



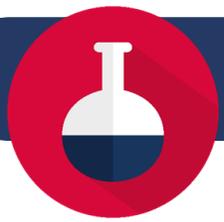
Availability of antimicrobials: situation in Human Medicine

Workshop on Veterinary Medicines: Improving the availability of antimicrobials and their alternatives

Andrea García Caballero
PRAN Coordination Unit



-  **01. ACCESS TO NEW ANTIMICROBIALS**
-  **02. ACCESS TO EXISTING ANTIMICROBIALS**
-  **03. SUPPORTING MEDICINES DEVELOPMENT: FINANCIAL INCENTIVES**
-  **04. ADDRESSING THE MARKET FAILURE**
-  **05. AEMPS STRATEGIES: LIST OF STRATEGIC MEDICINES & PRAN 2022-2024**



ACCESS TO NEW ANTIMICROBIALS: CURRENT PERSPECTIVE



Plan Nacional
Resistencia
Antibióticos

- AMR poses a **major threat** to human health
- In 2019:
 - **4.95 million deaths associated** with bacterial AMR
 - **1.27 million deaths attributable** to bacterial AMR

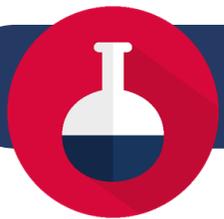


- The **development of new antimicrobial agents** is critical to tackle AMR



- **Fewer antibiotics** are **reaching the market**





ACCESS TO NEW ANTIMICROBIALS: CURRENT PERSPECTIVE



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Daptomycin, 1987



Last entirely original class of ABs discovered in the **late 1980s**



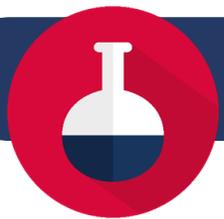
Bedaquiline (2014, MDR-TB); **fidaxomicin** (2011, CDI)



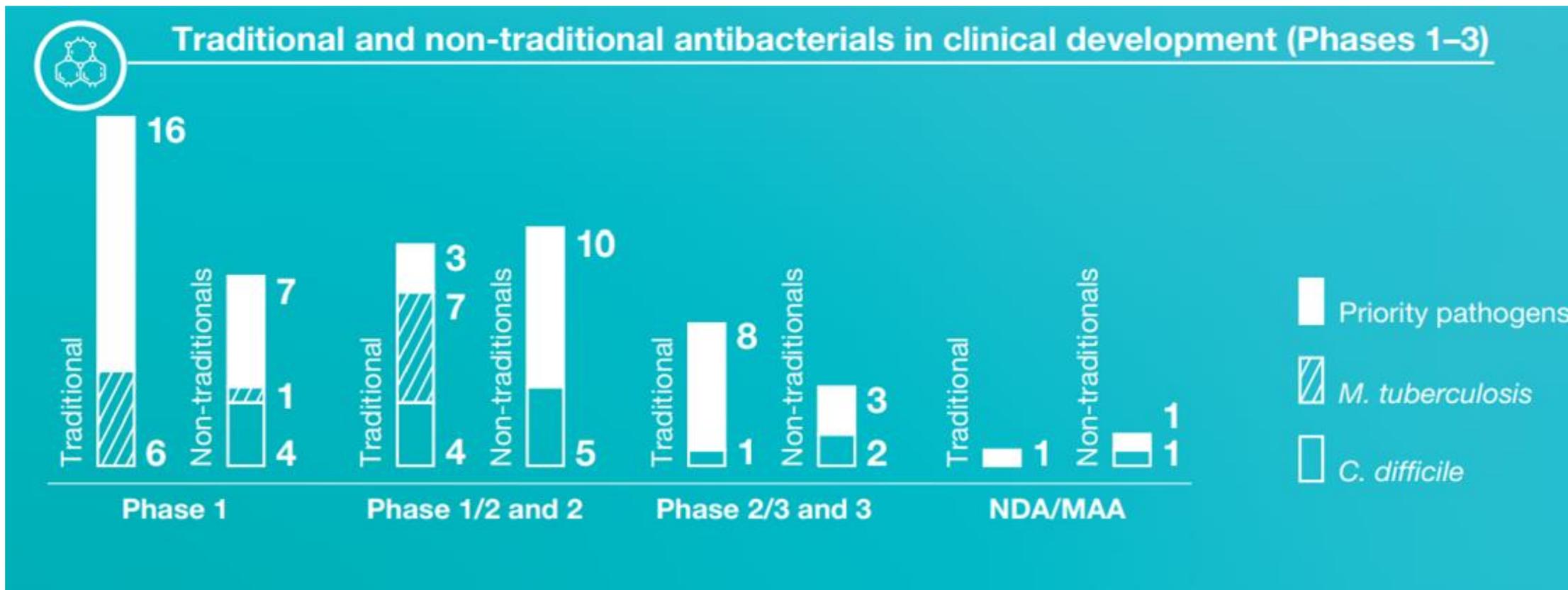
Current pipeline has **a few innovative medicines**

