



19th Congress of the European Association of Hospital Pharmacists
Barcelona, Spain, 26-28 March 2014

Seminar N6 – Drug shortages: Physicians‘ perspective

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Drug Commission
of the German Medical Association



HELIOS Clinic Berlin-Buch



Conflict of interest:

No financial relationships to disclose

Head of the Dept. of Hematology, Oncology, and Tumor Immunology
Chairman of the Drug Commission of the German Medical Association
Editor of „DER ARZNEIMITTELBRIEF“ (ISDB)

Member of the EMA Management Board



Drug shortages: Physicians' perspective - **Agenda**

- Essential medicines, drug shortages: **Definitions**
- Looking back at the (multifaceted) **root causes** of drug shortages
 - „Drug shortages: A complex health care crisis“.
- „**Medication shortages threaten cancer care**“.
- **Impact on patients and their care in oncology**
- **Ethical issue: Coping with critical drug shortages**
- „Near future: Drug shortages are anticipated to continue“.
- **Short/medium term actions to prevent/manage supply shortages**



Essential medicines - definitions

„A **medically necessary drug product*** is one that is used to treat or prevent a serious disease or medical condition for which there is no alternative drug, available in adequate supply, that is judged by FDA medical staff to be an adequate substitute“.

*Kweder SL & Dill SD: Clin. Pharmacol. Ther. March 2013

Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford.





Drug shortage - definitions

*Drug shortage**:

„The total supply of all clinically interchangeable versions of an FDA-regulated drug product is inadequate to meet the projected demand at the user level“.

*<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf>.

Drug shortage \neq supply bottleneck



Clinical Pharmacology & Therapeutics

Volume 31, No. 2, February 2013

Published for the American Society of
Clinical Pharmacology and Therapeutics
by Nature Publishing Group



Special issue devoted to

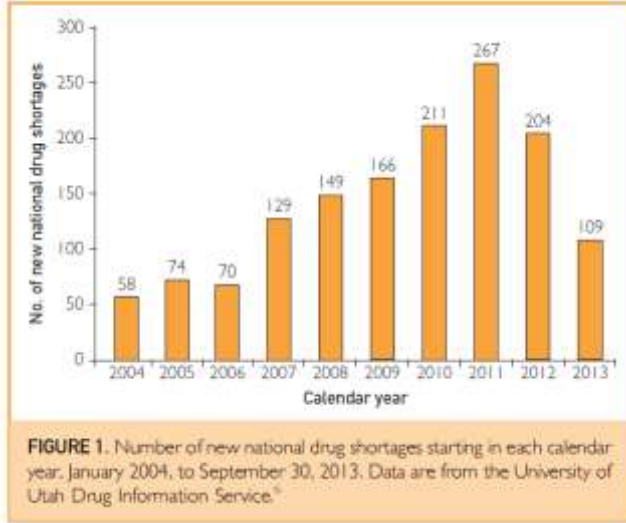
DRUG SHORTAGES

February 2013



Drug Shortages: A Complex Health Care Crisis

Erin R. Fox, PharmD; Burgunda V. Sweet, PharmD; and Valerie Jensen, RPh



2011: 267

73% generic injectable agents

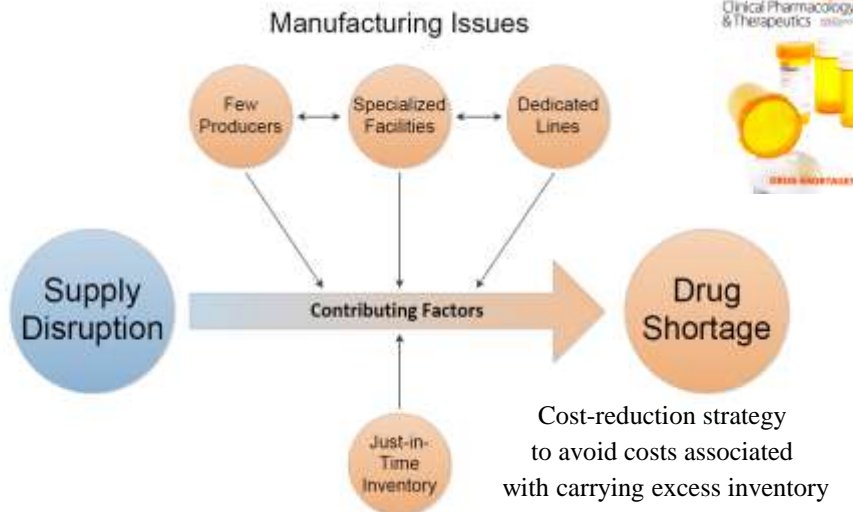
11% of all FDA-approved drugs, vaccines, and biologics in short supply

Mayo Clin Proc. ■ March 2014;89(3):361-373



Dynamics of Sterile Injectable Drug Shortages

Factors that turn a supply disruption into a shortage.



