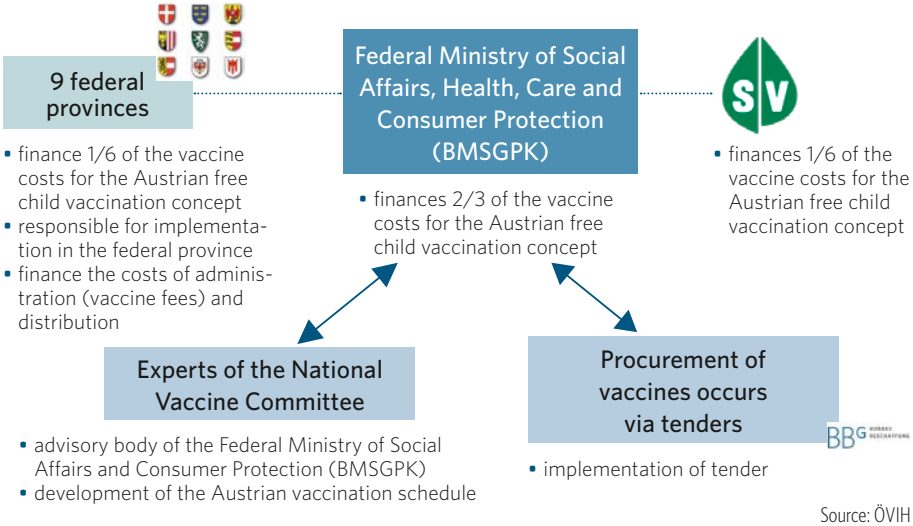
The Austrian vaccination schedule provides an overview of currently available vaccinations. It differentiates between vaccinations which are borne by public authorities within free child-vaccination programmes and those vaccinations which must be self-financed, but are recommended on the basis of scientific 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 2020 on the website of the Federal Ministry of Health:
https://www.sozialministerium.at/Themen/Gesundheit/Impfen/Impfplan-%C3%96sterreich.html

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 the age of 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 is made up as follows:



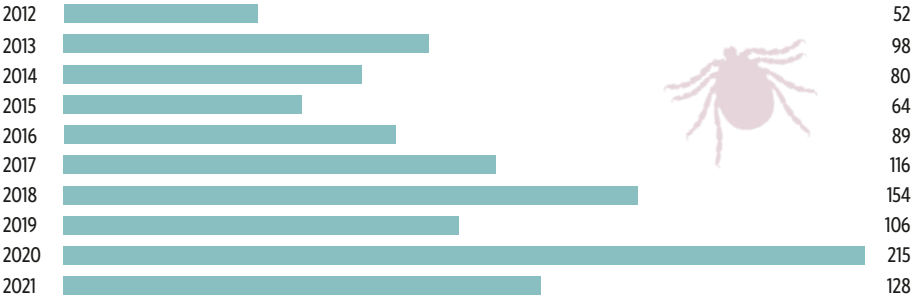
Source: ÖVIH

Current examples of important vaccination in Austria:

TBE (tick-borne encephalitis)

The vaccination rate for TBE is very high compared to other European countries and currently stands at 81 % in the Austrian population up to the age of 65. Austria is considered an endemic area. In 2021, despite the high vaccination coverage rate, 128 people were hospitalized with TBE disease. The number of cases has thus again significantly decreased to 2020 and is only slightly higher than in the last 20 years (excluding the outliers of 2018 and 2020). The correct vaccination scheme, which provides for basic and booster vaccinations, leads to almost complete (95–99 %) protection.

Number of TBE cases diagnosed in Austria over time



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Source: Virology MedUni Vienna, 2021

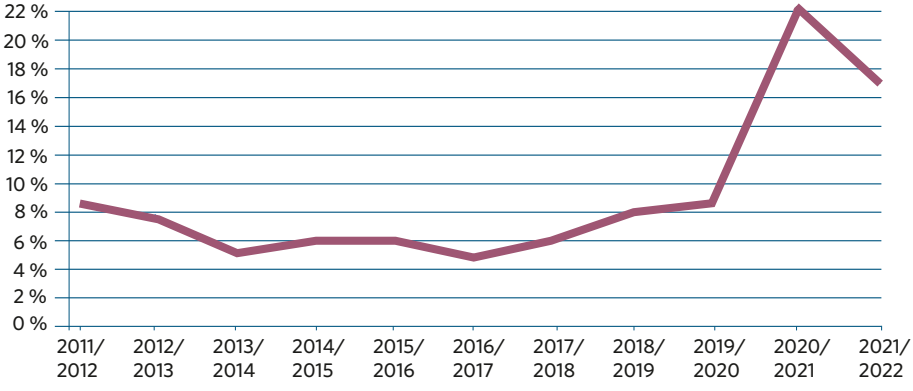
Influenza

According to AGES, there were 2,314 cases of flu and flu-like illnesses per 100,000 inhabitants in Austria at the peak of the flu season in 2019/20, which lasted almost three months. Small children (aged 0–4) fell ill particularly frequently.

Only low influenza activity was recorded in the 2020/2021 season and, therefore, the influenza epidemic was not declared in Austria

Model calculations by the BMSGPK have shown that vaccinating children makes a very good contribution to reducing or even preventing the spread of influenza: an 80 % coverage rate in children leads according to a study by Tsang et. al to a 61 % reduction in influenza cases in the unvaccinated adult population. To prevent concurrent influenza and COVID-19, influenza vaccination was included in the free Children's Vaccine Program for the first time in the 2020/21 season in Austria and is still included in it. In some federal states, there is a widespread offer of vaccinations, some of which are free or at reduced costs for adults.

Influenza-vaccination coverage over time



in percent

Source: ÖVIH

Vaccination coverage rate increased to approximately 21 % in the 2020/2021 season. Unfortunately, this rate could not be maintained in the 2021/2022 season. There was a decline to around 17 %.

Measles

According to WHO by 2020 Measles was supposed to be eradicated in at least five WHO regions. However, instead of being on the verge of elimination, they occure more frequently again, although 2020 is an exception. Despite the COVID-19 pandemic, including the associated precautionary measures, there were 25 registered cases of measles in Austria, according to the BMSGPK (for comparison, there were 151 in 2019). In the rest of Europe, the situation was similar: according to the ECDC (European Centre for Disease Prevention and Control), just over 2,000 cases of measles were documented in 2020, compared to more than 13,000 in 2019.
A vaccination coverage rate of 95 % with two doses is required for sufficient immunity in the population. Vaccination gaps exist in children ages 2–5 years and in people ages 15–30 years.

Virus-associated cancers

According to a study published by the NEMJ at the end of 2020, vaccination against human papillomavirus (HPV) contributes significantly to the reduction of cervical cancer: vaccinated women are significantly less likely to develop this type of cancer. The Austrian Vaccination Plan therefore provides HPV vaccination for girls and boys.

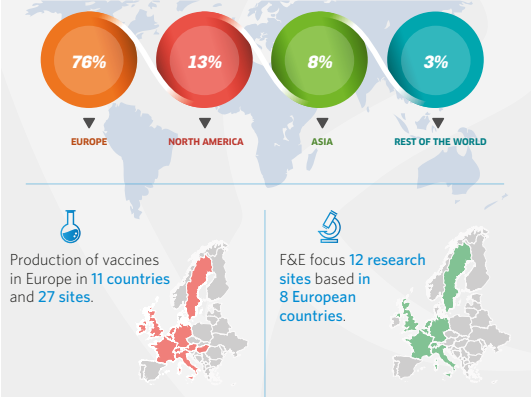
Bacterial diseases

In 2020, 356 invasive pneumococcal diseases were reported in Austria. People over 75 years of age were mainly affected. In addition, there were numerous cases of non-invasive diseases, such as pneumonia. To protect the population, vaccionation against pneumococci is included in the Austrian Vaccination Plan.