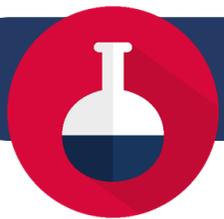


High attrition rate



2021 Antibacterial agents in clinical and preclinical development: an overview and analysis (WHO)





ACCESS TO NEW ANTIMICROBIALS: CURRENT PERSPECTIVE



Discovering and bringing antibiotics to the market is **not profitable** for the pharmaceutical industry.

variable
estimate

**COST OF
DEVELOPING AN
ANTIBIOTIC**



**US\$ 1.5 billion¹
US\$ 1.8-2.6 billion²
US\$ 447 million³**



**AVERAGE REVENUE
GENERATED FROM
ANTIBIOTIC SALES**

US\$ 46 million / year

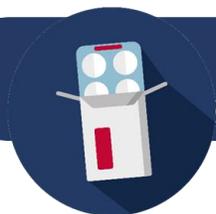
**> 10-30
years**

¹Towse A, Hoyle CK, Goodall J, Hirsch M, Mestre-Ferrandiz J, Rex JH. Health Policy. 2017

²Wellcome Trust. 2020

³Outterson. Health Aff (Millwood). 2021

Plackettm B. Nature 2020



ACCESS TO EXISTING ANTIMICROBIALS: CURRENT PERSPECTIVE

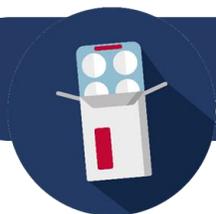


Drug shortage	Timeline	Cause	Consequences
Ceftolozane-tazobactam	2020 → 2021	Issues with compliance of GMP	Required for treatment of cIAI, UTI and other HAI. May necessitate use of carbapenems
Cloxacillin	2017 onwards	Disruption of manufacturing due to declining market returns	SoC for MSSA infections. Compels use of alternative agents (AMC, VAN) leading to worse outcome
Penicillin G	2015 onwards	Only four API producers. Low production levels due to lack of profitability	SoC for syphilis and rheumatic heart disease. Increased costs of therapy as substitute therapies more expensive and impact con AMR
Piperacillin-tazobactam	2017	Explosion at the sole factory in China supplying the API	Use of more broad-spectrum agents such as carbapenems. Increased use of cephalosporins with increasing risk of CDi