Cost-reduction strategy to avoid costs associated with carrying excess inventory

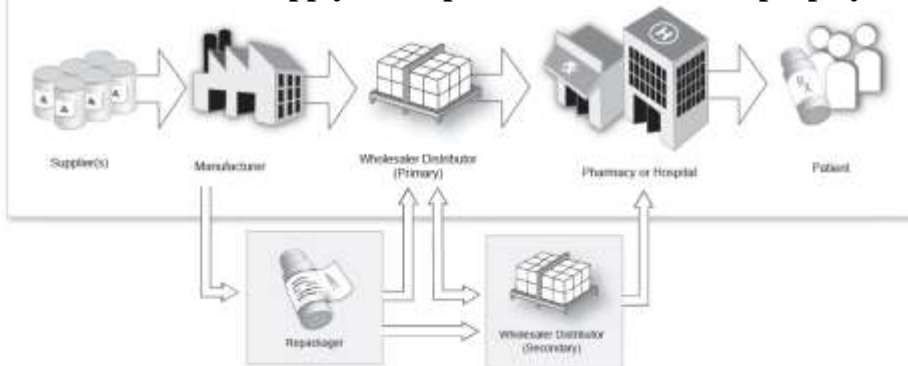
➤ „Available too late or not at all“



A Drug Supply Chain Example
From Supplier to Patient

**Root Causes
for drug shortages**

➤ **Pharmaceutical supply is complex and involves multiple players**



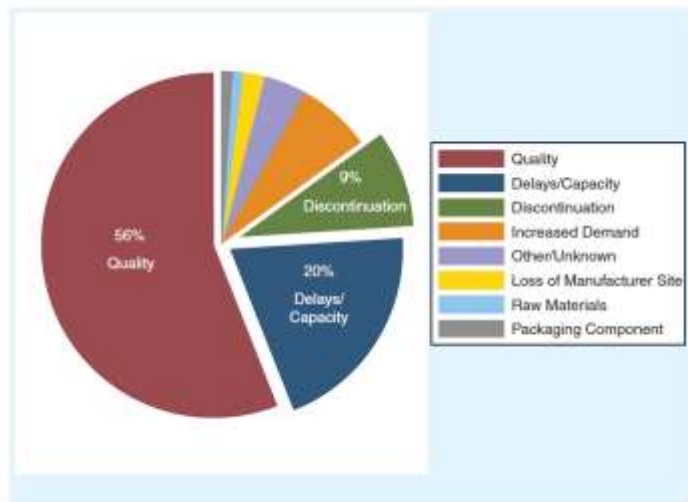
- **Quality aspects (e.g., manufacturing problems)**
 - **Delays in manufacturing or shipping**
- **Loss of manufacturing site; lack of availability of the active pharmaceutical ingredient; increased demand; economic reasons**