European production and vaccine supply

Europe represents the heart of global vaccine research and production. In 11 European countries, 1.7 billion doses (without COVID-19) of vaccine are produced. 76 % of the vaccine doses produced worldwide (exclusive COVID-19) come from the 27 European production sites. 86 % of the vaccine doses produced in Europe are distributed globally. More than 50 % go to humanitarian aid programmes. Vaccine research focuses on the development of "next-generation" vaccines and vaccines that protect against more diseases than ever before (such as research on vaccine against COVID-19, see chapter 7.8).

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



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.

For more information please visit: https://oevih.at/was_wir_tun/impfstoffproduktion.

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. In Austria there are 7 companies that sell vaccines, including COVID-19 vaccines. COVID-19 vaccines are also offered by 2 other manufacturers not operating in Austria.

Research into COVID-19 vaccines and the production of components of COVID-19 vaccines, which are being used worldwide, is carried out at 4 sites.

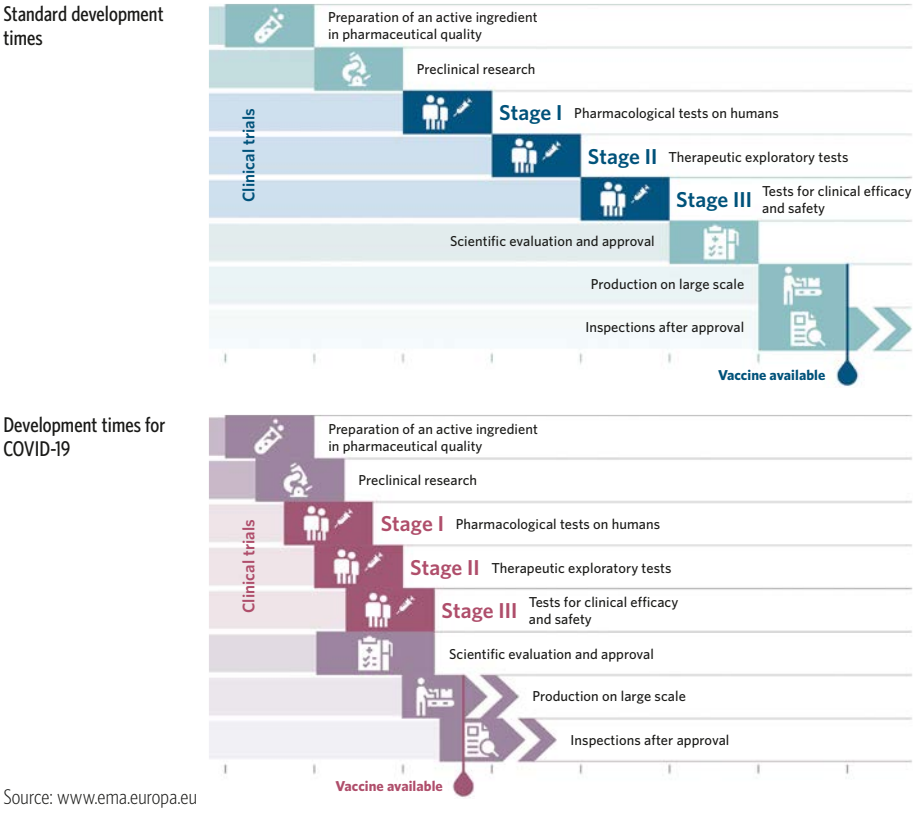
7.8 COVID-19 pandemic

With the announcement of the novel coronavirus SARS-CoV-2 on December 31st, 2019, numerous research and development projects for rapid and reliable tests to detect the virus, preventive-COVID-19 vaccines, and therapeutic drugs were launched worldwide within a very short time.

COVID-19 vaccines

It took 236 days for the first COVID-19 vaccine to become available. Contributing to this rapid development were **global collaborations between academia, organizations and companies**, rapid approvals of the study protocols and their designs, the conduct of the studies in multiple centers and countries, the high level of interest among volunteers to participate, and, last but not least, the early, cross-phase and parallel assessments (rolling review processes) by the regulatory authorities (see chapter 5.5 Regulatory characteristics).

Vaccine development in comparison



Source: www.ema.europa.eu

Overview: COVID-19 vaccines:

An **overview of vaccine research and development** is provide by WHO: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

An overview of the **status of vaccine approval in Europe** is provided by EMA: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines

Therapeutic Drugs

Existing drugs are being tested and new ones developed for the treatment of COVID-19. The first fundamentally new drugs were approved **less than two years after the project began**. The fast pace is partly due to prioritization in the companies and rapid study approval procedures in many countries.

Drugs of different types are needed. Most fall into one of the following five groups:

- **Antiviral drugs:** They are designed to prevent the viruses from entering body cells or from multiplying there.
- **Cardiovascular drugs:** These are designed to protect the blood vessels, heart and other organs from complications caused by the COVID-19 disease.
- **Attenuating immunomodulators:** In the advanced stage of the disease, they are intended to limit the body's defense reactions so that they do not cause even more damage than the viruses themselves.
- **Medications for lung function:** These are intended to help the lungs to maintain their function during the acute infection and to regenerate afterwards with as few consequences as possible.
- **Medications for long covid**, i. e. persistent symptoms after the actual COVID-19 disease has subsided.

Source: vfa

Overview: Drugs for the treatment of COVID-19

An **overview of the status of therapeutic drugs** in Europe is provided by the EMA: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines-covid-19

An interactive map of the industry associations vfa, BIO Deutschland and PHARMIG shows where pharmaceutical companies in the DACH region are working on vaccines or therapies against COVID-19.
www.vfa.de/corona-karte

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8 Pharmaceutical industry as an economic factor

Economic footprint of the pharmaceutical industry in Europe

The economic contribution of the pharmaceutical industry to the EU economy is estimated at 206 billion Euros in 2016 – of which 100 billion are direct effects and 106 billion are indirect effects, corresponding to approximately 1.4 % of total economic output (GDP). The pharmaceutical industry, thus, creates approximately 2.5 million jobs across Europe (with above-average levels of qualification and female). This is corresponding to 0,9 % of the total number of jobs in the EU. Source: PwC 2019

8.1 Pharmaceutical production in Europe

Pharmaceutical production in selected European countries

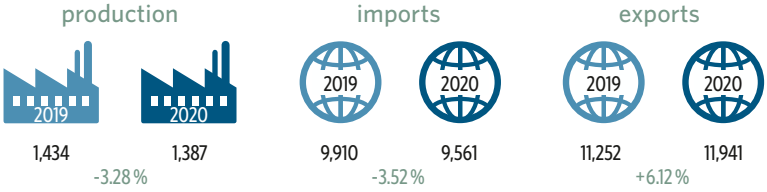
	million Euros	Euros per inhabitant	estimated population beginning 2019
Switzerland	54,305	6,274	8,655
France	35,848	549	65,274
Italy	34,000	562	60,462
Germany	33,158	396	83,784
United Kingdom	23,039	339	67,886
Ireland	19,305	3,909	4,938
Belgium	17,547	1.514	11,590
Spain	15,832	339	46,755
Sweden	9,840	974	10,099
Netherlands	6,180	361	17,135
Poland	2,550	67	37,847
Finland	1,877	339	5,541
Portugal	1,737	170	10,197
Austria	1,434	161	8,917
Norway	1,072	198	5,421

Source: EFPIA, Statistics Austria (changes in classification compared to previous years), Eurostat 2022

In 2019, Switzerland, France, Italy and Germany produced the majority of pharmaceuticals in Europe. Switzerland reported the highest production value per capita.

