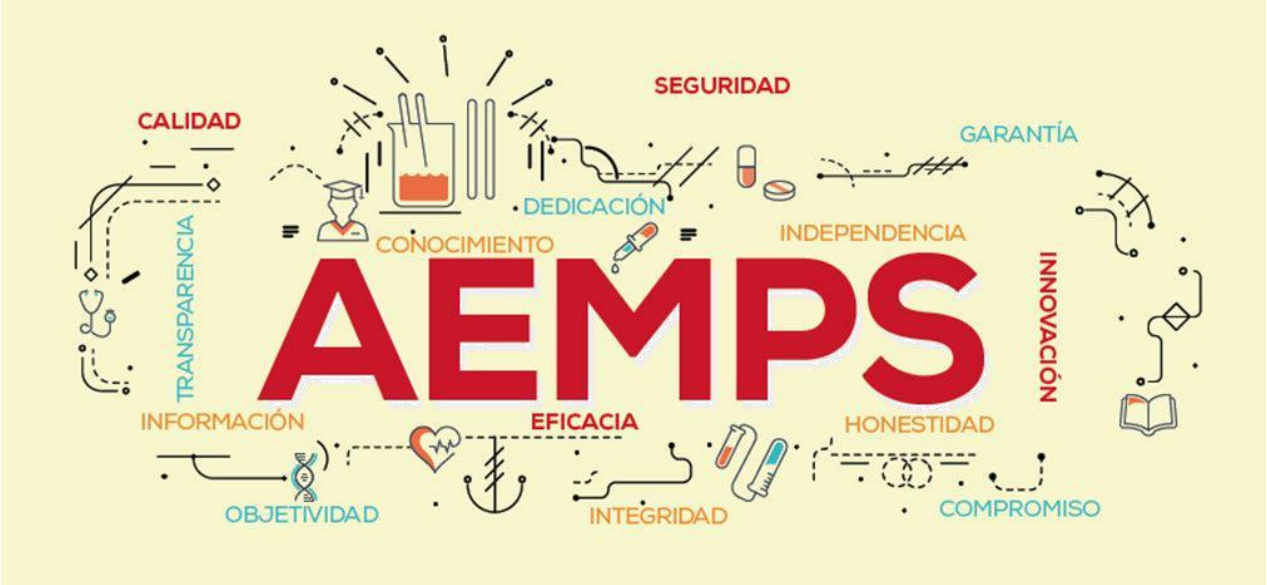
MINISTERIO
DE SANIDAD, CONSUMO
Y BIENESTAR SOCIAL

agencia española de
medicamentos y
productos sanitarios



MEDICINE SUPPLY GUARANTEE PLAN 2019-2022

EXECUTIVE SUMMARY

8 May 2019

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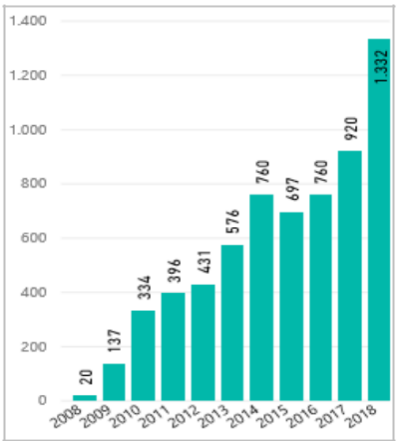
1. CURRENT SITUATION

Medicine supply problems arise when the units available in the supply chain are insufficient to cover national demand. The causes are many and varied and they are all closely interrelated. Solutions are difficult to implement due to these multiple causes, their interrelationships and to the fact that the problems are often global in scope and an exclusively national response is likely to be less effective than a coordinated international approach.

Supply Problem Notifications
(Control Panel / Labofar)



Regardless of this, the consequences of supply problems are suffered, primarily, by patients. But, furthermore, it also represents a significant overload for the doctors, pharmacists and health service administrations responsible for addressing the problems, leading to high direct costs (higher cost of the alternatives) and also of indirect costs (time spent on solving supply problems and monitoring of the alternative medicines).

