



Medicines shortages—unpicking the evidence from a year in South Africa

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BRIEF REPORT

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ABSTRACT

Although medicines shortages are a persistent and challenging problem for all health systems, the reasons for such shortages vary considerably between settings. Understanding the range of problems encountered, and the specific reasons for each medicines shortage event, may help to identify the most appropriate systems-wide responses.

South Africa's health system is, at this point, still clearly divided between a better-resourced private sector and an overwhelmed public sector. Medicines selection and procurement processes in the two sectors are markedly different. However, in both sectors there is a dearth of publicly accessible information about the incidence and consequences of medicines shortages.

This brief report describes the medicines selection and procurement processes currently applied in South Africa's public health sector, and then describes the nature of the medicines shortages that have been experienced in the KwaZulu-Natal provincial health services between July 2012 and June 2013. The degree to which these shortages might have been managed differently, had the recommendations developed by the International Pharmaceutical Federation Summit on Medicines Shortages been implemented, is then explored.

Key Words

Medicines shortages; South Africa; public sector selection and procurement; systems-wide responses

What this report adds:

1. What is known about this subject?

Medicines shortages have been most extensively documented in North American settings. National and international recommendations have been offered to reduce the incidence and impact of such shortages.

2. What new information is offered in this study?

This brief report provides an insight into the range of medicines shortages experienced in a middle-income country's public health sector.

3. What are the implications for research, policy, or practice?

Greater access to and sharing of information about medicines shortages and their causes can help to reduce the negative health impacts of such events.

Background

Shortages of medicines, unrelated to inefficiencies in the procurement and distribution system, have been documented for more than a decade in the United States of America.¹ However, significant prominence has been given to more recent shortages, especially of generic injectable products.²⁻⁵ Although initial analyses of the contributory factors had focused extensively on the effect of heightened regulatory interventions on the ability of manufacturers to ensure continued supply of injectable products, Woodcock and Wosinka showed how the lack of incentives to provide quality products lay at the core of the problem.⁶ Put simply, these authors argued that "the inability of the market to observe and reward quality" was driving excessive price competition and encouraging manufacturers to contain costs in every possible way, including "by minimizing quality investments".⁶ Medicines shortages in the US and Canada have predominantly involved generic versions of injectable medicines in a narrow range of pharmacological categories. However, the situation on a global level is far more mixed. Other categories of "fragile" markets have been identified, such



as the paediatric dosage forms for HIV/AIDS.⁷ Shortages have also been documented in a wide range of countries.⁸

Systems-wide responses

Although the analysis by Woodcock and Wosinka⁶ firmly put the procurement practices of health systems into the frame, previous interventions in the US have focused predominantly on early warnings and transparency.⁹⁻¹⁰ In this regard, while the requirements of the US Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) are important, they are clearly not sufficient.¹¹ FDASIA requires any manufacturer of a “life-supporting” or “life-sustaining” medicine or any medicine “used in emergency medical care or during surgery” to notify the regulator of a permanent discontinuance in the manufacture of the drug or an interruption of the manufacture of the drug that is likely to lead to a meaningful disruption in the supply of that drug in the United States” at least 6 months before that event.¹¹ Manufacturers are also required to provide the reasons for such discontinuance or interruption.

Outside of the US and Canada, publicly accessible sources of information about medicines shortages are generally lacking. Globally, it has been argued that “governments have a responsibility not only to ensure the quality of medicines and access to essential medicines, but also to create the necessary conditions for a sustainable, productive and responsible pharmaceutical industry”.¹² Active steps to improve access to information about medicines supply should be part of that government response.

In June 2013, the International Pharmaceutical Federation (FIP) and the Canadian Pharmacists Association co-hosted an International Summit on Medicine Shortages in Toronto, Canada. The Summit’s final communiqué offered recommendations on systems-wide responses to medicine shortages:¹³

- Each country should establish a publicly accessible means of providing information on shortages.
- A global process to determine the list of critical/vulnerable products should be developed.
- All procurers of medicines are urged to move towards active procurement processes that assure the continuity of supply of quality medicines.
- All countries are encouraged to remove unnecessary variability of regulatory practices within and between countries.