8.2 Pharmaceutical production in Austria

Pharmaceutical production in Austria, imports and exports



in million Euros

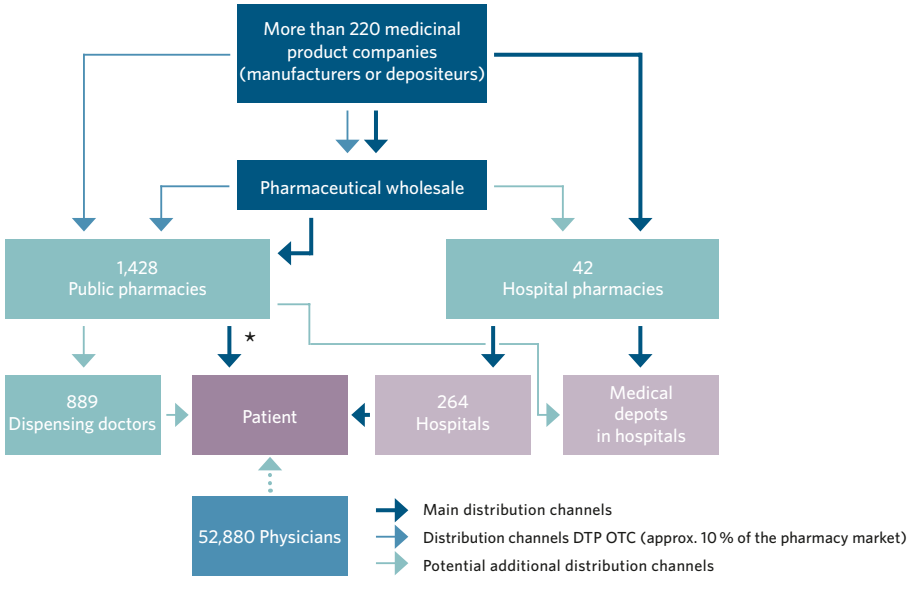
Source: Statistics Austria (changes in classification compared to previous years)

In the pharmaceutical industry, Austria is among the export countries: 2020 has a positive (+ 6.12 %) balance of trade. In 2020 compared to 2019 about - 3.28 % fewer pharmaceutical products were manufactured.

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, SV, BMSGPK, Austrian Chamber of Pharmacists, 2022

* 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).

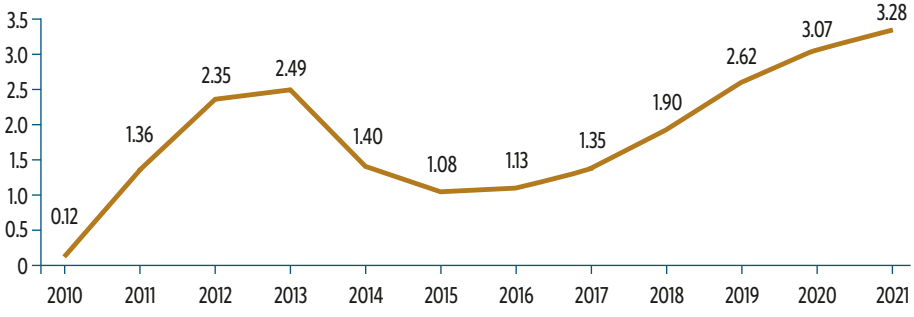
Parallel trade

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 for the supply. 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 health care 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.

In Austria, the share of parallel imports has been rising continuously for several years: in 2021 it amounted to 3.28 % (vs. 0,12 % in 2010) in the retail market and 2.01 % in the hospital market. Products from the nervous system and oncology sectors are particularly affected.

Parallel import in Austria



in percent

Source: IQVIA 2021

However, Austria is predominantly affected by parallel exports due to its low price level compared to the rest of the EU. In some cases, this leads to problems in supplying patients domestically despite the marketing authorization holder's proven ability to deliver. For this reason, the Ordinance on Securing Supply (BGBl 20/II/30) created the possibility for the BASG to issue a temporary parallel export ban for products with sales restrictions (cf. 9.4).

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.

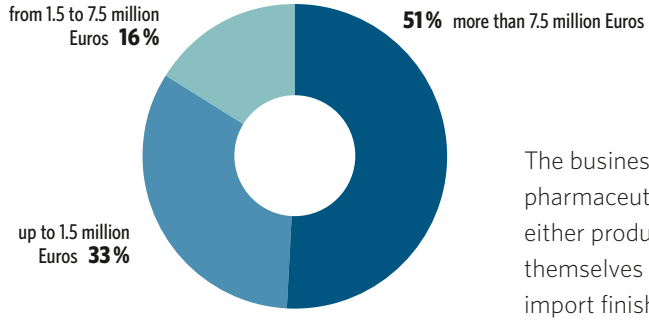
The implementation of the "falsification directive" (2011/62/EU) created a standardised logo for all member states to designate authorised internet pharmacies, leading to the introduction of distance selling, also in Austria.

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, 2021 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)

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

3.2 billion Euros
invested by pharmaceuticals companies in Austria (2013–2020)

Sources: Haber, G (2016): Life Sciences und Pharma: Economic impact analysis; internal publications 2013–2020)

* 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 health care. The interactive map www.pharmastandort.at visualizes the performance of the industry and shows what companies are constantly working for Austria.

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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 Social Affairs, Health, Care and Consumer Protection (BMSGPK) is responsible for the prices of medicinal products.
The manufacturer's price or depot selling price (MP/DSP) forms 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 the authorised pharmaceutical company, whereby the BMSGPK is informed about this price.

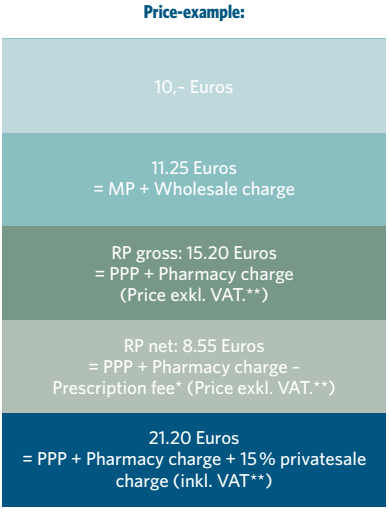
Prices of medicines

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

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

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

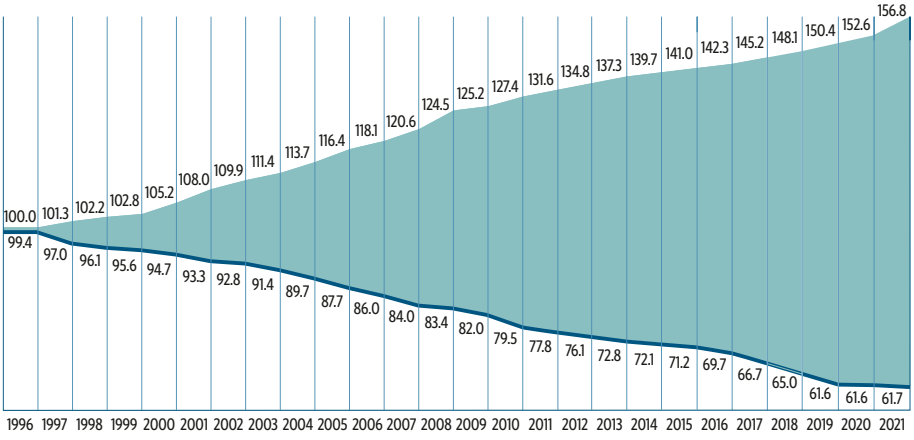
if a private purchase:
- Pharmacy selling price:
  Pharmacy –› Customer



* Prescription fee since 1.1.2022: 6.65 Euros; ** VAT. since 1.1.2009: 10 %

Source: PHARMIG

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 10 Euros in 1996 now only costs 6.17 Euros in 2021.

