"Rare essentials": drugs for rare diseases as essential medicines

Pieter Stolk,[a] Marjolein JC Willemen,[a] & Hubert GM Leufkens[a]

Abstract Since 1977, the WHO Model List of Essential Medicines (EML), published by WHO, has provided advice for Member States that struggle to decide which pharmaceutical technologies should be provided to patients within their public health systems. Originating from outside WHO, an incentive system has been put in place by various governments for the development of medicines for rare diseases ("orphan drugs"). With progress in pharmaceutical research (e.g. drugs targeted for narrower indications), these medicines will feature more often on future public health agendas. However, when current definitions for selecting essential medicines are applied strictly, orphan drugs cannot be part of the WHO Essential Medicines Programme, creating the risk that WHO may lose touch with this field. In our opinion WHO should explicitly include orphan drugs in its policy sphere by composing a complementary Orphan Medicines Model List as an addition to the EML. This complementary list of "rare essentials" could aid policy-makers and patients in, for example, emerging countries to improve access to these drugs and stimulate relevant policies. Furthermore, inconsistencies in the current EML with regard to medicines for rare diseases can be resolved. In this paper we propose selection criteria for an Orphan Medicines Model List that could form a departure point for future work towards an extensive WHO Orphan Medicines Programme.

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Voir page 750 le résumé en français. En la página 750 figura un resumen en español. يمكن الاطلاع على الملخص بالعربية في صفحة 750.

Introduction

This manuscript was based on an invited discussion paper for the 14th meeting of the WHO Expert Committee on the Selection and Use of Essential Medicines (7–11 March 2005, Geneva, Switzerland).

In all health-care systems, there is a struggle to decide which technologies should be provided to patients within the system. Criteria such as efficacy, need, prevalence and cost–effectiveness are used in this selection process. These struggles are particularly acute when considering pharmaceuticals. Since 1977, WHO has provided advice for countries by defining a WHO Model List of Essential Medicines (EML).[1] The concept of the EML as normative guidance and technical support has helped over 150 countries to establish the principle that essential medicines save lives and improve health, but only when they are available, affordable, of good quality, and properly used.[2] The fourteenth edition of the EML was published recently.[3] Originating from outside WHO, an "orphan drugs" movement has developed primarily in affluent countries since the early 1980s to create incentives for the development of medicines for rare diseases.[4] Because of their small market potential, such drugs are not attractive for pharmaceutical companies to develop and market.

While both are systems of prioritizing resources and allocating incentives for pharmacotherapy, the orphan drug movement and the WHO Essential Medicines Policy have many differences in background, goals and conceptual frame. However, it is becoming increasingly clear that they share common ground, i.e. there are essential medicines for rare diseases. Although orphan drugs have not been on the priority agenda of WHO because there are urgent population health needs with a high disease burden to be met, this may change as more orphan drugs come onto the market. For example, orphan drugs currently constitute about 15% of new centralized authorizations in the European Union (EU), there is increasing attention for "rare diseases" in emerging countries (e.g. Egypt, India) and more spin-offs of orphan drug innovations with implications for drug treatment in general (e.g. imatinib mesylate, used for the treatment of chronic myeloid leukaemia).[5] In this paper, we review recent advances in the fields of orphan drugs and essential medicines, and propose how WHO may develop an approach to provide useful advice to Member States that want to improve access to treatments using orphan drugs. For this purpose, we would like to recommend the creation of a complementary WHO Model List for Orphan Medicines as an addition to the current EML. Furthermore, we aim to provide a framework for analysing future questions surrounding the selection of "essential orphan medicines", or "rare essentials".

[a] Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, PO Box 80082, 3508 TB Utrecht, Netherlands. Correspondence to Professor Leufkens (email: H.G.M.Leufkens@pharm.uu.nl).

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Medicines for rare diseases: small numbers with impact

"Which diseases are classified as rare?" is not an easy question to answer, as we have to deal with a complex mosaic of hard-to-categorize conditions. Many rare diseases have a genetic basis. Often this is a monogenic modification, as in the case of X chromosome-linked haemophilia or the defect in transmembrane chloride ion transportation that causes cystic fibrosis.