The AEMPS (*Agencia Española de Medicamentos y Productos Sanitarios*, Spanish Agency for Medicines and Medical Devices) has undertaken different actions to ensure the availability of and access to authorised medicines. Addressing supply problems is also one of the priorities of the strategy of the EU's Heads of Medicines Agencies (HMA) up to 2020. The AEMPS is an active participant in these working groups for the prevention, early detection, monitoring and notification of supply problems affecting medicines for human and veterinary use.

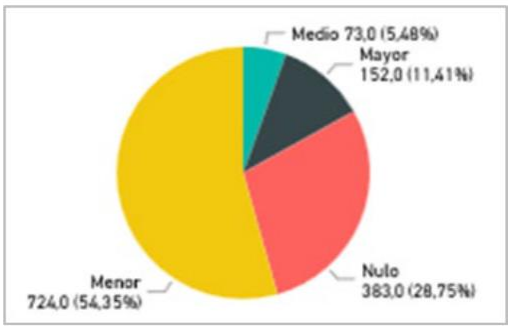
However, the number of supply problems notified grows every year and, although, marketing authorisation holders (MAH) are obliged to guarantee, within the limits of their responsibility, an adequate, continuous supply to the market, it does not appear that the actions currently being taken are reversing the upward trend of these problems.

The healthcare impact of these problems is classified as null, minor, medium or major, as follows:

- Null: if the supply problem is a short-term situation and normal supplies of the medicine to patients are maintained with the units currently in the distribution channel.
- Minor Impact: the pharmacist is able to substitute the medicine in most cases since other medicines are available on the market with the same active pharmaceutical ingredient and the same route of administration.
- Medium Impact: although alternatives exist on the market, the intervention of a prescribing doctor is necessary to determine the alternative medicine to be administered.
- Major Impact: the unavailability of a medicine causes a significant healthcare impact since there is no therapeutical alternative for one or any of its indications, and further action is necessary, beyond the

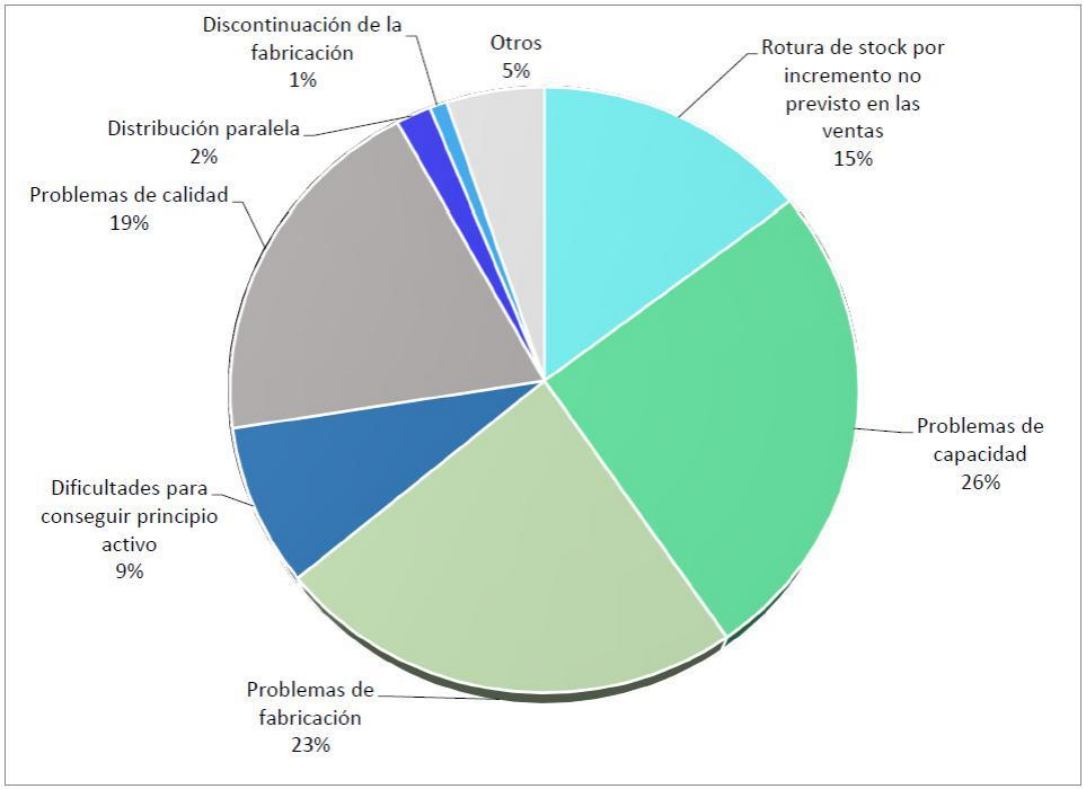
substitution of the medicine by the pharmacist or a change of prescription by the doctor (e.g., exceptional marketing or importation of foreign medicines).