www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm277626.htm



Economic and Technological Drivers of Generic Sterile Injectable Drug Shortages

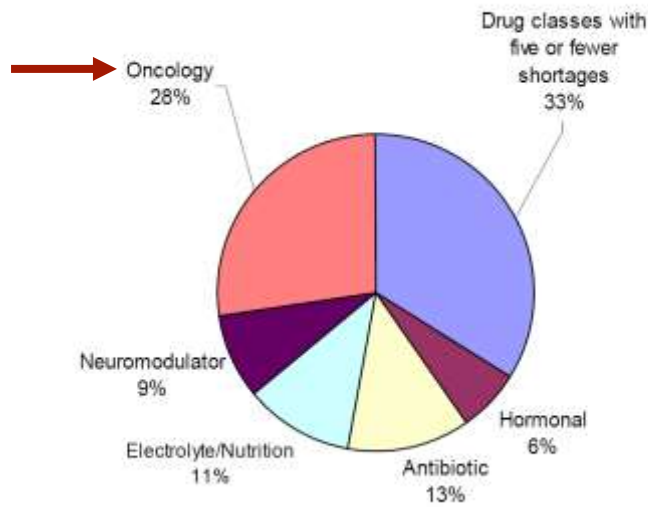
J Woodcock¹ and M Wosinska¹



CLINICAL PHARMACOLOGY & THERAPEUTICS | VOLUME 93 NUMBER 2 | FEBRUARY 2013



Drug shortages followed by FDA, by drug classes

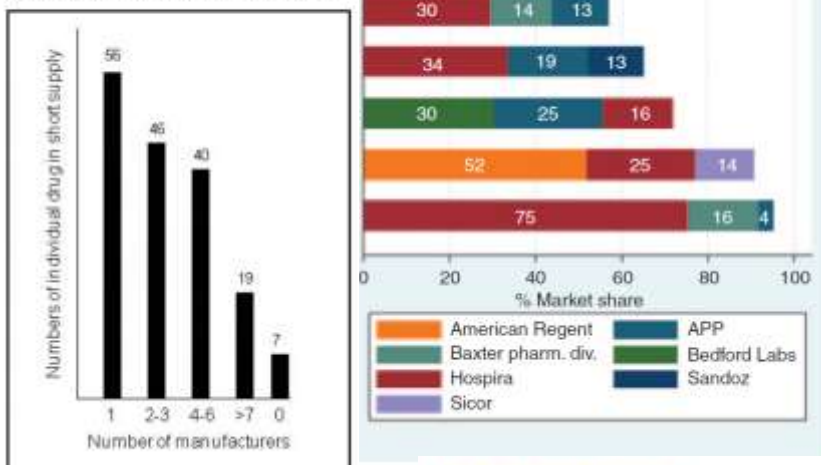


*Kweder SL & Dill SD: Clin. Pharmacol. Ther. March 2013



Market concentration in select generic sterile-injectable classes.

Figure 1. Correlation between individual drugs and number of suppliers.
Data adapted from IMS Institute for Healthcare Informatics, November 2011.



CLINICAL PHARMACOLOGY & THERAPEUTICS | VOLUME 93 NUMBER 2 | FEBRUARY 2013



The NEW ENGLAND JOURNAL of MEDICINE

The Shortage of Essential Chemotherapy Drugs in the United States

Mandy L. Gatesman, Pharm.D., and Thomas J. Smith, M.D.

For the first time in the United States, some essential chemotherapy drugs are in short supply. Most are generic drugs that have been used for years in childhood leukemia and curable cancers —

The main cause of drug shortages is economic. If manufacturers don't make enough profit, they won't make generic drugs.

Perspective
NOVEMBER 3, 2011

N ENGL J MED 365:18



Chemotherapy Drug Shortages in the United States: Genesis and Potential Solutions

Michael P. Link, Stanford University School of Medicine, Stanford, CA
Karen Hegerty, American Society of Clinical Oncology, Alexandria, VA
Hagop M. Kantarjian, MD Anderson Cancer Center, Houston, TX

Reason

- Increased national and worldwide demand for oncology drugs
- Shortages of supply of raw materials
- Production problems; contamination of materials
- Aging production plants
- Limited inventories of generic drugs to reduce company costs
- Limited profit margins for generic drugs; Medicare ASP + 6% reimbursement system

In Europe, where there is no such Medicare rule, the prices of generic drugs are higher than in the United States, and the prices of brand drugs are lower (because of agreements between drug companies and governments). This maintains a reasonable profit margin for generic drugs, allowing competition to continue and largely preventing drug shortages.

JOURNAL OF CLINICAL ONCOLOGY



Coming Up Short

These oncology drugs have experienced shortages in recent months.

- Bleomycin Injection
- Capecitabine Tablets
- Carboplatin Solution for Injection
- Cisplatin Injection
- Cytarabine Injection
- Daunorubicin HCl Injection
- Doxorubicin Injection
- Doxorubicin Liposomal Injection (Doxil)
- Etoposide Injection
- Flutasterone Injection
- Fluorouracil Injection
- Irinotecan Injection
- Leucovorin Calcium Injection
- Octreotide Injection
- Paclitaxel Injection
- Thyrotropin Alfa
- Vincristine Injection

Source: American Society of Health-System Pharmacists

Medication Shortages Threaten Cancer Care

The oncology community and the FDA tackle ongoing drug shortage problem Cancer January 18, 2012