- All countries should investigate the potential to establish a national body charged with gathering and sharing information about demand for, and supply of, medicines within their jurisdiction.
- All countries are encouraged to develop evidence-based risk mitigation strategies, which might include strategic buffer stockpiles, contingency plans, pandemic planning, and capacity redundancy appropriate to their national needs.

Medicines selection and procurement in South Africa

Medicines selection and procurement processes vary considerably between the South African private and public sectors. In the private sector, which caters predominantly for the approximately eight million inhabitants who are beneficiaries of medical schemes (private insurance), medicines selection is largely in the hands of individual prescribers, although some managed care interventions (such as formularies and treatment guidelines) do exist. In that sector, a number of pricing interventions have been implemented, including a single exit price at the factory gate and a maximum dispensing fee.¹⁴ Healthcare services are provided by a network of private medical practitioners, chain and independent community pharmacies, and private hospitals. By contrast, the public sector in South Africa bears responsibility for the provision of healthcare services to the balance of approximately 42 million inhabitants who do not have private insurance. In this sector, a national essential medicines list (EML), with accompanying extensive standard treatment guidelines (STGs), is in place and procurement is by local competitive bidding (tender), renewed every two years.¹⁵ Accordingly, in the public sector, there is usually only one contracted supplier of each medicine, unless the tender has been split between different suppliers. The prices obtained by this tender process are generally lower than the single exit prices charged to the private sector. However, in the event of a shortage, the options for obtaining alternative supplies may be limited. The ability to procure alternative supplies is also limited by the volumes required to meet the needs of the public sector. Healthcare services in this sector are provided by employed medical, nursing, and pharmacy staff located within clinics, community health centres and hospitals owned and operated by the provincial and local authorities. There are limited examples of public-private partnerships in the provision of personal health care.

Between July 2012 and June 2013, the KwaZulu-Natal Provincial Pharmacy and Therapeutics Committee faced a



number of medicines shortages. The reasons for each shortage varied considerably, but each provides insight into the problem in a middle-income country with some local pharmaceutical manufacturing capacity. This is not a comprehensive listing of every shortage or delay in supply that was experienced in this time period.

A recurring problem during this period was the supply of amoxicillin-clavulanic acid tablets. In this case, the tenderer was a generic firm. Another generic firm supplied a higher strength of the same product. In this particular case, a generic manufacturer is also the producer, under licence, of the branded version. The options for alternative supplies were therefore even more limited.

In July 2012, the generic manufacturer of a clomiphene tablet informed the provincial authorities that there was a global shortage of the product and that no further supplies would be expected until further notice. However, in this case, an alternative supplier was identified.

Although not on the EML, when the manufacturer of a methoxalen capsule withdrew this product from the market in July 2012, no alternatives were available. In this case, the manufacturer cited a “strategic alignment process and low volume demand” as the reason for the withdrawal. Also in July 2012, prescribers were informed of a decision to withdraw a triamcinolone ointment for oral administration. Here, again, the reason provided was rationalisation of the product portfolio. At the same time, the company also withdrew its cholestyramine sachets. No alternative source of this bile acid sequestrant was available.

In September 2012, a global shortage of glycopyrrolate injection was felt locally. No alternative suppliers were available at all, which necessitated using alternative anticholinergic agents.

A shortage of haloperidol injections was also noted in September 2012. In this case, the sole manufacturer indicated that “we are still unable to confirm when stock will be available”, but predicted that supplies would only resume in 18 months.

From October 2010, the sole manufacturer of human rabies immunoglobulin was unable to meet the increased demand for this product. The manufacturer reminded provincial authorities of the restricted source of the raw material (plasma from vaccinated donors) and the more than eight-month manufacturing time for a single batch.

In May 2013, shortages were experienced of sub-lingual tablets of isosorbide dinitrate. The withdrawal of flourescein sodium ophthalmic strips was easier to handle, as ophthalmic solutions were available in “minims” drop packs.

In June 2013, the combination antacid tablet containing aluminium hydroxide and magnesium trisilicate became unavailable from the contracted supplier. The only alternative supplier needed four to six months to manufacture a quantity sufficient to meet the state’s needs. Moving to more liberal use of a protein pump inhibitor at primary care level required additional training as well as supply arrangements.

