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Letter to the Editor

Oncologic drug shortages also in Italy

Dear Editor,

Health care providers are increasingly faced with the issue of drug shortages. Drug shortages are a phenomenon where drugs may be (temporarily) unavailable and result in patients not getting the best treatment possible. This lack of drugs may mean that patients do not get treated appropriately, or that treatment may be delayed until the drug is available.

An American hospital association analysis of survey data collected in June 2011 from 820 non federal, short-term acute care hospitals showed that almost all hospitals reported experiencing one or more drug shortages in the past six months, with 24% reporting 21 or more shortages[1]. The survey also showed that three out of four hospitals reported rationing or restricting drugs that were in short supply. The list of generic drugs in short supply mainly consists of antibiotics, anaesthetic agents, cardiovascular agents, common electrolyte solutions, and vitamins.

In the past several months, the United States media have extensively reported on shortages of cancer drugs, too. These cancer drugs are usually cheap and are the backbone of curative therapies for cancers in children and adults, in particular acute leukaemias, lymphomas, breast cancer, and testicular cancer. They include vincristine, 5-FU, methotrexate, ARA-C, etoposide, paclitaxel, cisplatin, BCNU, the anthracyclines, etc. Interestingly, very little has been reported in medical journals until an article appeared in the New England Journal of Medicine of November 3, 2011, and few data are available for Europe as well[2].

However, recently the lead pharmacist of the Cambridge University Hospitals of Cambridge, United Kingdom[3] reported that intravenous lorazepam, which is the first line treatment of status epilepticus, has not been available since May 2010, causing great difficulty in treating patients with status epilepticus as well as those with agitation. In the same issue of the British Medical Journal, Pfizer reported manufacturing problems, but is expecting to return to market with intravenous lorazepam by the second quarter of 2013[4].

In the United States, many treatment facilities are turning to the grey market. For example cytarabine, which is one of the basic drugs for the therapy of acute leukaemias typically sold at 12 USD per vial, is now being offered on the grey market for nearly 1000 USD. In some cases, hospitals are turning to alternative suppliers and pay anywhere from 10 times to 1000 times more for medications. So far, the American Society of Health System Pharmacies reported at least fifteen deaths that are directly attributable to the drug shortages[5].

Difficulties in finding low-cost drugs have also involved treatment programs using stem cells at the National Cancer Institute of Aviano, Italy, within the Department of Medical Oncology.

The first signs of shortages emerged in May 2011 with the non-delivery of an order of 100 vials of carmustine, an essential high-dose therapy drug required with stem cell transplantation. Carmustine stocks ran out in June 2011, when nine patients with lymphoma were already undergoing a care program that was to be completed in August with autologous bone marrow transplantation. We were forced to modify treatment plans – with significant difficulties in finding alternative routes that would not change the expected results – for nine patients, causing great anxiety and concern for patients and their families. Our choice was to lengthen the waiting period for those patients who had already achieved good results with the preparatory treatments for the transplant, and to replace carmustine with experimental alternative drugs in

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the most urgent and demanding cases in whom the postponement of care could have seriously compromised the final results. This is not the first time we were faced with great distress and concern, especially for patients and their families, because of a shortage of essential medicines that cannot be substituted unless experimentally. The lack of carmustine continued for three months in 2009 and bleomycin, a drug needed for treatment of lymphomas and testicular tumours, was not available for two weeks at the beginning of 2011.

These shortages have also forced delays in United States clinical trials for cancer which use these drugs as a baseline to test the efficacy of new therapies. It is important to note that these new therapies are almost exclusively biological drugs that are so expensive that cost-effectiveness analysis is not supported in some cases. For example, the National Institute for Clinical Excellence (NICE) in the United Kingdom is not approving the same drugs that have been approved by the European Medicines Agency (EMA) and the Food and Drugs Administration (FDA) in the United States.

Finally, hundreds of thousands of patients in the United States, and probably the same number in Europe, may not get the full care they need in the near future. The FDA acknowledges some manufacturers may have less financial incentives to make older and cheaper generic drugs. In 2010, 11% of shortages were due to the fact that companies stopped making certain drugs, usually for business reasons. Various proposals to address the long-term problem in the United States have stalled, not least because of disagreement over the cause.

We believe that we should create a stock pile of emergency injectables as well as vaccines, or offer tax incentives for the manufacturing of low-cost but lifesaving products. If this policy does not produce the desired outcome, it might be necessary to put pressure on those pharmaceutical companies that are not producing these old drugs by not be allowing them to get approval for their new, more expensive therapies.

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