8.2 Cytotoxic and adjuvant medicines	
Complementary List	
aliquantol [E]	Tablets 200 mg; 200 mg
asparaginase	Powder for injection: 20 000 IU in vial
bleomycin	Powder for injection: 15 mg (in sodium) in vial
capecitabine	Tablets 500 mg; 200 mg
carboplatin	Powder for injection: 150 mg (in sodium) in vial
cisplatin	Powder for injection: 50 mg (in sodium) in vial
cytarabine	Powder for injection: 100 mg in vial
daunorubicin	Powder for injection: 100 mg in vial
doxorubicin	Powder for injection: 500 micrograms in vial
epidolone	Powder for injection: 50 mg (hydrochloride) in vial
etoposide	Tablets 100 mg; 50 mg
flutasterone	Powder for injection: 250 mg (hydrochloride) in vial
fluorouracil	Powder for injection: 20 mg; 50 mg (hydrochloride) in vial
irinotecan	Capsules 100 mg
irinotecan	Injection 20 mg/ml in 5 ml ampoules
irinotecan	Injection 20 mg/ml in 5 ml ampoules
irinotecan	Solid oral dosage forms: 200 mg; 250 mg; 300 mg; 400 mg; 500 mg; 1 g
irinotecan	Powder for injection: 1 g vial; 2 g vial
irinotecan	Tablets 30 mg
irinotecan	Injection: 100 mg/ml in 2 ml and 10 ml ampoules; Tablets: 400 mg; 600 mg
irinotecan	Powder for injection: 20 mg (in sodium salt) in vial; Tablets: 2.5 mg (in sodium salt)
irinotecan	Powder for injection: 0.1 mg/ml
irinotecan	Capsules 30 mg (in hydrochloride)

WHO Model List of Essential Medicines

18th List (April 2013)

(Last Assessment - October 2012)

Cytotoxic drugs N = 22
‘Supportive drugs’ N = 3

irinotecan	Solid oral dosage forms: 40 mg
irinotecan	Powder for injection: 30 mg (sodium) in vial
irinotecan	Powder for injection: 1 mg; 1 mg (sodium) in vial



Clinical Dilemmas and a Review of Strategies to Manage Drug Shortages
Anne Elise Rider, Derek J. Templet, Mitchell J. Daley, Carrie Shuman and Leticia V. Smith
Journal of Pharmacy Practice 2013 26: 183 originally published online 3 April 2013
DOI: 10.1177/0897190013482332

Regimen	Medications
FOLFOX	5-fluorouracil, oxaliplatin, leucovorin
XELOX	capecitabine, oxaliplatin
ABVD	doxorubicin, bleomycin, vinblastine, dacarbazine
Stanford V	mechlorethamine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide, prednisone
MOPP	mechlorethamine, vincristine, procarbazine, prednisone

- One chemotherapy agent in short supply or unavailable impacts multiple treatment regimens for several types of cancer (e.g., doxorubicin)
- Chemotherapy shortages may contribute to adverse patient outcomes (e.g., increased toxicities, decreased efficacy) and/or elimination of a curative regimen (e.g., shortage of cytarabine, backbone of AML treatment)
- Drug shortages likely contribute to delays in providing chemotherapy



National survey on the effect of oncology drug shortages on cancer care

ALI MCBRIDE, LISA M. HOLLE, COLLEEN WESTENDORF, MARGARET SIDEBOTTOM, NIESHA GRIFFITH, RAYMOND J. MULLER, AND JAMES M. HOFFMAN

Table 2.
Most Difficult Oncology Drugs to Obtain, as Reported by Survey Respondents (n = 239)*

- Standard treatment of many oncology protocols for childhood, hematologic, and gynecologic protocols
- Equivalent dosing for substitute regimes often absent, substitutions not based on evidence gathered from randomized controlled trials
- Medication errors



The impact of drug shortages on patient care and clinical trials in oncology

- Many shortages invisible to the ordering prescriber – because they can be managed by the pharmacists
- Number of pts. harmed difficult to quantify
- Risks of drug shortages: increased risk of medication errors and/or adverse patient outcomes
- Patients treated with an alternative therapy (for which clinicians may have limited familiarity)
- Drug of choice unavailable/delay in therapy
- real patient harm; e.g., higher relapse rate/reduced survival
- Rationing of chemotherapy because of shortages