Currently, several criteria to identify and classify rare diseases are found in orphan drug legislation, which provides incentives for the development and marketing of medicinal products for diseases that may otherwise suffer from nonviability of the market. These market failures are mainly caused by scientific deficiencies (e.g. small numbers of subjects for clinical trials, lack of knowledge about the cause of the disease, absence of valid biomarkers), greater regulatory demands on new drugs in terms of safety and effectiveness, possible obstacles in patenting, and a lack of public awareness of the issue.[6] In response to this, the first orphan drug legislation was introduced in the United States of America (USA) in 1983. Other countries (e.g. Australia, Japan, Singapore) followed in the 1990s, and in 2000 the EU established its own orphan drug legislation. Table 1 provides an overview of the main features of orphan drug systems in the EU and USA. Methods used in regulations to stimulate research and development of orphan drugs include extended regulatory guidance and advice, waivers of regulatory fees and market exclusivity. It is important to note that there are differences between the USA and EU definitions of a rare disease. In the USA Orphan Drug Act, the definition relates to an absolute number (<200 000 patients in the USA), while the European regulation uses a relative measure (<5 cases per 10 000 inhabitants) and requires disorders to be life-threatening and/or chronically debilitating. When these definitions are used, it is estimated that between 5000 and 7000 conditions qualify as rare diseases, bringing the total number of patients suffering from these diseases in Europe and the USA alone to 55 million.[4,7] For many other countries data are scarce, but the prevalence of rare diseases is likely to be comparable.

To prioritize limited public health resources it is important to possess reliable data on disease burden, course of disease and long-term prognosis. This has been a difficult task for rare diseases. A primary reason why sound epidemiological data is often lacking is the absence of proper classification and coding for the disease and the absence of registration of the patients suffering from rare conditions. Although International Classification of Disease (ICD) codes are available for some of the better-known rare diseases, such as thalassaemia, cystic fibrosis and haemophilia, many orphan drugs are not included in medical registries and databases. Often these rare disorders are grouped under higher classification levels such as "endocrine metabolic disorders". A second reason for the lack of reliable epidemiological data is the frequent absence of appropriate biochemical and genetic diagnostic data. Generally speaking, indicators to quantify disease burden, such as the disability-adjusted life year (DALY), are not very useful in the case of rare diseases, as the low prevalence brings DALY estimates for these diseases to the bottom of any list created on the basis of burden of disease.

The impact of the Orphan Drug Act on drug development and public health in the USA was evaluated in 2003, the 20th anniversary of its establishment.[4] Since the introduction of this legislation, about 1100 drugs have received an orphan drug designation. Of these, 231 were marketed, providing an estimated 11 million patients in the USA with a new treatment for their disease. In the EU, the first 5 years of orphan drug legislation were recently evaluated by the European Medicines Agency (EMEA). Overall, the experience was positive; by April 2005, more than 260 products had acquired an orphan drug designation, and 22 of these received a marketing authorization, creating new treatment options for more than one million patients in the EU.[8]

Access to and affordability of medicines for rare diseases

Despite this progress, no effective and safe treatment is available for many rare diseases. Furthermore, when treatments are available, obstacles are encountered that hinder access and use of these drugs.

- **Challenges in assessing clinical relevance and cost–effectiveness.** The methodology for evaluating orphan drug treatments is often still in an experimental phase, hampering positioning in clinical practice.
- **Lack of knowledge and training.** For many rare diseases, available information is inadequate. Health professionals are often deficient in appropriate training and awareness to be able to diagnose and adequately treat these diseases. The aim of initiatives like Orphanet[7] is to address this issue.
- **Deficient diagnostic systems.** For many diseases no diagnostic methods exist, or diagnostic facilities are unavailable. In these cases, diagnosis may be problematic. Consequently, validity, coding and reproducibility are problems.
- **High prices.** Prices of orphan drugs per treatment episode can be very high. For example, the cost of treatment with enzyme replacement therapies may reach more than US$ 150 000 per treatment-year. The affordability of orphan drugs has become a major issue for payers and is a strong driver of tensions between the different stakeholders.[9] Some companies have responded to this by developing programmes to facilitate access to orphan drugs.[10]

These obstacles to treating rare diseases with orphan drugs exemplify and mirror the global debate of deficiencies in bringing new drugs to patients who need them. The recent WHO report *Priority medicines for Europe and the World* gives a thoughtful account of this and has provided a priority listing of gaps in pharmacotherapy.[11] One of these gaps is the crisis in the development of new antibiotics. This crisis was linked to the orphan drug issue in a more general context in *Science* magazine: "Will all drugs become orphans in the future, not because of the rareness of the disease, but because other factors hinder investment in drug discovery and development?"[12]

Furthermore, advances in pharmacogenomics may lead to treatments benefiting a small subgroup of patients.[13] Whatever the outcome, it seems inevitable that with an increasing number of drugs specifically indicated, and effective, for rare diseases, these medicines will feature more often on future public health agendas.