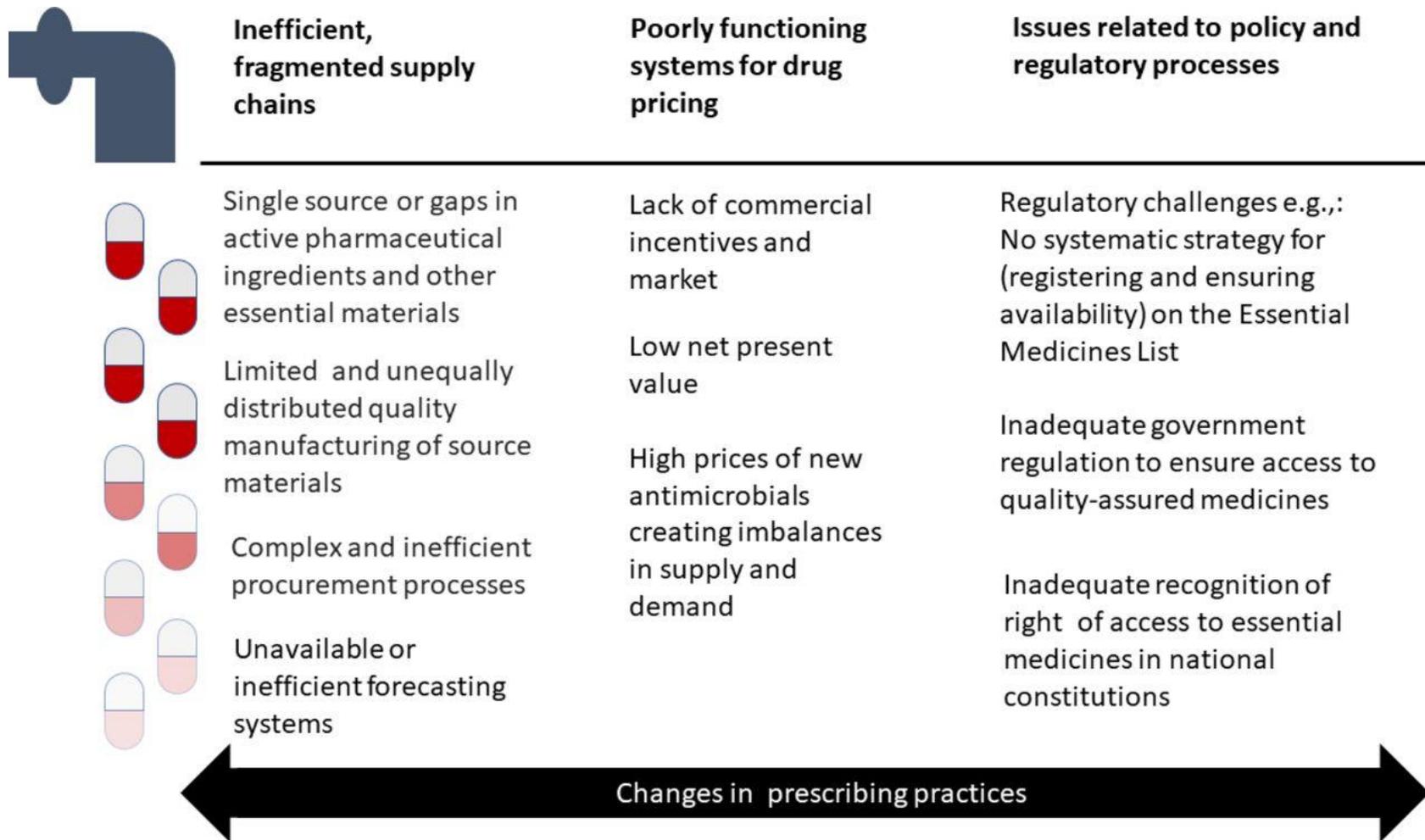
Adapted from Shafiq N, Pandey AK, Malhotra S, Holmes A, Mendelson M, Malpani R, Balasegaram M, Charani E. BMJ Glob Health. 2021

Meeting Report Antibiotic Shortages: Magnitude, Causes and Possible Solutions. Norwegian Directorate of Health, Oslo, Norway 10-11 December 2018.