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

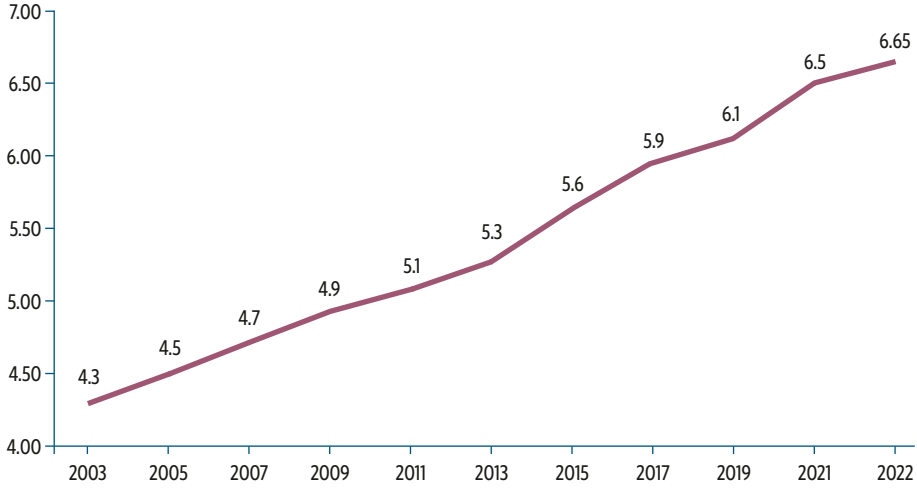
The divergence between consumer price index and pharmaceutical price index continues year to year. The pharmaceutical price index decreases continuously.

In 2021 43 % of all *reimbursable drug packages (measured by volume in units) was below the prescription fee of 6.30 Euros due to price adjustments.

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

The annual adjustment of the prescription fee is regulated by law and has increased by approx. 56 % in the period from 2022 vs. 2003. The earnings from prescription fees generated income of 427 million Euros for health insurance in 2020.

Development of prescription fees 2003–2022



in Euros

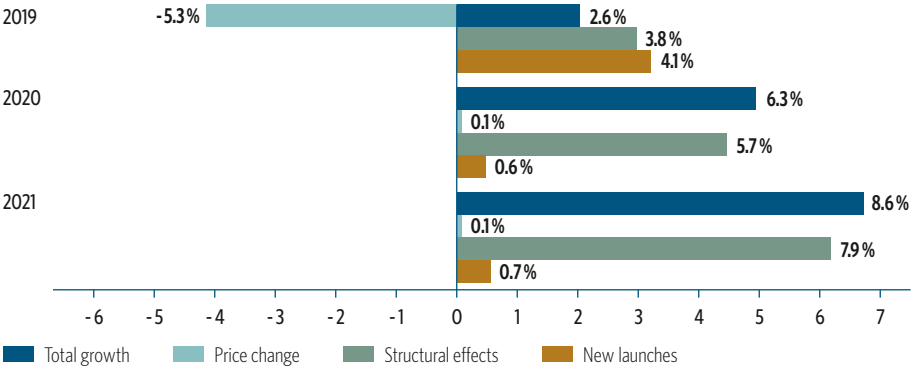
Source: BMSGPK

In addition to a general exemption from the prescription fee for social reasons, since January 2008 there has been an annual prescription fee cap of 2 % of the insured person's annual net income (excluding special payments such as holiday or Christmas bonuses). As of the date on which this limit is exceeded, insured persons and co-insured relatives are exempt from the prescription fee for the rest of the calendar year.

9.2 Elements of growth

The growth of the retail RX market – amounting to + 6.3 % in 2021 – 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 specific product that has already been launched on the market compared with the price of the previous period. **In 2021 – as in 2020 – these amount to 0.1 % and have a marginal impact on market development**.

- **New launches** include those products that contain new active substances, in the first year after market launch. These products replace existing therapies or enable new drug therapies for the first time. **In 2020, new launches influence market growth to a minor extent of + 0.7 %** – similar development as in 2020 with a value of + 0,6 %.

- **Structural effects** include factors such as changes in prescribing habits, replacement and expansion of previous forms of therapy, new dosage forms, volume increases, and much more. **In 2021, the structural effects amount to + 7.9 %** – and are significantly higher than the 2020 value of + 5.7 %.

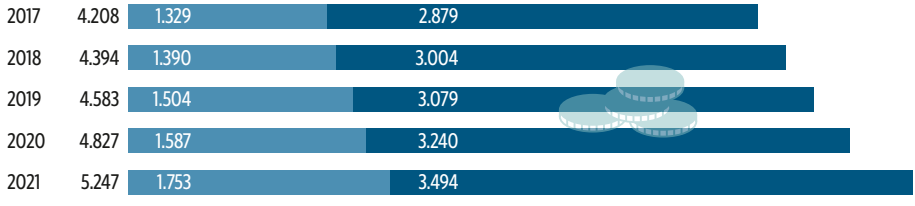
9.3 Hospital and pharmacy market

In 2021, the Austrian pharmaceutical market reported sales of 5.2 billion Euros and a sales volume of 222 million packages. This represents a growth rate of 8.6 % in value and a decrease in volume of - 0.9 %.

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*)



in million Euros

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

Hospitals
Pharmacies

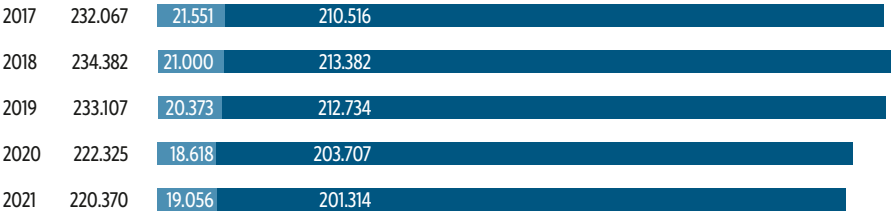
* Not taking discounts and refunds into consideration

In 2021, compared to 2020, both the pharmacy and hospital market have grown in terms of value. In terms of volume, the pharmacy market is declining.

- Pharmacy market: + 7.8 % regarding value according to Euro in turnover or - 1.2 % regarding volume according to packages
- Hospital market: + 10.3 % regarding value according to Euro in turnover or + 2.3 % regarding volume according to packages

In 2021, 222 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



in units of 1,000 Source: IQVIA DPMÖ next level with adapted data source (incl. RX direct to pharmacy business)/DPMÖK

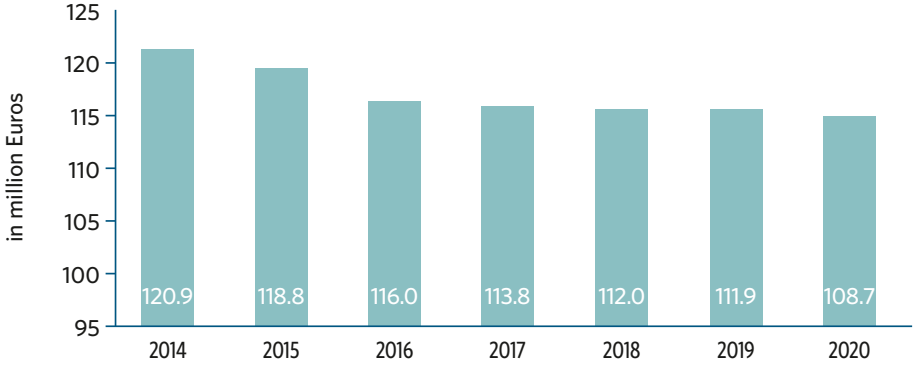
Hospitals
Pharmacies

In 2021 vs. 2020 the number of sold packages increased by - 0.9 %.