Essential medicines: big numbers with impact

In 1977, the first Essential Drug List was published, containing medicines that were indispensable for the health needs of the majority of the population.[1] By 2002,

Table 1. **Features of orphan drug incentive systems[11] in the USA[a] and EU[b]**

Feature	USA	EU
Programme established	1983 — the Orphan Drug Act modified the Federal Food, Drug and Cosmetic Act	2000 — Orphan Medicinal Products Regulation
Prevalence criterion for rare disease	<200 000 patients in the USA (<7.5:10 000)	Life-threatening or chronically debilitating disorder that affects <5:10 000 in the EU
Requirements for orphan drug designation	Rare disease, or research and development costs cannot be recovered in 7 years	Rare disease, or product unlikely to be developed without incentives or new product will be of significant benefit
Products eligible for orphan drug designation	Drugs and biologicals (including vaccines and in-vivo diagnostics)	Drugs and biologicals (including vaccines and in-vivo diagnostics)
Market exclusivity	7 years; prevents same product being approved for the same indication unless clinical superiority is shown	10 years; can be reduced to 6 years if orphan drug criteria no longer met
Other benefits	Regulatory fee waivers, 50% tax credit on clinical research after designation; grants for clinical research (pharmaceutical companies and academia eligible); protocol assistance; faster review if indication warrants; research grants for medical devices and medical food	Regulatory fees can be reduced or waived; access to centralized procedure; protocol assistance. Individual Member States have to implement measures to stimulate the development of orphan medicinal products.

[a] USA = United States of America.
[b] EU = European Union.

the definitions of the EML had changed. From then on essential medicines were selected with "priority conditions" in mind: they had to be evidence-based, safe and cost-effective. Priority conditions were selected considering current and future public health relevance.[14] The EML consists of two sections, which are published together: a "core" list representing the minimum medicine needs for a basic health-care system, and a "complementary" list for medicines that address priority health-care needs, but require specialized facilities/services, or are costly. Within the context of the EML, medicines for "neglected diseases" may be included in the list on the basis of the criteria described above since they meet the priority needs of a specific population (e.g. local high-prevalence conditions such as trypanosomiasis), in contrast to "rare diseases" (diseases with a low prevalence everywhere).

Three major functions for the EML (and other WHO medicines policies) have been identified: operational, educational and symbolic purposes.[15] As an operational tool, the EML is an important guide for policy-makers and programme managers to identify medicines that require priority attention in terms of production, and access. Furthermore, the list is an educational tool for health professionals and policy-makers, not only through improvement of formulary building and utilization, but also through the procedures used to select WHO committee members and candidate medicines for the EML. Finally, the list has a significant symbolic value. Classification as an essential medicine confers worldwide recognition, preferred position in pharmaceutical management and may stimulate related policies (e.g. production, infrastructure investments or the establishment of quality systems).[16–18]

While selection occurs at a global level, the EML concept should be implemented nationally. Countries are invited and encouraged to formulate national policies with the EML as a model to be adapted. This results in separate national lists, which vary from the WHO list due to local circumstances such as demographics, epidemiology, public health relevance, financial resources or capacity of the health system. Whether a medicine is included in a national list can be considered as an indicator for the level of adoption and dissemination of the EML. A comprehensive overview of the differences between the EML and national lists can be found in an analysis published in the *Lancet*.[1] Although there is an ongoing debate about the impact of these lists on national drug use, the balance sheet for the EML, particularly in less affluent countries, looks very positive.[19]

Orphan drugs and essential medicines

Although the fields of essential medicines and orphan drugs share principles of social justice and equity, Table 2 lists some important ways in which the two groups of medicines differ.