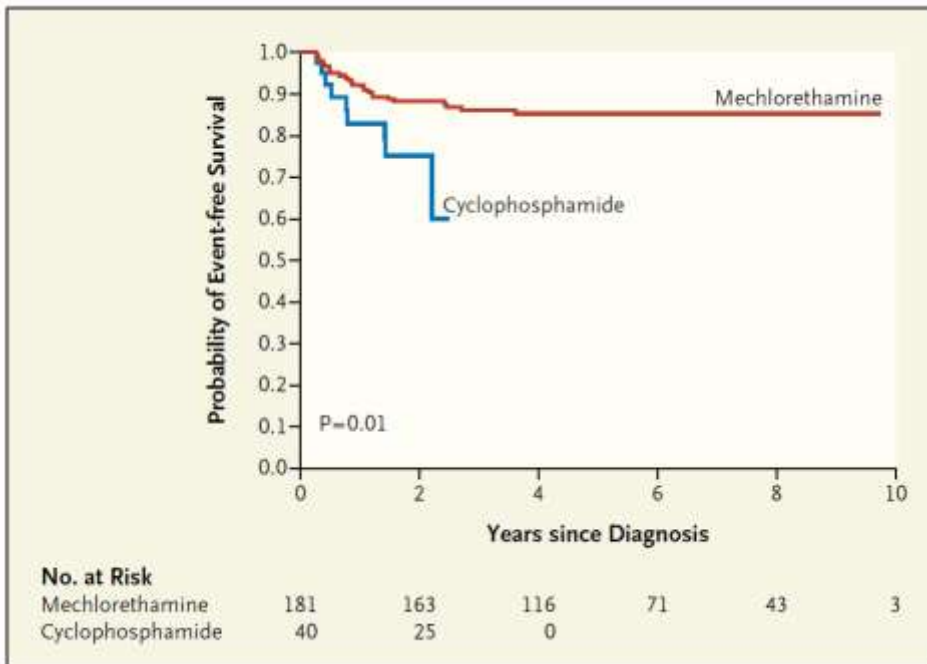


National survey on the effect of oncology drug shortages on cancer care

ALI MCBRIDE, LISA M. HOLLER, COLLEEN WESTENDORF, MARGARET SIDERBOTTOM, NIESHA GRIFFITH, RAYMOND J. MULLER, AND JAMES M. HOFFMAN

Table 3.
Medication Errors and Shortage-Associated Adverse Outcomes, as Reported by Survey Respondents

Event	No. (%) Respondents*
Near-miss medication error (n = 39)	
Wrong drug	11 (28)
Wrong dosage conversion	10 (26)
Wrong drug concentration	8 (21)
Delayed or omitted drug	3 (8)
Inadequate supply to prepare dose	3 (8)
Details unknown	4 (10)
Medication error that reached a pt (n = 15)	
Wrong drug	2 (13)
Wrong dosage conversion	7 (47)
Wrong drug concentration	3 (20)
Delayed or omitted drug	1 (7)
Extra dose	2 (13)
Adverse pt outcome (n = 40)	
Increased toxicity	20 (50)
Disease progression	6 (15)
Cardiac event	2 (5)
Emotional stress	1 (3)
Details not disclosed	11 (28)



N ENGL J MED 367;26 NEJM.ORG DECEMBER 27, 2012

What impact do drug and biological product shortages have on research and clinical trials? What actions can FDA take to mitigate any negative impact of shortages on research and clinical trials?

The impact of drug shortages on cancer clinical trials

The shortage of some cancer drugs is not just affecting patients currently undergoing standard or non-investigational treatment, but it is also having a significant negative impact on current and future cancer clinical trials. Approximately half of all active cooperative group cancer clinical trials have at least one drug on the shortages list.

Furthermore, as patients are recruited for clinical research trials with the intent to receive an investigational therapy, the treatment described in the consent form details both the benefits, side effects, and other standard of care treatment options. It is concerning that a patient who opts to receive an investigational treatment in combination with an existing drug, which is short supply, could have instead elected to receive alternative, standard treatment – perhaps in a more timely way. Treatment delays of days to months are critical in the life of a cancer patient and could limit their chances for a cure or remission of their disease.

Another residual impact of drug shortages is the delay in obtaining the data necessary to bring new cancer therapeutics to patients. With more than 400 cancer agents in various stages of development, it is imperative that cancer clinical trials continue uninterrupted in order to obtain the necessary data to seek approval of new anti-cancer drugs as soon as possible.



Why drug shortages are an ethical issue

Wendy Lipworth^{1,2} and Ian Kerridge^{2,3}

Australasian Medical Journal [AMJ] 2013, 6, 11, 556-559]

Chemotherapy Drug Shortages in Pediatric Oncology: A Consensus Statement
Matthew DeCamp, Steven Joffe, Conrad V. Fernandez, Ruth R. Faden and Yoram Unguru

Pediatrics 2014;133:e716

Coping With Critical Drug Shortages

An Ethical Approach for Allocating Scarce Resources in Hospitals

Philip M. Rosoff, MD, MA; Kuldip R. Patel, PharmD; Ann Scates, PharmD;
Gene Rhea, PharmD; Paul W. Bush, PharmD; Joseph A. Goyert, MD

Arch Intern Med. 2012;172(19):1494-1499.