Notifications, 2nd half, 2018, broken down by healthcare impact (Control Panel / Labofar)



According to an analysis of the second half of 2018 undertaken by the AEMPS, this type of problem is due especially to problems arising in the manufacture of medicines (including logistical problems related to capacity and planning), and, proportionally, they have a greater impact on medicines used in hospitals and in groups C (cardiovascular system), J (anti-infectives), L (antineoplastics and immunomodulators) and S (sensory organs). Of all the supply problems notified during this period, 17% of the cases were deemed to have had a medium or major healthcare impact.

The causes identified in the supply problems notified by the MAH are shown in the following chart.



It is necessary, therefore, to continue to address the causes and to work on the reduction of the impact of the consequences. The AEMPS has launched this new Medicine Supply Guarantee Plan for 2019-2022, coordinating the activities within the Ministry of Health, Consumer Affairs and Social Welfare (MSCBS)

and including the participation of different agents, represented by patients' associations, healthcare professionals, health administrations, distributors, the pharmaceutical industry and other stakeholders.

2. PURPOSE AND FOCUS

There are three general objectives, which give rise to specific measures that, in most cases, can be implemented in parallel. The tasks involved in these three lines of work can also generate measures that are not contemplated in this initial plan, being adapted in line with the evolution of the situation and the analyses available. The general objectives are:

- **To prevent** supply problems.
- **To manage** supply problems.
- **To inform** about supply problems.

There is also a fourth transversal objective: **coordination with other EU countries**, and the participation and involvement of stakeholders (patients, healthcare professionals, health administrations, distributors and industry).

3. ACTION PLAN

At the end of this document, there is a schedule of the deadlines laid down for the performance of the actions described below.

3.1. Prevention of supply problems

3.1.1. Plan for the control of medicines on the market

The purpose of this measure is to continue the strategy that was initiated in 2018 to increase the capacity for control of the market for authorised medicines, which will improve early detection of quality deficiencies, giving the system the flexibility it needs to avoid any resulting supply problems, and to verify the effective marketing of medicines.

In the first quarter of 2019, on the basis of the results of the actions taken in 2018, a quadrennial strategy will be designed together with the stakeholders.

3.1.2. Regulatory measures to prevent supply problems

The objective of this action is, firstly, to implement new regulatory instruments or take advantage of existing instruments that can help to prevent supply problems, and also to anticipate the impact that regulatory measures may have on supply problems.

The regulatory measures consist of:

a) A requirement for Marketing Authorisation Holders (MAH) which have generated supply problems of critical medicines (quality), or those which have suffered higher numbers of supply shortages in the half-year, to prepare **prevention plans** in order to raise their awareness and for the implementation of effective prevention measures.

b) In inspections of MAH laboratories, review all ***procedures related to continuous supply guarantees*** for medicines whose shortage has a healthcare impact.

c) Minimise the impact of ***Brexit*** on supply problems in Spain.

d) Elaborate a guide, which must be accessible by stakeholders, that includes all of the ***regulatory tools*** available in the fields of notification, evaluation, coordination and communication, facilitating its use in order to minimise supply problems.

e) Introduce ***indicators*** that allow analysis of the repercussion of regulations on supply problems and to optimise AEMPS databases in order to do so.