Two recent examples illustrate the tensions in the discussion about orphan drugs within the WHO Expert Committee on the Selection and Use of Essential Medicines: the cases of fludrocortisone and factor VIII/IX concentrates. Fludrocortisone, indicated for adrenal insufficiency, was deleted from the EML in 2003, because its rare indication did not meet the criterion of "satisfying the priority health-care needs of the population", it was on few national lists, and was not stocked by some major international suppliers.[20] In contrast, just 2 years later the 2005 Expert Committee decided to retain factor VIII and IX concentrates as essential medicines, even though haemophilia is a rare disease, like adrenal insufficiency.[21] Important arguments for keeping factor VIII/IX on the EML were the lack of safety and cost of the alternatives, and logistical arguments, such as the organization required by blood transfusion services for the production of plasma fractions.

At the same meeting in 2005, the Committee suggested that there was a need for WHO to establish a policy advisory group on rare diseases to study this issue in light of its increasing importance.[21]

Rare essentials

We started this paper with the notion that there is common ground between the EML and orphan drugs. However,

Table 2. **A comparison of essential medicines and orphan drugs**

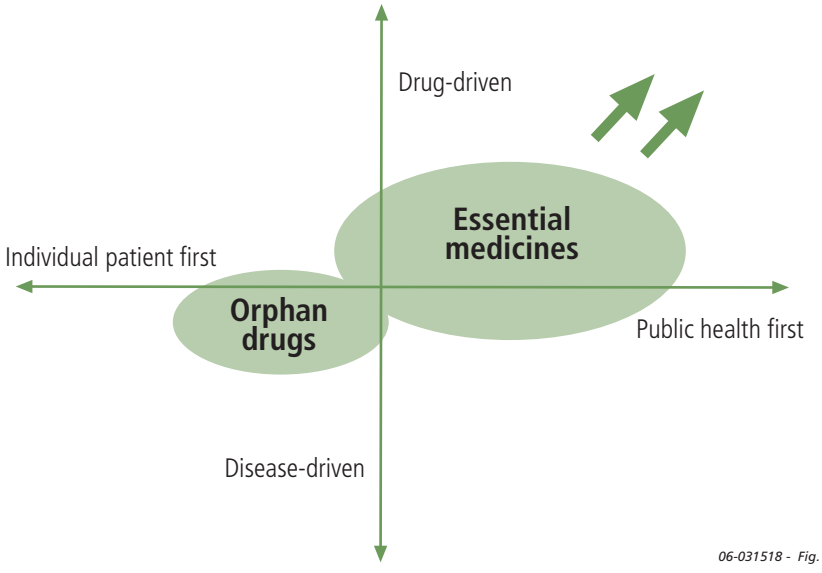
Aspect	Essential medicines	Orphan drugs
Concrete policies in place since:	1977 worldwide	1983 in USA,[a] 2000 in EU[b]
Primary focus:	Public health: bringing effective medicines to as many patients as possible	Individual patient: even a single patient warrants all possible treatment
Initiated and developed by:	WHO, and Member States	Governments of Australia, EU, Japan, and USA; patient groups
Criteria:	Drug driven (i.e. drug to be listed on EML[c] is efficacious, safe, cost-effective, based on evidence based data, etc.)	Disease driven (i.e. disease to be classified as an orphan drug has low prevalence <5–7.5 : 10 000, is life-threatening, etc.)
Policies aim to:	Provide established medicines to patients	Provide new medicines to as yet untreatable patients
Target populations:	Initially low-income countries, now all countries	High-income countries, developed countries
Economics:	Cost–effectiveness, sustainable and affordable access	Relatively high prices per individual patient, cost-maximization per population

[a] USA = United States of America.
[b] EU = European Union.
[c] EML = Model List of Essential Medicines.

developments in policies affecting the EML may result in these fields becoming more and more distinct in the future. The primary focus in the orphan drug arena is the individual patient, irrespective of the demands of society at large. This contrasts with the more "utilitarian" public health approach of the current EML definitions. Moreover, the two systems also differ in their drug/disease orientation. Fig. 1 captures these two dimensions. The domain of the EML is dominated by public health concerns (i.e. priority diseases) and proven effectiveness of medicines through the methods of "evidence-based medicine". The 2002 revisions of the EML entry criteria show an increased move towards the upper-right quadrant. Therefore, if current EML definitions are applied strictly, both fields may "lose touch". We believe that this is an unwanted situation given future developments in the pharmaceutical field. Below we propose criteria to compose a complementary Orphan Medicines Model List to assist policy-makers.