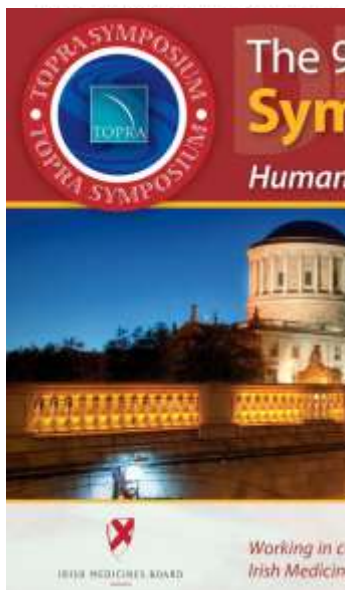
Ethical issues that need to be considered attempting to understand or address drug shortages

- Drug shortages are a major threat to the delivery of „beneficent“ , „non-maleficent“ and equitable health care
- Compelling evidence that pts. can be harmed by drug shortages
- Moral imperative to prevent further drug shortages
- Ethical approach includes transparency, fairness for pts. and health care providers, and its ability to be rapidly put in practice
- Initial response: an attempt to maximize efficiencies and to minimize wastage
- Pts. should not be treated differently depending on their (non-clinical) circumstances, e.g., insurance status, ethnicity etc.
- Youth of pts. should play a determinative role in forced rationing decisions ????



Drug shortages

**Solutions:
no main targets
many side paths**



REPORT OF THE INTERNATIONAL SUMMIT ON MEDICINES SHORTAGE

Toronto, Canada
20-21 June 2013





22 November 2012
EMA/590745/2012
Patient Health Protection

Reflection paper on medicinal product supply shortages
caused by manufacturing/Good Manufacturing Practice
Compliance problems

4. Envisaged activities

While the causes of shortages are varied and complex, the challenge remains to effectively co-ordinate an assessment, to develop risk minimisation measures to alleviate the impact on patients, and to communicate within the Network, with international partners and with healthcare professionals, patients and the general public. On occasions EMA is being asked to coordinate the follow-up to an emerging event in the absence of an appropriate legal framework.

In some cases, the need for rapid implementation of risk minimisation measures is paramount. Short and medium term measures will be undertaken to enhance the current approach. In addition, there are some aspects which will require discussion with bodies outside the Network, e.g. in the area of medical devices.



Workshop on product shortages due to manufacturing and quality problems: Developing a proactive approach to prevention

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Details Documents Multimedia

Title	Workshop on product shortages due to manufacturing and quality problems: <u>Developing a proactive approach to prevention</u>
Date	14/10/2013 - 14/10/2013
Location	European Medicines Agency, London, UK
Summary	The workshop discusses how to improve existing risk-management strategies to prevent shortages due to <u>manufacturing and quality issues, as well as how to mitigate the impact of shortages.</u> Registration was by invitation only due to limited places and is now closed. However, the workshop will be broadcast live.

Related information

- EMA workshop on prevention of product shortages due to manufacturing and quality problems takes place today (14/10/2013)
- EMA to host workshop on prevention of product shortages due to manufacturing and quality problems (10/10/2013)
- [Reflection paper on medicinal-product supply shortages caused by manufacturing / good-manufacturing-practice compliance problems \(23/11/2012\)](#)

Contact point:
shortagesworkshop@ema.europa.eu



Key recommendations to prevent and to manage drug/supply shortages of medicines

- Improved communication among the regulatory agencies, manufacturers, and stakeholders
- Increase authority of EMA and national agencies (e.g., FDA Safety and Innovation Act, FDASIA)
- Examine impact of current requirements on drug shortages
- Develop a National Registry
- Compile a list of essential medicines by specialty organizations
- Provide economic incentives to manufacturers of critical drugs
- Civil or monetary penalties for industry noncompliance

23 March 2014

Current Drug Shortages Index

The majority of information in this section is provided to FDA by manufacturers. We appreciate their timely reports and also encourage healthcare professionals and health consumers to notify FDA of shortages. You can send reports by email to: drugshortages@fda.hhs.gov.

A-Z Index **Chemotherapy**

Drugs are listed by generic name or active ingredient

A-Z Index

A

Amikacin Injection
 Amoxicillin, Clavulanate Injection (oral pending) (see 282212)
 Arzoxifen Hydrochloride Tablets (oral pending) (see 12728712)
 Atropine Sulfate Injection

B

Baclofen Tablets for Suspension (oral pending) (see 18122212)
 Bupivacaine Hydrochloride (Bupivacaine, Bupivacaine) Injection

C

Ceftriaxone and Zidovudine, Tablets (Ceftriaxone) Tablets (oral pending) (see 282212)
 Ceftriaxone Hydrochloride (Ceftriaxone), Sodium Succinate (Ceftriaxone) Injection
 Calcitonin Receptor Receptor (oral pending) (see 12122212)
 Calcitonin Receptor Receptor (oral pending) (see 11822212)
 Chlorambucil Sodium Succinate Injection (oral pending) (see 11822212)
 Chlorine Chloride Injection
 Clonidine Injection (oral pending) (see 17822212)
 Clonidine Hydrochloride (Clonidine) Injection (oral pending) (see 18222212) **11/2014**
 Copper Injection (oral pending) (see 47822212)
 Cyclosporine Injection (oral pending) (see 12822212)