Prescription trends

The number of prescriptions has declined since 2015. In 2020 compared to 2014, it has decreased by approximately 10 %.

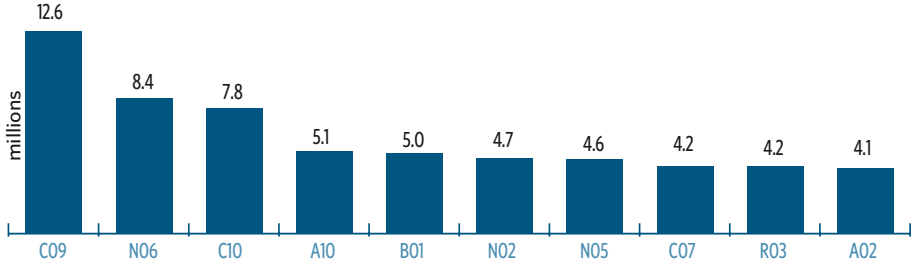
Number of reimbursed prescriptions



in million Euros Number of prescriptions Source: SV

9.4 Pharmaceutical consumption by indication groups

The most frequently prescribed therapeutic subgroups ATC-level 2*, 2020



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)
A10 anti-diabetics (medicine against diabetes)
B01 Antithrombotic agents (inhibits clotting)
N02 Analgetics (pain medication)
N05 Psycholeptics (for treatment of psychotic illnesses such as psychosis, schizophrenia. Medication for the treatment of sleep and anxiety problems)
C07 Beta-adrenoreceptor antagonist medication (e. g. for high blood pressure, cardiac insufficiency, angina pectoris)
R03 Agents for obstructive respiratory diseases (e. g. bronchial asthma, chronic lung disease/COPD, etc.)
A02 Medicine for the treatment of acid complaints (for neutralising stomach acid, e. g. with heartburn, acid indigestion)

in packs Source: SV

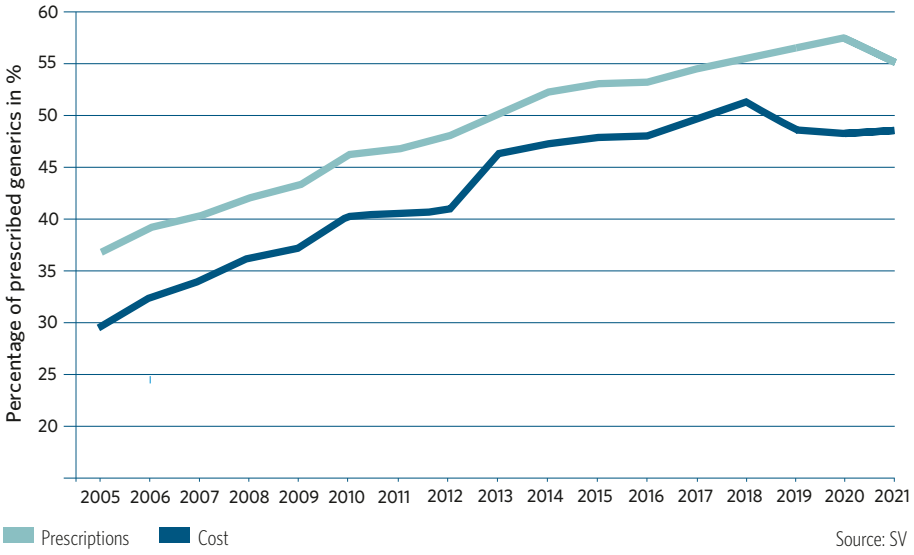
* ATC Code: Anatomical Therapeutic Chemical Classification System of the WHO

More than 60 % of all prescriptions account for the top 10 indication groups with the highest number of prescriptions.

The most frequently prescribed medications according to the ATC system are: Medicinal products for the treatment of the renin-angiotensin system (e. g. with high blood pressure), psychoanaleptics (for the treatment of psychological illnesses, e. g. depression) as well as agents which influence lipid metabolism. These 3 indication groups with the highest prescription volume account for around 29 % of all prescriptions.

9.5 Generics in the reimbursement market

Prescribed generic products in the reimbursement* market



Source: SV

* 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 55 % (according to billing records of the health insurance funds for 2021), this means more than every second prescription is accounted by a successor product and about 48 % of the costs are accounted by successor products on the reimbursable market.

9.6 Biosimilars

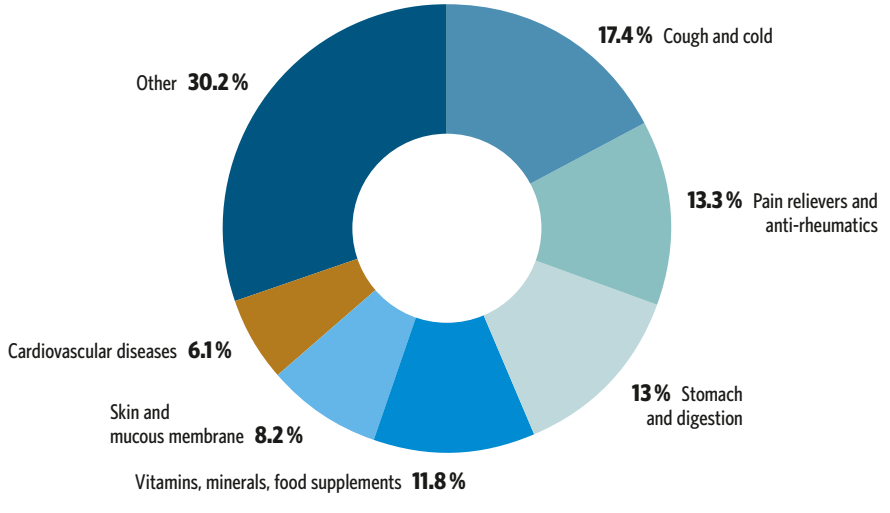
In Austria, 49 approved biosimilars (for 14 different active substances) are available for the treatment of serious diseases such as cancer, autoimmune diseases, growth disorders, osteoporosis or blood coagulation (EMA approvals: 70, status 04/2021). **Just under a quarter (29 %) of the total biosimilar-eligible market in Austria (in terms of sales) is accounted for by biosimilars in 2020: in the retail market, this share is around 17 % and in the hospital market 45 %.**

Source: IQVIA, Association for Biosimilars Austria, 2022

9.7 Self-medication market

In terms of value, the OTC market grew by + 4.4 % to Euro 1,247 million (AVP) in 2021 compared to 2020 – this is significantly better than the growth of + 1.1 % from 2019 to 2020. In terms of volume, there is also a positive development of + 2.3 % in the OTC market; in 2020, sales in packages declined by - 5.6 %.
Agents for the treatment of coughs and cold continue to represent the largest indication group in 2021 with a share of 17.4 % (measured in terms of sales in AVP), with a sales growth of + 1.7 % compared to 2020 despite lockdowns and hygiene measures (e. g. distancing rules, and mandatory masks).

Indication groups in self-medication (based on pharmacy sales price) 2021



Source: IGEPHA/IQVIA

Drugs in self-medication, so-called "over the counter" drugs (OTC), are effective, safe and make good health economic sense. They are therefore an integral part of health care and therapy for many diseases. About every fourth drug dispensed in pharmacies in Austria is such a prescription-free OTC drug.