Fig. 1. **Priorities in bringing important drugs to patients: two dimensions**

In this figure, "Drug-driven" refers to more emphasis on the drug compound for decision-making (e.g. cost–effectiveness, evidence base). "Disease-driven" refers to more emphasis on the characteristics of the disease in the decision-making process. The arrows indicate a future trend based on recent developments.



Priority-setting on medicines for rare diseases requires a thoughtful weighing of issues associated with disease prevalence, drug effectiveness, safety and costs. Although the driver of such a weighing process should be scientific evidence, it is important to note that for orphan drugs it is not always possible to meet state-of-the-art standards of evidence-based medicine, particularly when an orphan drug is newly developed and limited data are available on effectiveness, safety, tolerance, etc.[22] Therefore, we propose the following, primarily "drug-driven", criteria for inclusion on a complementary WHO Orphan Medicines Model List, i.e. designation as a "rare essential".

1. **Prevalence:** the rare disease has a prevalence <5–7.5 cases per 10 000 persons (EU/USA criteria) and is life-threatening or chronically debilitating.
2. **No alternatives on EML:** no other medicine on the EML is an effective alternative treatment (the medicine may be on the EML for a different indication).
3. **Effectiveness:** the treatment is effective.
4. **Safety:** the treatment has a positive safety profile.
5. **Availability:** sustained supply of the product is feasible.
6. **Diagnosis:** the diagnosis of the disease is technically feasible (in most countries).

Table 3. **The evaluation of factor VIII concentrates according to the proposed criteria for an Essential Orphan Medicines List**

Criteria	Assessment of factor VIII concentrate
1. Prevalence	In the USA[a] about 18 000 people have haemophilia,[23] bringing the prevalence to <1 per 10 000 inhabitants. Prevalence in low-income countries is comparable.
2. No alternatives on EML[b]	No alternative treatments are available on the EML.
3. Effectiveness	The treatment is regarded as highly effective for haemophilia A.
4. Safety	With a safe supply of blood products, factor VIII is a safe product considering its indication.[24]
5. Availability	Programs like 'Operation Access' have improved the supply of this product in many countries.[25]
6. Diagnosis	Although laboratory infrastructure is often lacking,[26,27] good progress in diagnosis has been made; although this is still a problem in many countries. Several programmes have increased knowledge about the diagnosis and treatment of haemophilia A.[28]
7. Expertise infrastructure	Inclusion of blood products on the EML has been an important factor to facilitate and stimulate local infrastructure and training.

[a] USA = United States of America. [b] EML = Model List of Essential Medicines.

7. **Expertise infrastructure:** the specialist knowledge, training and infrastructure to diagnose and to treat the disease is available (in most countries).

When a medicine does not fulfil the first criterion it should be evaluated according to the existing (2002) criteria for inclusion on the EML. The exact cut-off value for rare diseases used on the Orphan Medicines Model List can be the subject of future debate. When the disease prevalence is appropriate, criteria 2–7 should be evaluated. Especially for criteria 5–7, evaluation on a case-by-case basis is required. However, rules on how to weigh the evidence can be decided beforehand. If any of the criteria 2–7 cannot be met, the medicine would not be suitable to be included in a complementary Orphan Medicines Model List.

Using the criteria introduced above, we evaluated factor VIII concentrate as an example (Table 3). From this assessment it can be concluded that, although problems in diagnosing haemophilia and ensuring access to factor VIII concentrate remain, factor VIII fulfils all criteria and could be included on a complementary WHO Orphan Medicines Model List. The selection process proposed here is stringent. However, only a rigorously selected list can aid policy-makers in the target Member States.

Options

We propose three possible routes which WHO could take to address the issue of medicines for rare diseases:

- do not include medicines for rare diseases in WHO's policy sphere;
- create an Orphan Medicines Model List as a complement to the current EML;
- create a dedicated Essential Orphan Medicines Programme alongside the current Essential Medicines Department.