The economic cost of the shortage of just one antimicrobial is estimated to be €20-30 million



ACCESS TO EXISTING ANTIMICROBIALS: CURRENT PERSPECTIVE



Shafiq N, Pandey AK, Malhotra S, Holmes A, Mendelson M, Malpani R, Balasegaram M, Charani E. BMJ Glob Health. 2021



SUPPORTING MEDICINES DEVELOPMENT: FINANCIAL INCENTIVES



Plan Nacional
Resistencia
Antibióticos



PUSH

PULL



RESEARCH AND
DISCOVERY



NON-CLINICAL
DEVELOPMENT



CLINICAL
DEVELOPMENT
Phase I, II & III



POST-APPROVAL LIFE-
CYCLE MANAGEMENT &
PHARMACOVIGILANCE



Marketing
authorisation



SUPPORTING MEDICINES DEVELOPMENT: FINANCIAL INCENTIVES



Plan Nacional Resistencia Antibióticos

Dynamic Dashboard

INVESTMENTS IN AMR R&D

GLOBAL AMR R&D HUB



Last updated: 08.03.2023



Parameter

Number of Projects

Total Investments

Currency

USD EUR

Status

Active Closed

Reset filter

*by year = incomplete years

Funders 227

Number of Projects 13051

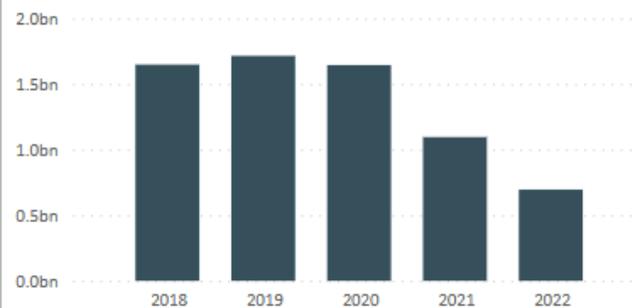
Total Investment EUR 8.89bn

Research Organisations (RO) 2808

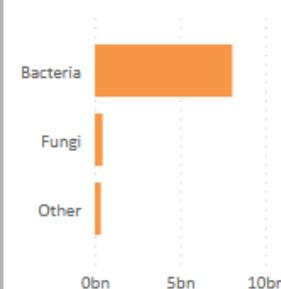
Countries of RO 90

One Health Sectors 4

by Year (Total Investments in EUR)

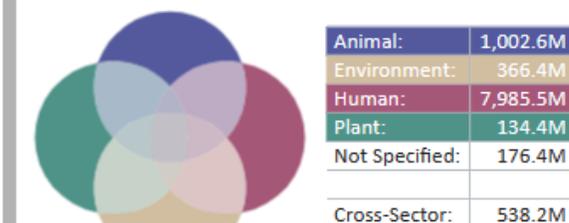


by Infectious Agent (Total Investments in EUR)

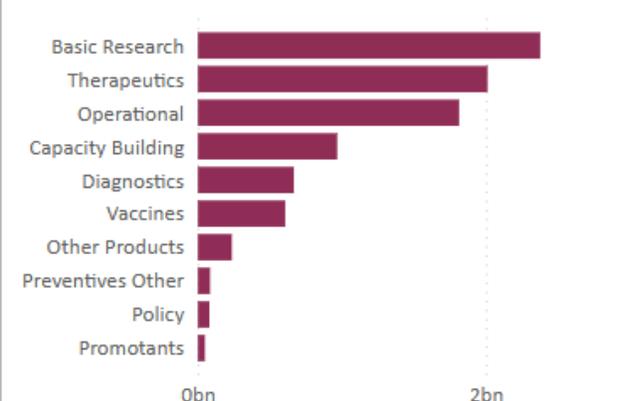


by One Health Sectors (Total Investments in EUR)