9.8 Drug supply

Despite all efforts in the distribution chain to ensure the supply of patients, there may be selective restrictions in availability. The reasons for this are multifactorial and can be found in all areas of the distribution chain. Under the leadership of BASG, a collaborative approach for dealing with or reducing distribution restrictions was outlined in a position paper https://www.basg.gv.at/fileadmin/redakteure/04_Marktbeobachtung/Vertriebseinschr%C3%A4nkungen/Positionspapier_Vertriebseinschr%C3%A4nkungen.pdf of all stakeholders in the distribution chain.

According to the Regulation on Security of Supply (BGBl 20/II/30), marketing authorization holders have to report any distribution restrictions for prescription-only human pharmaceuticals since 1 April 2020. The notifications are published in the distribution restriction register on the BASG website. Based on an evaluation scheme, BASG decides on a temporary parallel export ban for the notified products. https://medicineshortage.basg.gv.at/vertriebseinschraenkungen

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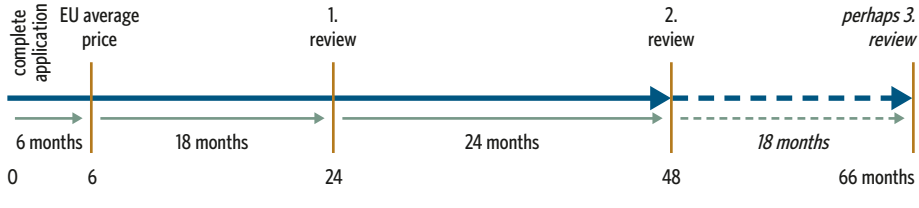
10 Pharmaceuticals reimbursement through health insurance

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.



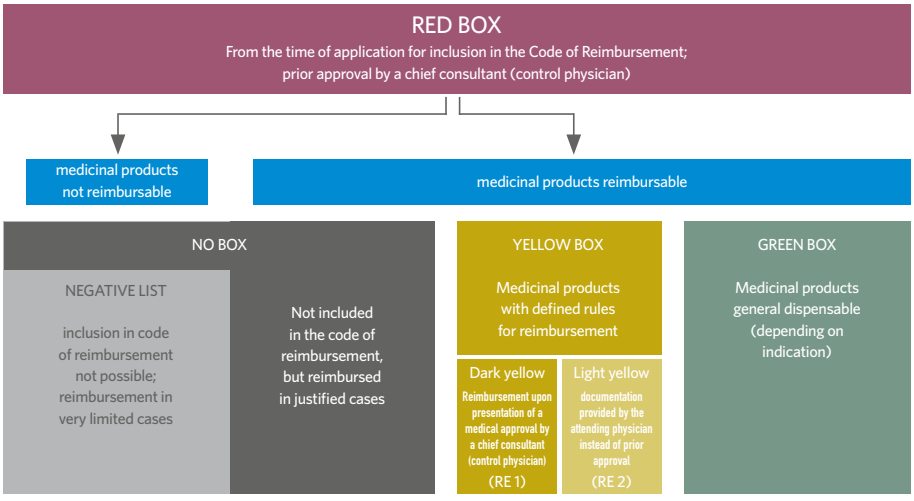
Source: PHARMIG

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 "free prescription" (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



Source: PHARMIG

- 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 EKO 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, the inclusion of which relates to a specific application, the Dachverband der österreichischen Sozialversicherungsträger 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).

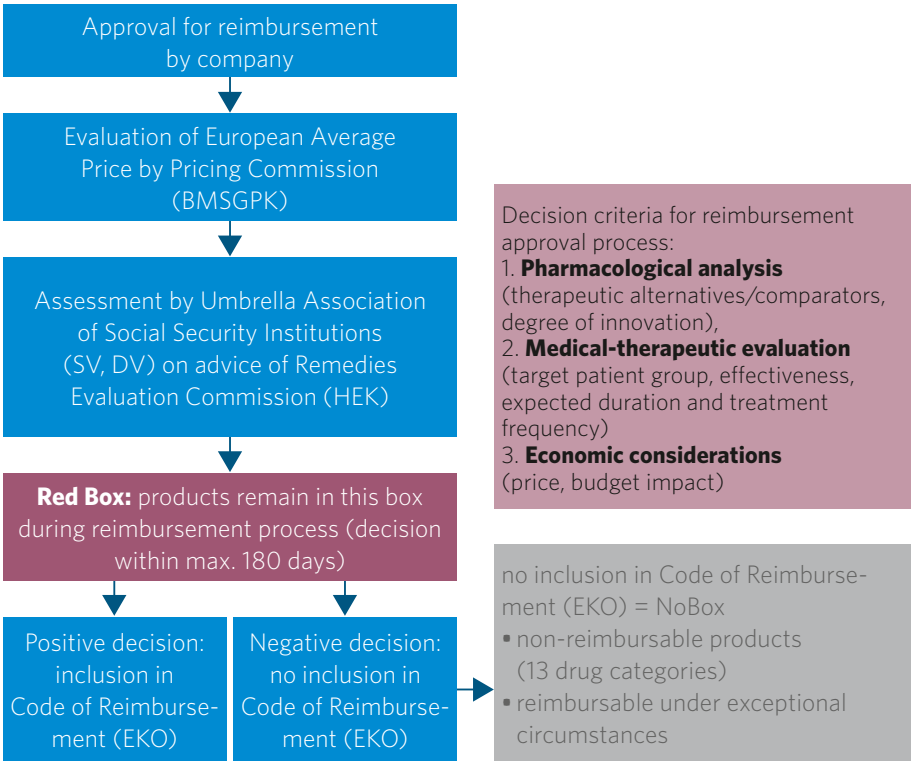
- The **Red Box** temporarily comprises all medicinal products for which an application for inclusion in the EKO was submitted. The price of the proprietary medicinal product may not exceed the EU average price. The costs are assumed by the health insurance only upon presentation of a medical approval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

All other medicinal products not included in the EKO 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.

This "chief medical approval requirement" was suspended by the Austrian Health Insurance Fund (ÖGK) starting in March 2020 for the duration of the pandemic.

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 EKO. The inclusion procedure is an administrative procedure and is 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 – https://www.ris.bka.gv.at/SVRecht/.



Source: PHARMIG

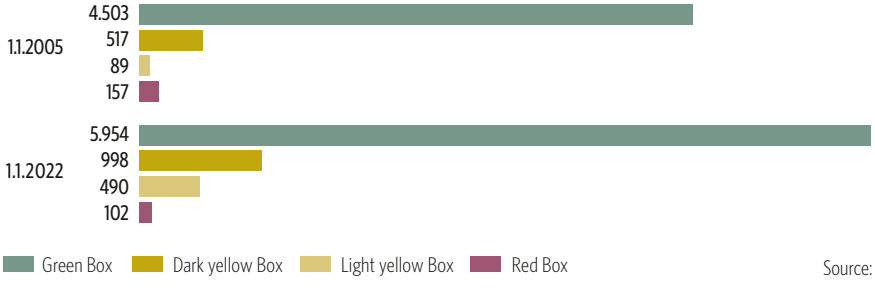
Specific groups of medicinal products are fundamentally excluded from inclusion in the EKO (Official Bulletin No. 34/2004: List of non-reimbursable medicinal product categories pursuant to § 351c Para.2 ASVG) and as a rule must be paid by patients themselves, unless the absorption of costs is authorised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

Remedies Evaluation Commission (HEK [Heilmittel-Evaluierungs-Kommission])

The Remedies Evaluation Commission is the advisory body of the Umbrella Association of Social Security Institutions (DV). All applications for inclusion (including amendments) of a medicinal product in the reimbursement codex must be submitted to the HEK. The HEK must also be heard if the DV intends to make a change in the EKO on its own initiative. The HEK makes a written recommendation to the Umbrella Association of Social Security Institutions (DV).