Doing nothing is not a viable option. With interest in rare diseases increasing, WHO should not exclude itself from this debate. Furthermore, the impact of granting a special status to the treatment for a specific rare disease can be illustrated by the case of haemophilia. Being listed on the EML has contributed to increased national investments in local safe blood transfusion infrastructure, education and training. If the WHO medicines policy does not give such symbolic attention to orphan drugs, these valuable opportunities may be missed, which would be a loss for all parties involved. These consequences and the need for action were also recognized by the WHO Expert Committee on the Selection and Use of Essential Medicines at its most recent meeting in March 2005.[21]

We want to argue for the second option presented above: creating an Orphan Medicines Model List as a complement to the current EML, using the experience and expertise available in the Essential Medicines Programme and Expert Committee. Furthermore, inconsistencies in the composition of the EML, as is the case with the current inclusion of factor VIII and IX concentrates, can be avoided. The selection criteria we have suggested above could aid in the process of selecting candidate drugs for an Orphan Medicines Model List. When this list appears to be successful, an extension to a more expensive independent WHO Orphan Medicines Programme can be considered.

Conclusion

We believe that WHO should explicitly include orphan drugs in its policy sphere as more orphan drugs will become available in the next decades and more Member States will face tough questions about how to address the need and demand for treatment by patients with a rare disease. High costs, the imbalance between industry and public health interests, problems with access and a lack of an evidence base are features that may hamper such an activity. However, considering orphan drugs solely as an issue for high-income countries does not help policy-makers and patients in low-income countries to tackle the need for treatment. The establishment of an easily retrievable, international expert opinion on effective therapies for rare diseases would aid in formulating specific national policies aimed at improving access to orphan drugs. The EML has been an important symbolic, operational and educational tool for the past three decades. The same could be true of a complementary Orphan Medicines Model List that identifies "rare essentials". ■

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Résumé

«Rares et essentiels» : considérons les médicaments destinés au traitement des maladies rares comme des médicaments essentiels

Depuis 1977, la Liste modèle des médicaments essentiels (LME) publiée par l'OMS fournit des indications aux États Membres qui peinent à décider des technologies pharmaceutiques à appliquer dans le cadre de leur système de santé publique. Lancé au départ indépendamment de l'OMS, un système d'incitation a été mis en place par divers gouvernements pour favoriser la mise au point de médicaments contre les maladies rares («médicaments orphelins»). Avec les progrès réalisés par la recherche en pharmacie (médicaments visant des indications plus étroites par exemple), ces médicaments seront plus souvent considérés comme des priorités de santé publique. Cependant, si l'on applique strictement les définitions actuelles des médicaments essentiels, les médicaments contre les maladies orphelines ne peuvent être intégrés au Programme d'action pour les médicaments essentiels auquel participe l'OMS, d'où le risque que celle-ci perde contact avec le domaine concerné. Il faudrait, à notre avis, que l'OMS inclue explicitement les «médicaments orphelins» dans sa sphère d'action en constituant une Liste modèle complémentaire des médicaments orphelins s'ajoutant à la LME. Cette liste complémentaire de médicaments «rares et essentiels» pourrait aider les décideurs et les patients, notamment des pays émergents, à améliorer l'accès à ces médicaments et à stimuler des politiques analogues. Il est en outre possible d'éliminer les incohérences de la LME actuelle à propos des médicaments destinés à traiter des maladies rares. Le présent article propose des critères de sélection pour l'établissement d'une Liste modèle des médicaments orphelins, qui pourrait servir de point de départ à la mise en place d'un programme complet de l'OMS en faveur de ces médicaments.

Resumen

«Medicamentos esenciales raros»: los fármacos contra enfermedades raras como medicamentos esenciales

Desde 1977 la Lista Modelo de Medicamentos Esenciales (LME) de la OMS, publicada por esta organización, ha servido de orientación a los Estados Miembros a la hora de determinar el tipo de tecnologías farmacéuticas que se debe proporcionar a los pacientes en el marco de los sistemas de salud pública. Una iniciativa que tiene su origen fuera de la OMS es un sistema de incentivos puesto en marcha por diversos gobiernos para desarrollar medicamentos contra enfermedades raras («medicamentos huérfanos»). Conforme avancen las investigaciones farmacéuticas (por ejemplo mediante el desarrollo de medicamentos focalizados en indicaciones más limitadas), estos fármacos aparecerán con más frecuencia en las futuras agendas de salud pública. Sin embargo, si se aplican estrictamente las actuales definiciones para seleccionar los medicamentos esenciales, los medicamentos huérfanos no pueden formar parte del Programa de Medicamentos Esenciales de la OMS, lo que conlleva el riesgo de que ésta quede marginada en este asunto. A nuestro juicio, la OMS debería incluir explícitamente los medicamentos huérfanos en su esfera normativa, confeccionando una Lista Modelo de Medicamentos Huérfanos como complemento de la LME. Esta lista complementaria de «medicamentos esenciales raros» podría ayudar a las autoridades y los pacientes, por ejemplo de los países emergentes, a mejorar el acceso a esos medicamentos y potenciar las políticas relacionadas. Además, es posible corregir las incoherencias que presenta la actual LME en lo referente a las enfermedades raras. En este artículo proponemos varios criterios de selección para elaborar una Lista Modelo de Medicamentos Huérfanos que podría constituir el punto de partida para futuras ampliaciones con miras a establecer un vasto Programa OMS de Medicamentos Huérfanos.