3.1.3. Guarantee of supply of essential medicines

The objective is the adoption of special measures for those medicines which are necessary for certain illnesses or pathologies, which have no therapeutical alternative and are susceptible to supply problems with a high healthcare impact.

a) The elaboration and approval of a reference framework on the basis of existing lists, such as the WHO list, and the prioritisation of actions on these medicines, establishing actions to ensure their continued provision by the national health services.

3.1.4. Review of sanctions policy

The objective is to establish and provide a legal framework that allows the management of a sanctions regime which reflects the clinical impact and gravity of the supply problem caused, in order to deliver a dissuasory effect on supply problems. To this end, the following actions will be taken:

a) ***Modify the current sanctions regime***. Include a "serious" sanction for the health impact in Royal Legislative Decree 1/2015, of 24 July, which approved the revised text of the Law on Guarantees and the Rational Use of Medicines and Medical Devices (pending).

b) In parallel, and while the legal framework is being modified, generate an indicator and ***move forward on sanctions policy***, exploring the flexibility offered by current legislation and discussing the aspects required to make it effective: delimitation of the obligations and non-compliances of the agents in the chain in their respective areas of responsibility, quantification of the impact, detection of loopholes, etc.

3.1.5. Development of regulations

a) Development of the provisions of Article 28.5 of Royal Decree 1345/2007, of 11 October, which regulates the procedure for the authorisation, registration and dispensing conditions of industrially-produced medicines for human use, **in order to encourage interest in the production and marketing of critical medicines** which are in short supply.

b) Development of Article 3.3 of the revised text of the Law on Guarantees and the Rational Use of Medicines and Medical Devices approved under Royal Legislative Decree 1/2015, of 24 July: **medicines of no commercial interest**.

3.2. Management of supply problems

Three groups of measures are proposed to manage supply problems efficiently.

3.2.1. Early detection of supply problems

This is the implementation of measures that will allow supply problems to be detected proactively, establishing information channels from different points in the system. This foresees:

a) The amendment of the regulations governing the ***notification*** of supply problems by the MAH or any other agent that is aware of a possible incidence.

b) Confirmation with the Marketing Authorisation Holder and the integration of all the information received from all sources, mainly community pharmacies and hospital pharmacy services, which will allow the ***early detection of cases not notified by the MAH.***

c) The creation of a network of sentinel pharmacy services

d) The creation of a working group with representatives of distributors and community pharmacies for the early detection of problems.

e) A review of Circular 3/2011 and the concepts of ***temporary suspension vs non-marketed medicines***, and their impact on other aspects of the regulation and provision of pharmacy services, in line with criteria for inclusion in the invoicing nomenclature.

3.2.2. Improvement of supply problem management tools

The objective is to improve existing tools in order to optimise the management of supply problems in the AEMPS and of the relationship between all the stakeholders, and to create new tools where necessary.

a) Generation of the necessary ***indicators***, establishment of the ***sources*** for those indicators, and upload the relevant accessible data to the ***control panel.***

3.2.3. Improvement of the provision of alternative therapies

All measures should be aimed at prevention and, when a shortage occurs, at minimising the impact on the patient and on healthcare. In general, measures which are closest to the usual healthcare practice are preferable, and so these should be given priority over other solutions. Criteria to address them should be established which allow them to be prioritised. It is considered that, without prejudice to the identification of others, the measures described below should be implemented.