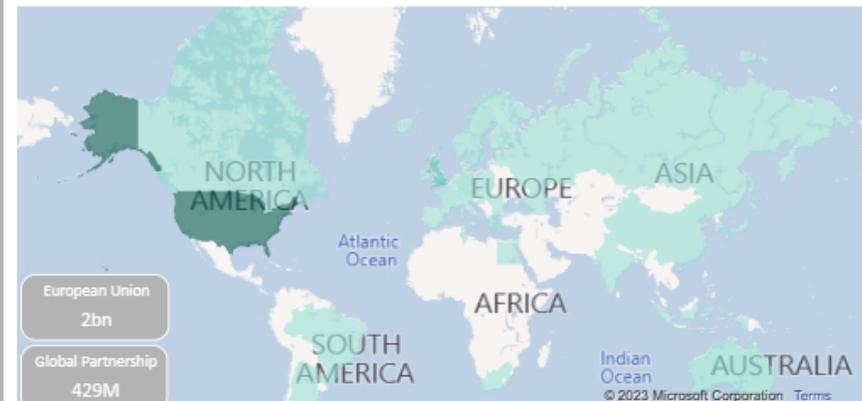
Move cursor over the colored shapes to show values



by Research Area (Total Investments in EUR)



by Location of Funder (Total Investments in EUR)



Suggested reference: Global AMR R&D Hub, 2020. Dynamic Dashboard: AMR R&D Investments Gallery. Last update date | 08.03.2023



PUSH



Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)

A global platform of 29 members which fund multi-sectorial AMR research on a global scale and coordinate national research funding.



Combating Antibiotic-Resistant Bacteria (CARB-X)

A global non-profit partnership for antibacterial research, funded by BARDA (US), BMBF (DE), GAMRIF (UK), Bill & Melinda Gates Foundation, NIAID (US).



AMR Action Fund

A global public-private partnership, created by industry and supported by the WHO, the EIB and the Wellcome Trust. Seeking to invest 1bn USD to bring 2-4 new antimicrobials to market by 2030.



INCATE (INCubator for Antibacterial Therapies in Europe)

Founded in 2021, it is a partnership of research institutions and pharma companies that provides advice, and funding to start-up companies, including academic spin offs



Horizon Europe
THE NEXT EU RESEARCH & INNOVATION PROGRAMME (2021 – 2027)

EU4Health programme
for a healthier and safer Union
#EUBudget #EU4Health

European Commission



SUPPORTING MEDICINES DEVELOPMENT: FINANCIAL INCENTIVES

PULL



UK: cefiderocol, ceftazidime-avibactam

SW: cefiderocol, imipenem-cilastatin/relebactam, meropenem varbobactam, fosfomycin

US: PASTEUR Act (under discussion)

EC's Pharmaceutical Strategy for Europe



European Health Emergency Preparedness and Response Authority (HERA)

Launched by
the European
Commission
in 2021

Aims to develop, produce,
and procure medical
countermeasures before
and during a health crisis.

Feasibility study on stockpiling
of medical countermeasures in
the area of AMR

- Identification of **AM with critical need** for uninterrupted access
- Analysis of **supply chain vulnerabilities**
- Review of **existing AM stockpiling systems** (EU & global level)
- Identification and **assessment of options for stockpiling of AM** at EU level (physical vs virtual alternatives)





ADDRESSING THE MARKET FAILURE



Plan Nacional Resistencia Antibióticos

Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG)

Established in March 2022 in accordance with the Regulation on EMA's Reinforced Role (Regulation (EU) 2022/123).

Coordinates urgent actions within the EU to manage medicine supply issues and issues related to the Q, S & E of medicines.



Role: to ensure a robust response to medicine supply issues caused by major events or public-health emergencies.