ملخص

الأدوية الأساسية النادرة:
أدوية الأمراض النادرة كأدوية أساسية

منذ عام 1977، تقدِّم القائمة النموذجية التي أَعَدَّتها وطبعتها منظمة الصحة العالمية للأدوية الأساسية المشورة والنُّصح للبلدان الأعضاء التي تكافح من أجل اتخاذ قرار حول أي المستحضرات الصيدلانية وأي تكنولوجيا ينبغي تقديمها للمرض من خلال النظام الصحي العام. وقد بدأ العديد من الحكومات العمل بنظام للحوافز أُعِدَّ خارج منظمة الصحة العالمية لابتكار أدوية للأمراض النادرة أطلق عليها اسم الأدوية اليتيمة. ومع التقدُّم المُحْرَز في البحوث الصيدلانية والتي أصبحت الأدوية نتيجة له تستهدف دواعي استخدام أكثر تحديداً، فإن هذه الأدوية اليتيمة ستظهر أكثر فأكثر على خطط عمل الصحة العامة. وعندما تطبَّق التعريفات الحالية لبعض الأدوية الأساسية بدقة أكثر، فلن يكون بالمقدور وضع الأدوية اليتيمة كجزء من برنامج منظمة الصحة العالمية للأدوية الأساسية، وذلك يؤدِّي لخطر احتمال أن تفقد منظمة الصحة العالمية التماسّ مع الواقع الميداني. وفي وجهة نظرنا فإن على منظمة الصحة العالمية أن تضع وبوضوح الأدوية اليتيمة ضمن سياساتها وذلك بتأليف قائمة نموذجية متـتمة للأدوية اليتيمة إلى جانب قائمة الأدوية الأساسية؛ فمن شأن القائمة المتـتمة للأدوية النادرة أن تساعد أصحاب القرار السياسي والمرضي في البلدان التي تعاني من أمراض مستجدَّة أو طارئة على سبيل المثال، في إتاحة هذه الأدوية وفي وضع سياسات خاصة بها؛ إلى جانب أنه يصبح بالإمكان التخلُّص من حالة عدم التنسيق الذي تعاني منه قائمة الأدوية الأساسية في الوقت الحاضر عند تعاملها مع الأمراض النادرة. ونقدِّم في هذه الورقة بعض المعايـير المنتقاة لقائمة نموذجية للأدوية اليتيمة يمكن الانطلاق بها للتوسُّع نحو برنامج شامل للأدوية اليتيمة.