Furthermore, a procedure for the response to a supply problem should be defined, in which the actions to be taken by the different agents involved are established (Regional Authorities, AEMPS, MAH, etc.), and which includes the maximum deadlines for the performance of the different actions:

a) Enhance the ***collaboration of the MAH*** of the medicines affected, as well as the manufacturers of the alternatives available on the market, in order to meet demand with other authorised medicines and, if this is not possible, by means of the authorisation of exceptional manufacture or marketing operations in order to obtain sufficient additional units to meet demand.

b) By agreement with the competent bodies, **develop the policy for the substitution** of publicly-financed medicines which are in short supply by non-financed medicines which are available, with prior notification to the patient.

c) Review the ***application and approval procedure for foreign medicines***, developing criteria which will vary in accordance with the market situation of the alternative(s): number of holders, market share, number of manufacturers, price, etc.

d) **Propose the inclusion of agreements** between Official Pharmacists' Associations and Regional Ministries of Health covering **officinal formulae** to temporarily substitute the publicly-financed medicine which is in short supply and for individualised treatments for the duration of the shortage and when there is no commercial alternative available.

e) Define a procedure for coordination with the Directorate General of Basic National Health Services and Pharmacy in order to obtain ***information regarding prices of medicines*** in the EU, to minimise the economic impact on Spanish health services.

f) Elaborate a white paper or ***guidelines for action*** with the participation of representatives of the agents in the medicine chain, healthcare professionals and patients, for information about and the presentation of ***foreign medicines*** or the ***exceptional marketing/manufacture*** of medicines, including a labelling guide that takes into consideration the possibilities offered by information technology in the case of foreign medicines as a reference framework.

g) Agree with the representatives of the pharmaceutical industry the ***principles that govern the return to the market of medicines*** once the supply problem has been solved, informing of when it is again in the supply chain and available to the patient.

h) Take advantage of the work of scientific associations in providing further possible therapeutical alternatives.

3.3. Information on supply problems

This is a key aspect in which the improvements are aimed at meeting, as far as possible, the expectations of patients and healthcare professionals.

The following measures are going to be applied in order to improve information about supply problems, involving patients and healthcare professionals to this end, so that the information provided is of maximum utility.

3.3.1. Optimisation of online public information of the AEMPS. Updates.

The objective is to continue providing accurate, permanently updated, accessible information about supply problems, improving the current contents of the Agency's website, and incorporating aspects that are relevant to the different stakeholders.

a) ***Review and update the contents of the website*** to expand the information offered, improving the messaging about each different problem to make it more comprehensible to patients and also to facilitate the measures to be taken by healthcare professionals, taking as a basis the proposals for improvement made in a survey of the targets of the information: patients, healthcare professionals and the pharmaceutical industry.

b) Provide an ***active communication service*** to facilitate access to the information by professionals and patients' organisations.

c) Publish an online ***half-yearly report*** analysing the evolution of supply problems.

3.3.2. Integration of information regarding supply problems with healthcare IT systems (prescribers)

The objective is to make information about supply problems available in the applications of healthcare professionals, for both prescribing and dispensing purposes, providing primary information to the systems, and reinforcing the role of the AEMPS as a reference point in the dissemination of this information.

a) The creation of a ***system to transmit information*** about supply problems with a healthcare impact involving risks and critical medicines to the information systems of the Regional Authorities, the General Council of the Official Pharmacists' Associations (CGCOF), the Spanish Society of Hospital Pharmacies (SEFH), the Spanish Society of Family and Community Pharmacies (SEFAC) and other scientific and patients' associations.

b) To continue improving the availability of systems providing ***active information through community pharmacies to patients*** who request medicines with supply problems, based on the integration of the information held by the AEMPS with the BOT+ database.

c) The improvement of the ***content of the information received by professionals,*** integrating the shortage situation in the Vademecum and in the Alcántara nomenclature system so that it can be used by prescription systems, defining the cases in which it should be included and the frequency of updating.

3.3.3. Improvement of the reach of information

The objective is to design a communication strategy for supply problems that ensures that complete information reaches its targets, depending on the type of problem and the repercussions.

a) To create an ***information network*** that encompasses all of the stakeholders sequentially (in waves) with criteria for each one of them: from what information should be provided online to what should be the subject of an informative notice.

b) To establish with each ***stakeholder*** what messages they wish to receive about supply problems, and when, how and where they wish to receive them.

c) To offer the information to the general public in the AEMPS External Communication Plan.