Members of the Remedies Evaluation Commission or their representatives
https://www.sozialversicherung.at/cdscontent/?contentid=10007.855429&portal=svportal

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



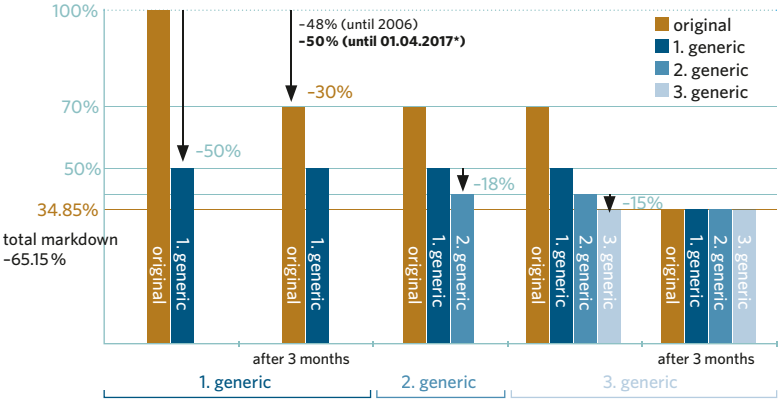
Source: WVZ

As of 1 January 2022, a total of 7,534 packages were listed in the EKO. There were 5,266 packages upon its introduction in 2005.

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 with regard to generics) for the inclusion or the continuance of interchangeable products with identical active substances (original and successor products):

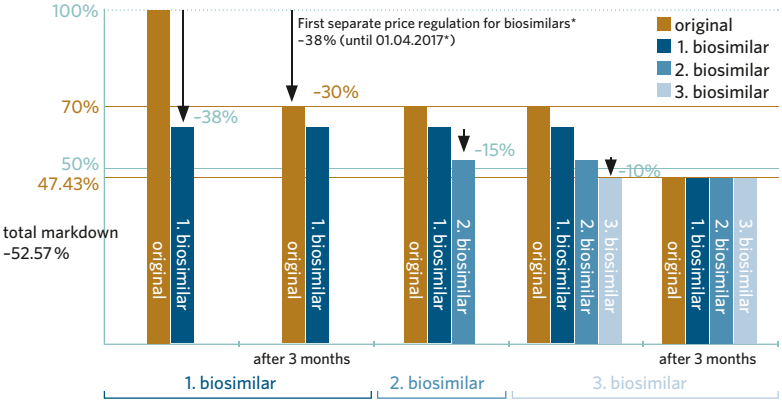


* ASVG amendment from BGBl. No. I, 49/2017 § 351c Para. 10 in force as of 1 April 2017, limited until 31 December 2023

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 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 2023

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

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

Due to price divergences of individual active ingredients within the Green Box, a price range was established for the purpose of alignment in 2017, 2019 and 2021. The price of the affected medicinal products with the same active ingredient in the Green Box may not exceed the price of the cheapest medicinal product with the same active ingredient by more than 30 % on the reference date (1 February of the respective review year) (ASVG amendment 2017, Section 351c (11)). In turn, cancellation procedures for those products will be eliminated until 1 April 2022, for economic reasons.

In 2022, BGBL. 32/2022 decided to implement the price range for 2023 for the last time, with a corridor of 20 % to the cheapest drug speciality with the same active ingredient in the same or practically the same dosage form. The relevant strength within an active ingredient is the respective key strength (the most frequently prescribed). The price reduction is necessary to a maximum of the prescription fee, i. e., drug specialties with a price charged to the social insurance below the prescription fee are excluded from this regulation. However, these are used to determine the maximum price. In return, there will be no cancellation procedures for those products until December 31, 2023 for economic reasons.

According to social insurance, the annual savings from the implementation of the price band in 2017 amounted to approximately Euro 46 million (on the basis of the reimbursed price, KVP). In 2019, the annual savings amounted to approximately Euro 12 million, and potential savings of around Euro 16 million are expected for 2021.

Source: Parlamentarische Anfragebeantwortung 8908/AB

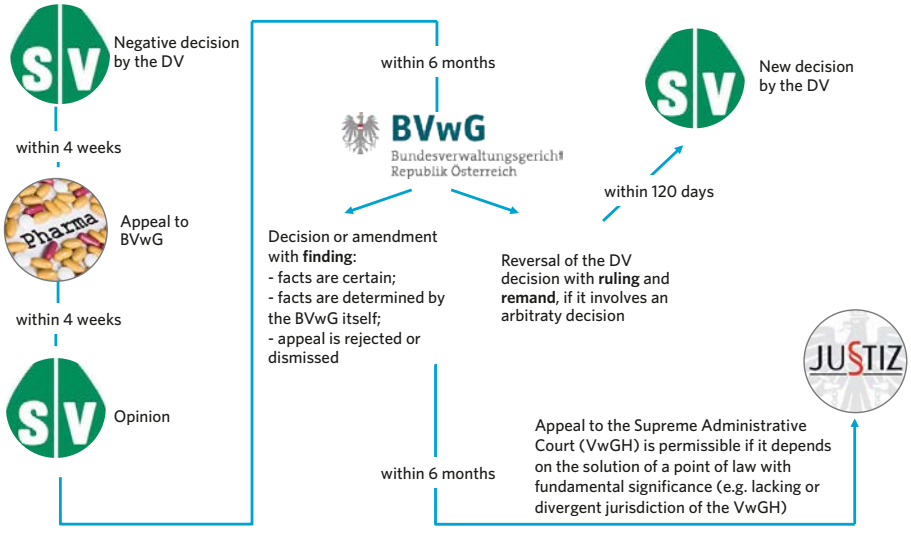
Special provisions for proprietary medicinal products outside of the EKO ("No Box")

The special provisions (Section 351c (9a) ASVG) that have been in force since the 2017 ASVG amendment for pharmaceutical specialties that are not listed in the EKO (see chapter 10.1) but are reimbursed in certain exceptional cases were tightened in 2022 (BGBL. 32/2022). For these pharmaceutical specialties, if annual sales exceed Euro 750,000, a partial amount must be repaid to the social insurance by the pharmaceutical companies. The price commission establishes the EU average price for these products as a benchmark. If the MP charged by social insurance exceeds the determined EU average price, a repayment obligation in excess of the difference arises for these pharmaceutical specialties.

10.4 Federal administrative court

The Federal Administrative Court is competent for appeals against a decision of the Umbrella Association of Social Security Institutions. An appeal must be submitted within four weeks after the decision has been served via the Internet portal www.sozialversicherung.at. The appeal has a suspensive effect. The decision is made by a 5-member senate (deliberation and voting of the senate not public). The findings of the Federal Administrative Court (BVwG) are published in the Legal Information System of the Federation (RIS) – https://www.ris.bka.gv.at/Bvwg/.

Process flow



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

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11 PHARMIG Code of Conduct

Pharmaceutical companies develop, produce and sell medicinal products. They are also responsible for updating doctors, pharmacists, patients and the general public about their medicinal products, and so to contribute to the safety as well as the correct use of the pharmaceutical products. In this context, the exchange of the respective experience is an essential aspect, which also flows into the further development of therapy concepts. All these aspects require a reasonable basis for the cooperation of several partners in the health care system. In this context, it is important to focus on the respective scientific context when collaborating with health care professionals or institutions and to design the framework for the collaboration in a comprehensible and transparent manner.