References

1. Laing R, Waning B, Gray A, Ford N, 't Hoen E. Twenty-five years of the WHO essential medicines lists: progress and challenges. *Lancet* 2003;361:1723-9.
2. Quick JD. Ensuring access to essential medicines in the developing countries: a framework for action. *Clin Pharmacol Ther* 2003;73:279-83.
3. WHO Expert Committee on the Use of Essential Drugs. *WHO model list of essential medicines: 14th list, March 2005.* Geneva: World Health Organization; 2005. Available from: http://whqlibdoc.who.int/hq/2005/a87017_eng.pdf
4. Haffner ME, Whitley J, Moses M. Two decades of orphan product development. *Nat Rev Drug Disc* 2002;1:821-5.
5. Bosanquet N, Domenighetti G, Beresniak A, Auray J-P, Crivelli L, Richard L, et al. Equity, access and economic evaluation in rare diseases. The impact of orphan drug legislation on health policy and patient care. *Pharm Dev Regul* 2003;1:151-7.
6. European Platform for Patients' Organisations, Science and Industry. *Orphan therapies: from clinical development to equitable access. Proceedings of the 4th EPPOSI Workshop on Partnering for Rare Disease Therapy Development, 13–14 November 2003, The Hague.* Available from: http://www.epposi.org/DenHague%20ProceedingsFinal[1].pdf
7. Orphanet [online database]. Available from: http://www.orpha.net/
8. European Medicines Agency. *COMP report to the commission in relation to article 10 of regulation 141/2000 on orphan medicinal products.* London: EMEA; 2005. Available from: http://www.emea.eu.int/pdfs/human/comp/3521805en.pdf
9. McCabe C, Claxton K, Tsuchiya A. Orphan drugs and the NHS: should we value rarity? *BMJ* 2005;331:1016-9.
10. Genzyme. *Gaucher Initiative.* Available from: http://www.genzyme.com/commitment/patients/gaucher_initiative.asp
11. Van Weely S, Leufkens HGM. Background paper: orphan diseases. In: Kaplan W, Laing R, editors. *Priority medicines for Europe and the World — a public health approach to innovation.* Geneva: World Health Organization; 2004. Available from: http://mednet3.who.int/prioritymeds/report/index.htm
12. Service RF. Orphan drugs of the future? *Science* 2004;303:1798.
13. Ginsburg GS, Konstance RP, Allsbroook JS, Schulman KA. Implications of pharmacogenomics for drug development and clinical practice. *Arch Intern Med* 2005;165:2331-6.
14. WHO Expert Committee on the Selection and Use of Essential Medicines. *The selection and use of essential medicines: report of the WHO Expert Committee 2002.* Geneva: World Health Organization; 2003. WHO Technical Report Series 914. Available from: http://www.who.int/medicines/publications/essentialmeds_committeereports/TRS_914.pdf
15. Chirac P. Translating the essential drugs concept into the context of the year 2000. *Trans R Soc Trop Med Hyg* 2003;97:10-2.
16. Loff B. Patents and access to essential drugs. *Trans R Soc Trop Med Hyg* 2003;97:6-9.
17. Ford N. Patents, access to medicines and the role of non-governmental organisations. *J Generic Med* 2004;1:137-45.
18. Health Action International, Campaign for Access to Essential Medicines, Médecins Sans Frontières, Oxfam International, Voluntary Service Overseas, Save the Children. *Drug policy at the 55th World Health Assembly — ensuring accessibility of essential medicines. Resolution EB109.R17.* Available from: http://www.oxfam.org/eng/pdfs/pp020511_WHA_briefing.pdf
19. Levy M, Reidenberg M. What has been the impact of the concept of essential drugs? *Clin Pharm Ther* 2003;73:275-8.
20. WHO Expert Committee on the Selection and Use of Essential Medicines. *The selection and use of essential medicines: report of the WHO Expert Committee 2003.* Geneva: World Health Organization; 2003. WHO Technical Report Series 920. Available from http://whqlibdoc.who.int/trs/WHO_TRS_920.pdf
21. WHO Expert Committee on the Selection and Use of Essential Medicines. *Expert Committee Report 2005, unedited version.* Available from: http://mednet3.who.int/EML/expcom/expcom14/14Expcom_ReportFinal-unedited_040705.pdf
22. Leonard JV. Evidence-based medicine. *Lancet* 2005;366:979.
23. National Heart, Lung and Blood Institute. *Diseases and Conditions Index. What is hemophilia?* Available from: http://www.nhlbi.nih.gov/health/dci/Diseases/hemophilia/hemophilia_what.html
24. Farrugia A. Safety and supply of Haemophilia products: worldwide perspectives. *Haemophilia*, 2004;10:327-33.
25. Srivastava A. Choice of factor concentrates for Haemophilia: a developing world perspective. *Haemophilia* 2001;7:117-22.
26. Srivastava A, Chuansumrit, Chandy M, Duraiswamy G, Karagus C. Management of Haemophilia in the developing world. *Haemophilia* 1998; 4:474-80.
27. World Health Organization. *Control of haemophilia: haemophilia care in developing countries. Report of a Joint WHO/World Federation of Haemophilia Meeting, Geneva, 16–17 June 1997.* Geneva: WHO; 1998. Available from: http://whqlibdoc.who.int/hq/1998/WHO_HGN_WFH_WG_98.3.pdf
28. Giangrande PLF, Mariani G, Black C. The WFH Haemophilia Centre Twinning Programme: 10 years of growth, 1993–2003. *Haemophilia* 2003;9:240-4.