Medicines Shortages Single Point of Contact (SPOC) Working Party

Responsible for monitoring and reporting events that could affect the supply of medicines in the EU

Provides recommendations to the MSSG



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 January 2023
EMA/27040/2023

Shortage of amoxicillin and amoxicillin/clavulanic acid Various presentations including paediatric formulations and presentations

Indication	Amoxicillin, alone or in combination with clavulanic acid, is an antibiotic used to treat a wide range of bacterial infections.
Reason for shortage	The shortage has several root causes, but the main one is a surge in respiratory infections that has led to an increase in demand for antibiotics. This is compounded by manufacturing delays and production capacity issues (lack of personnel). EMA has been closely monitoring the situation since November 2022 and has been engaging with key players in the supply chain of amoxicillin in order to agree possible mitigating measures, such as increasing manufacturing capacity. Based on current information from companies and stakeholders, it is expected that the situation will improve in the coming months.
Member States affected¹	Austria, Belgium, Bulgaria, Croatia, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Spain, Lithuania, Latvia, Luxembourg, Malta, Netherlands, Norway, Portugal, Poland, Romania, Slovenia, Slovakia and Sweden.



The MSSG also discussed the current amoxicillin shortages and whether the ongoing situation meets the definition of a **'major event'** as foreseen in Regulation (EU) 2022/123, and the consequences and added value that this would have in terms of mitigating those shortages.

The MSSG came to the conclusion that at present this ongoing shortage situation is not considered to be a major event and that **current mitigating measures are improving the supply situation in the short-term.**



AEMPS STRATEGIES: LIST OF STRATEGIC MEDICINES



Plan Nacional
Resistencia
Antibióticos

Subgroup of medicines for which **additional measures** need to be adopted in order to **guarantee its availability** in the market, due to their essential role in maintaining basic health protection and their supply vulnerabilities

Castellano | Català | Euskera | Galego | València | English

GOBIERNO DE ESPAÑA MINISTERIO DE SANIDAD **am** agencia española de medicamentos y productos sanitarios SÍGUELOS

La AEMPS Medicamentos de uso humano Medicamentos veterinarios Productos sanitarios Cosméticos Biocidas y cuidado personal Comunicación Industria farmacéutica Profesional Sanitario Ciudadanía CNCps



Medicamentos estratégicos

Inicio > Medicamentos de uso humano > Medicamentos estratégicos

Última actualización: 22 de diciembre de 2022

En el contexto de distintas medidas, tanto en el ámbito europeo como nacional, para garantizar el acceso a los medicamentos, así como fomentar la competitividad, la capacidad innovadora y la sostenibilidad de la industria farmacéutica, se ha hecho necesaria la elaboración del listado de medicamentos estratégicos.

En primer lugar, se han definido tres tipos de medicamentos muy relevantes para el sistema sanitario para poder identificar cuáles, dentro del conjunto de los medicamentos autorizados en España por la AEMPS o por la Comisión Europea, deben ser considerados estratégicos:

- **Medicamentos esenciales:** de acuerdo con la definición de la OMS son los medicamentos mínimos necesarios para un sistema básico de salud.
- **Medicamentos críticos:** un subgrupo de los medicamentos esenciales para los que nunca deberían existir problemas de abastecimiento en el sistema sanitario.
- **Medicamentos estratégicos:** un subgrupo de los medicamentos críticos para los que se considera necesario adoptar medidas adicionales, bien regulatorias, económicas o de otra índole para garantizar su mantenimiento en el mercado tanto por su necesidad para la atención básica de la salud como por la vulnerabilidad de su cadena de suministro.