3.4. Principles for transversal actions and coordination

3.4.1. Coordination with EU countries

Supply problems are global problems and, as such, the national plan must be aligned with the actions taken by other national agencies and the EMA.

a) ***Maintaining the level of participation.***

b) Implementation in Spain of the ***consensual European definition of supply problems.***

3.4.2. Participation and involvement of stakeholders

The launch of the plan will count on the active participation of patients, healthcare professionals, health administrations, distributors and industry.

a) Compilation and inclusion of ***commitments and actions by stakeholders*** in this plan.

   a. Professional organisations and scientific associations: CGCOF, OMC, SEFH, SEC, Spanish Allergy and Clinical Immunology Society, SEOM, SEHH, FACME, SEFAC, SEFAP.

   b. Representatives of patients: Patients' Forum, AGP, Platform of Patients' Organisations.

   c. Representatives of the Pharmaceutical industry: Farmaindustria, AESEG.

   d. Representatives of Pharmaceutical Distribution: FEDIFAR.

   e. Directorate General of Basic Health Services and Pharmacy of the MSCBS, INGESA, Defence Pharmacy (Ministry of Defence), regional health authorities.

   f. Other stakeholders.

3.4.3. Continuous evaluation of the plan

The plan should include ongoing analysis of the causes and determining factors affecting supply problems in Spain, since the situation on the ground is in constant evolution, involving multiple causes.

a) Include a ***module in the control panel*** for supply problems.

b) Continue to perform a ***half-yearly analysis of supply problems*** and continue to add content to the analysis depending on the indicators chosen.

c) Hold ***at least two meetings per year with the representatives*** of the agents involved in order to analyse progress and difficulties, and to propose any necessary changes.

4. CALENDAR

Action	2019				2020				2021				2022			
	1T	2T	3T	4T	1T	2T	3T	4T	1T	2T	3T	4T	1T	2T	3T	4T
1. PREVENTION OF SUPPLY PROBLEMS																
1.1. **Plan for the control of medicines on the market**																
1.2. **Regulatory measures** to prevent supply problems																
1.3. **Guarantee of supply of essential medicines**																
1.4. Review of **sanctions policy**																
1.5. Development of regulations																
2. MANAGEMENT OF SUPPLY PROBLEMS																
2.1. **Early detection** of supply problems																
2.2. **Improvement of management tools** (Control Panel indicators)																
2.3. Improvement of the **provision of alternative therapies**																
3. INFORMATION ON SUPPLY PROBLEMS																
3.1. **Optimisation of online public information**																
3.2. **Integration of information** with healthcare IT systems																
3.3. **Improvement of the reach of information**																
4. TRANSVERSAL ACTIONS AND COORDINATION																
4.1. **Coordination with EU countries**																
4.2. **Participation and involvement** of stakeholders (*)																
4.3. **Continuous evaluation** of the Plan																

(*) *Professional organisations, patients' organisations, representatives of industry, representatives of distributors, Directorate General of Basic Health Services and Pharmacy (MSCBS), INGESA, Defence Pharmacy (Ministry of Defence), representatives of the regional health authorities and other stakeholders.*

Texto de los gráficos

Notifications, 2nd half, 2018, broken down by healthcare impact

Nulo	Null
Menor	Minor
Medio	Medium
Mayor	Major

The causes identified in the supply problems notified by the MAH are shown in the following chart.

Rotura de stock por incremento no previsto en las ventas	Shortage due to unforeseen increase in sales
Problemas de capacidad	Capacity problems
Problemas de fabricación	Manufacturing problems
Dificultades para conseguir principio activo	Difficulties in obtaining active pharmaceutical ingredient
Problemas de calidad	Quality problems
Distribución paralela	Parallel distribution
Discontinuación de la fabricación	Discontinued product
Otros	Other