Draft common position between patients', consumers,
and healthcare professionals' organisations on

Supply Shortages of Medicines

October 2013

- Article 81 of the EU Directive on Medicines for Human Use¹¹ was intended to ensure adequate supply of any given product to the market. However, there is extensive evidence of situations where pharmacies can't obtain the medicines that they need for their patients. Consideration should be given to strengthening the provisions of Article 81;

- Françoise Charnay-Sonnek, European Specialist Nurses Organisations ([ESNO](#))
- Roberto Frontini and Richard Price, European Association of Hospital Pharmacists ([EAHP](#))
- David Haerry, European Aids Treatment Group ([EATG](#))
- Dr Carla Hollak, Academic Medical Centre, Amsterdam ([AMC](#))
- François Houyez, European Organisation of Rare Diseases ([EUROORDIS](#))
- Sascha Marschang, European Public Health Alliance ([EPHA](#))
- Jurate Svarcaite, Pharmaceutical Group of the European Union ([PGEU](#))



**Thank you
for your attention**

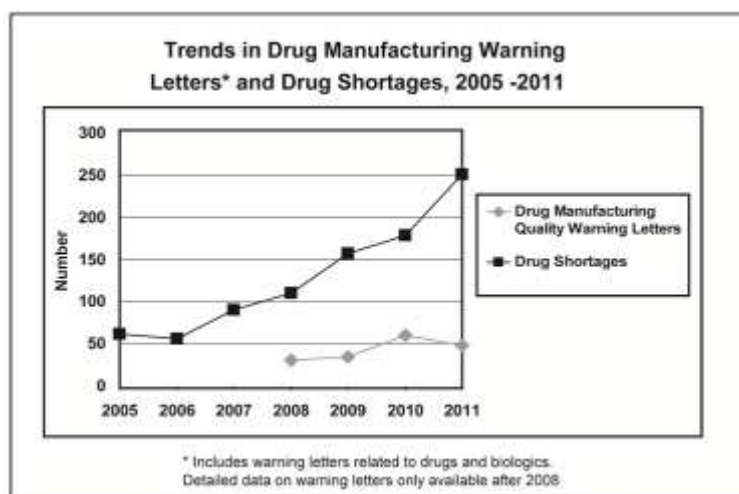
*Antonello
da Messina
(ca. 1430-1479)
Saint Jerome in
His Study*

Latest Reports

Type	Active substance	Brand	Form of administration	Revision Date	Impact
🚫	Corifollitropin alfa	Elonva	Liquid Injection	08-07-2013	Substitution is possible
🚫	Levothyroxine (sodium)	Euthyrox 75 mcg	tablet	08-07-2013	Solved
🚫	Alendroninezuur colecalciferol	Fosavance 70/5600	tablet	08-07-2013	Solved
🚫	Epirubicin	Epirubicin PCH	infusion, injection	09-07-2013	Substitution is possible
🚫	Lactulose	Lactulose PCH, RP	syrup, powder for oral use	09-07-2013	Substitution is possible
🚫	Enalapril	Enalapril PCH, Apotex, CF	tablet	09-07-2013	Substitution is possible
🚫	Isosorbide dinitrate	Isordil, Titradose	tablet	09-07-2013	Substitution is possible
🚫	Ascorbic acid	250 and 500 mg ascorbic	tablet	10-07-	Substitution



Drug Shortages: The Cycle of Quantity and Quality



*Kweder SL & Dill SD: Clin. Pharmacol. Ther. March 2013



FDA reveals new initiatives to deal with drug shortages

Michael McCarthy

BMJ 2013;347:f6646 doi: 10.1136/bmj.f6646 (Published 4 November 2013)

Seattle, USA

Under proposed rules announced on 31 October by the US Food and Drug Administration, drug makers will be required to notify the government at least six months in advance, or as far in advance as practical, if they intend to stop making a medically important drug. This rule will also apply to any interruption in a drug's manufacture that is likely to lead to a disruption in supply.¹

The FDA said it prevented just under 200 shortages in 2011 and more than 280 in 2012 by working with existing and new manufacturers to ensure supply, expediting reviews to prevent shortages, and exercising "enforcement discretion in appropriate circumstances, if this would not cause undue risk to patients."

As a result of such efforts, the number of products in short supply dropped to 117 last year, the agency said. Numbers for this year are not yet available.