In the same month, increasing difficulty was experienced with obtaining stocks of prazosin tablets from the sole supplier. A shift to doxazosin was the only option.

By mid-2013, the international shortage of the active pharmaceutical ingredient (API) of cloxacillin was affecting the ability of local formulators to meet demand. With all other manufacturers similarly affected, an alternative antibiotic had to be sought.

Supply problems were also experienced with erythromycin suspension.

In June 2013, a global decision to withdraw an effervescent potassium tablet was announced “with immediate effect”.

Discussion

As the examples cited show, medicines shortages in the South African public sector have affected a wide range of products, not only generic injectables. At times, unpredictable and increasing demand has clearly been a contributory factor. Though not listed, the challenges of moving the world’s largest antiretroviral treatment programme from reliance on single agents to fixed-dose combinations have not been trivial. However, other shortages have resulted from global problems with APIs or manufacturing, or have been the result of strategic withdrawals from the market for purely economic reasons. A number of these withdrawals have been made at short notice and in instances where alternatives were not easily identified. The recommendation that each country should establish a publicly accessible means of providing information on shortages is therefore important to consider carefully.



The first of the recommendations from the International Summit on Medicine Shortages dealt with the need for a list of critical/vulnerable products. Cloxacillin is an example of an essential medicine, which may be increasingly difficult to procure, unless global API stocks are secured. Where products are to be withdrawn globally, an FDASIA-style warning would be useful, even if an alternative supplier cannot be identified and authorised within the six-month time period. This is a particular problem with older products for which there is only one supplier. Previous examples that have affected South Africa have been shortages of injectable beta-blockers and injectable phenobarbitone.

When South Africa became a member of the Pharmaceutical Inspection Co-operation Scheme in 2009, the resultant tightening of Good Manufacturing Practice requirements resulted in a number of shortages as local plants were upgraded. Going forward, there is still room for harmonisation of regulatory requirements, as urged by the International Summit.

The Summit recommended that all procurers of medicines move towards what it termed “active procurement processes”, in order to assure the continuity of supply of quality medicines. In a winner-take-all competitive bidding (tender) system, the drive towards lower prices can have a negative impact on investments in quality. The South African public sector is increasingly using split tenders, and is committed to using public procurement to enhance the capacity of local production. However, it also needs to be seen to clearly value quality in its procurement practices.

Unlike the US FDA, the South African medicines regulatory authority (Medicines Control Council) does not provide any information on medicines shortages on its website. The provincial health authorities also do not provide such resources. No publicly accessible sources cover private sector supply problems. The Summit’s recommendation that countries investigate the potential to establish a national body charged with gathering and sharing information about demand for, and supply of, medicines is thus of critical importance. In a closed healthcare system such as the South African public sector, ethically sound allocation of available stock at times of scarcity is far easier than it is in the private sector. However, as South Africa implements its planned national health insurance system, those differences will become less evident.

The Summit’s final recommendation was that all countries should develop evidence-based risk mitigation strategies. As the examples cited above show, some of these (such as strategic buffer stockpiles) would have been of little use.

However, the rabies immunoglobulin example shows how necessary contingency plans would be, but also how difficult it is to ensure capacity redundancy.

Conclusion

Medicines shortages can have local as well as global causes, but every shortage occurs in an increasingly globalised and connected pharmaceutical marketplace. While no country can stand aside from the problem, or consider itself immune, national solutions alone are of limited utility. Some of the problems encountered in KwaZulu-Natal in the past year will also have affected health systems in other parts of the world. A combined effort is needed to address these problems, using every tool in reach. A good starting point is to ensure greater access to and sharing of information about medicines shortages and their causes, so that the negative health impacts of such events can be reduced or even prevented.

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PEER REVIEW

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CONFLICTS OF INTEREST

The author discloses that he is chairman of the Board of Pharmaceutical Practice of the International Pharmaceutical Federation and has also served on the KwaZulu-Natal Provincial Pharmacy and Therapeutics Committee. This brief report is written in his personal capacity and does not reflect the position of any organisation or structure.