This is precisely where industry-wide compliance regulations come in: the pharmaceutical industry did pioneering work in this area. The CoC has been making a valuable and important contribution since 1970: the regulations ensure that legal requirements are complied with, that the freedom of procurement, decision-making and therapy of health care professionals is not unfairly influenced, and that ultimately this strengthens the confidence of the public and patients in the necessary cooperation.

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.

Companies live ethical responsibility

The pharmaceutical companies that have submitted to the CoC demonstrate a high sense of responsibility and set a clear example of integrity.
To fulfill this responsibility, compliance advisors exist, which support the companies from within as business partners of integrity. Compliance is the responsibility of all employees and business units and primarily concerns:

- Promoting **ethical** and **legally compliant behavior** between the pharmaceutical industry, business partners (such as health care professionals), and stakeholders
- Ensuring **fair competition** within the pharmaceutical industry
- Ensuring that physicians are informed about therapeutic options in an **objective** and **legally** compliant manner
- Consistent **compliance** with the established principles of conduct and their monitoring
- **Training** for employees and external cooperation partners regarding ethical principles and anti-corruption regulations
- A **compliance program** implemented in all departments to protect the integrity of the company

Compliance in all phases of a drug's life cycle

Transparency creates trust

Since 2014, the CoC also contains provisions on how pharmaceutical companies disclose pecuniary benefits when they cooperate with for example physicians or hospitals or support the work of patient organizations. Essentially, the individual disclosure of pecuniary benefits resulting from this cooperation is to be aimed for. Individual disclosure must be based on data protection law. Depending on the situation, this may be consent or an overriding legitimate interest. In the event that this is not the case, disclosure shall be made in aggregated form. Disclosure is made annually as of June 30 on a publicly accessible website. More information on the transparency initiative can be found at: 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 2020.

The rules of procedure for the committees of experts 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 against 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.

In the interest of legal certainty, the results of the CoC-procedures are published in anonymized form on our website www.pharmig.at.

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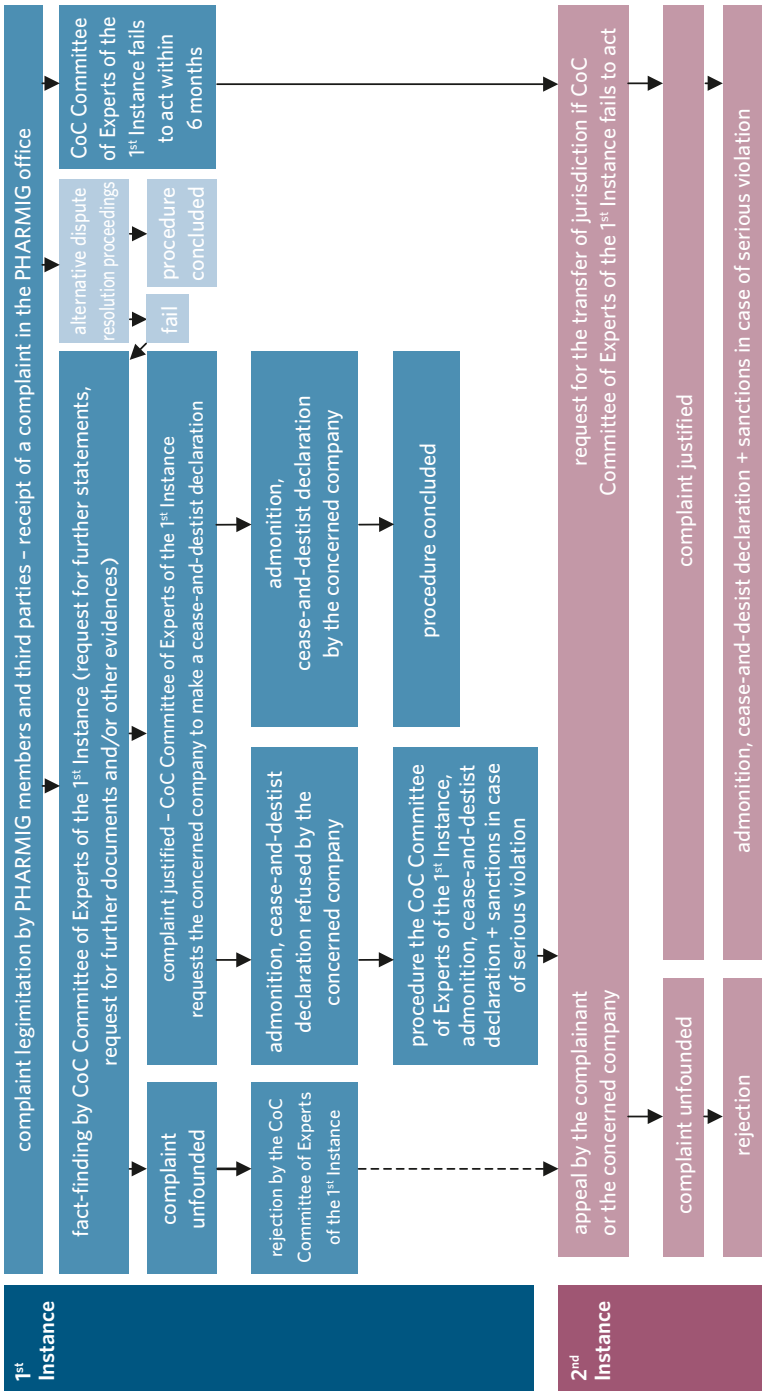
Flowchart – procedure of the CoC committees of experts of the 1st and 2nd instance



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
Federal Law 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
Bundesstatistikgesetz (BStatG)	Provision of data by the federal government to certain recipients; regulations on "Statistics Austria"; basis for the implementation of the Austrian Micro Data Center
Forschungsorganisationsgesetz (FOG)	Support of science and research; framework conditions for data processing for the purpose of research and statistics; access to register data for operational research

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
AMDC	Austrian Micro Data Center
AMVO	Austrian Medicines Verification Organisation
AMVS	Austrian Medicines Verfication System
BASG	Federal Office for Safety in Health Care
BGBL	Federal Law Gazette
BMGF	Federal Ministry for Health and Women until 7.1.2018
BMSGPK	Federal Ministry of Social Affairs, Health, Care and Consumer Protection
c4c	Collaborative Network for European Clinical Trials for Children
CHMP	Committee for Medicinal Products for Human Use
CoC	PHARMIG Code of Conduct
CPI	Consumer Price Index
DCP	Decentralised Procedure
DTP	Direct to Pharmacy
ECDC	European Centre for Disease Prevention and Control
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHDS	European Health Data Space
EKO	Code of Reimbursement
EMA	European Medicines agency
Enpr-EMA	European Network of Pediatric Research at the 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
HTA	Health Technology Assessment
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
KVP	Box office price
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

OKIDS	Child Research Network
OTC	Over The Counter
ÖVIH	Austrian Vaccine Manufacturer Association
PedCRIN	Pediatric Clinical Research Infrastructure Network
PHAGO	Austrian Association of Full-Line Pharmaceutical Wholesalers
PIP	Paediatric Investigation Plan
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
QP	Qualified Person
R&D	Research & Development
SHA	System of Health Accounts
SPC	Supplementary Protection Certificate
SV	Main Association of Austrian Social Insurance Institutions
UHK	Independent Medicinal Products Commission
VAT	Value-Added Tax
VO-EKO	Ordinance on the code of Reimbursement (EKO) according to § 351g ASVG
WHO	World Health Organization
WKÖ	Austrian Federal Economic Chamber

PHARMIG

Verband der pharmazeutischen
Industrie Österreichs