Shortages catalogue [Send](#) [Print](#) [Help](#) [Share](#)

The shortages catalogue contains information on medicine shortages that affect or are likely to affect more than one European Union (EU) Member State, where the European Medicines Agency has assessed the shortage and provided recommendations to patients and healthcare professionals across the EU.

It does not give a complete overview of all medicine shortages occurring in the EU, as most shortages are dealt with at a national level.

For each shortage listed below, additional information about the situation in a specific country may be available from the national competent authority.

There may be medicines in short supply that are not listed here, if you cannot find information on a medicine in short supply or you would like further information, please visit the website of your national competent authority.

If you are having difficulty obtaining a medicine that has been prescribed to you, talk to your doctor or pharmacist.

Table of contents

- Current shortages
- Resolved shortages

Current shortages [Back to top](#)

Document(s)	Language	Status	First published	Last updated	Effective date
Etidrel (etidrelast) supply shortage	(English only)		19/10/2014		
Cerezyme (imiglucerase) supply shortage	(English only)		04/11/2013		
Fibractone (agalsidase beta) supply shortage	(English only)		04/11/2013		
Vivade (vidofin) supply shortage	(English only)		04/11/2013		

Resolved shortages [Back to top](#)

Document(s)	Language	Status	First published	Last updated	Effective date
Droscix (mexaserone) shortage resolution	(English only)		20/12/2013		

BfArM für Bürger

ENGLISH PREISE RSS GLOSSAR KONTAKT LEICHTE SPRACHE

BfArM
Bundesinstitut für Arzneimittel und Medizinprodukte

Über das BfArM • Arzneimittel • Medizinprodukte • Bundesopiumstelle • Forschung • Service

Lieferengpässe

STARTSEITE • ARZNEIMITTEL • PHARMAWIRTSCHAFT • RISIKOINFORMATIONEN
LIEFERENGAPPE • LIEFERENGAPPE VON HUMANARZNEIMITTELEN

Lieferengpässe von Humanarzneimitteln

Das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) bietet eine Übersicht zu aktuellen Lieferengpässen für Humanarzneimittel in Deutschland auf der Basis freiwilliger Informationen der Zulassungsinhaber an:

[Tabelle der Lieferengpässe - Stand: 05.03.2014 \(PDF, 165KB, Datei ist barrierefrei/nachname\)](#)



Update: March 5, 2014

Drug shortages: N=13



LIEFERENGAPPE FÜR HUMANARZNEIMITTEL IN DEUTSCHLAND*

Vertriebsart	W. Nr.	Arzneimittel (INN)	Lieferengappestärke / Hersteller	Verfügbarkeit	Ursache für Engpass	Zusatzinformationen	Kontakt (Tel. Nr.)	Letztes Update	Mitteilung in Fachzeitschrift
Keinprospekt	1811	Pellets 4 Angulus (Nahrung, 5 mg/m ²) Nahrungsmittel (FN 1423089)	Ophthal Europe GmbH / Ophthal Europe (Deutschland) GmbH	Daum der Lieferengpass nicht mehr besteht.	Probleme bei der Herstellung	Ein Ausschichtspezialist mit dem Werkstoff konnte zur Erzeugung des Beschichtungsfilms bei STI 400, 8 4000 über Ophthal Europe (Deutschland) Kontakt hergestellt werden.	0712/140 55 40	09.07.2013	ja
Keinprospekt	1814	Cantrivin 100 mg Tabletten (FN 0007500)	Chemie Pharma (GmbH)	Nicht verfügbar bis Anfang Oktober 2014.	Probleme in der Herstellung	-	0044788752900	06.08.2013	nein
Multiprospekt	1819	MTX 25 mg (1x1) ¹ injekt., Injektionslösung, 25 mg (FN 0792390, 07923400) MTX 50 mg (1x1) ¹ injekt., Injektionslösung, 50 mg (FN 0402746, 00131438) Methotrexat 100mg, 25	Novartis AG	Lieferengpass auf unbestimmte Zeit	Probleme in der Herstellung	-	060047604100	27.06.2013	nein
Multiprospekt	1920	Mikrocyclin 10 mg (1x1) ¹ , Pulver zur Herstellung einer Injektions- oder Infusionslösung oder Lösung für intravenöse Anwendung, 10 mg (FN 0046020) Mikrocyclin 20 mg (1x1) ¹ , Pulver zur Herstellung einer Injektions- oder Infusionslösung oder Lösung für intravenöse Anwendung, 20 mg (FN 0007400, 01248130, 00566612, 00566610)	Novartis AG	-	Probleme in der Herstellung	-	002047604100	27.06.2013	nein