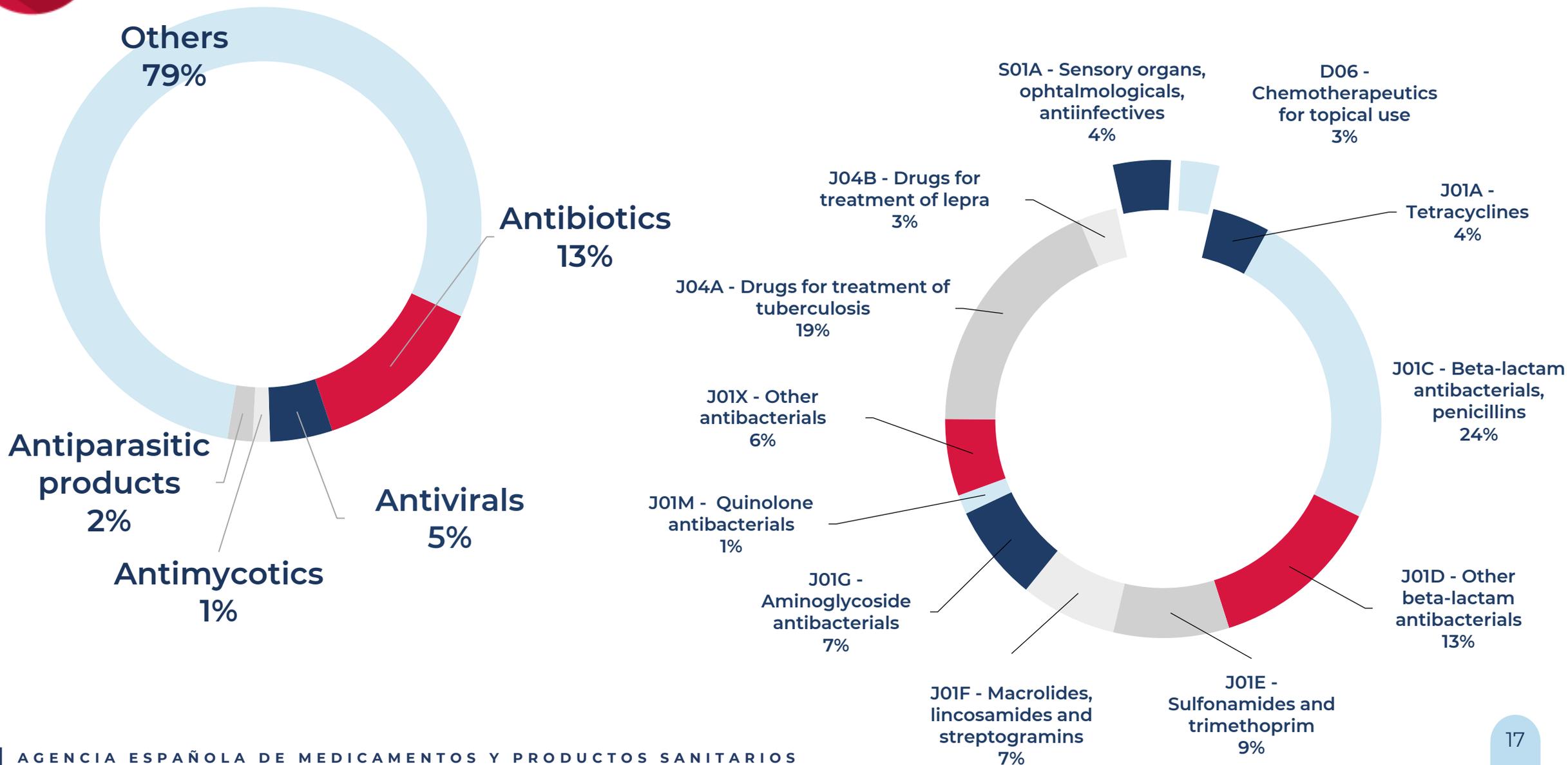
Dentro del marco de actuación de la AEMPS se han adoptado medidas encaminadas a la protección regulatoria de estos medicamentos, estimulando el interés de la industria farmacéutica nacional en la fabricación y comercialización de los mismos y promoviendo su autorización en España.

541 medicinal products containing **295 active ingredients**, expressed as VirtualMP

VirtualMP = abstract representation of an active medicinal ingredient + strength information + route of administration



AEMPS STRATEGIES: LIST OF STRATEGIC MEDICINES





Study how regulatory and financial incentives agreed at EU level can be applied nationally



Collaboration with AEMPS medicine supply guarantee plan → FEDIFAR-AEMPS collaboration: supply problem analysis



RAVARA: registry of real-world data from antimicrobials of high strategic value and recent approval

¡Thanks for your interest!

www.resistenciaantibioticos.es

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