On behalf of the Swiss Federal Office of Public Health

External evaluation of the early revision of the Swiss Therapeutic Products Act (TPA)

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Abstract

Pharmacy preparations also known as unlicensed pharmaceutical preparations are produced by establishments with manufacturing approval for the supply of their own customers, if for example no authorised medicinal product is available for treatment. The objective of the early revision of the Therapeutic Products Act (TPA; HMG) was to improve the balance between security of supply and product safety for magistral medicinal products (MPs). According to the findings of the present evaluation, good progress is being made towards achievement of this objective. The legal framework is largely appropriate for achievement of this objective, and enforcement (for which the cantons are mainly responsible) is underway. However, widespread implementation will still take some time to complete. The recommendations of the evaluation are primarily aimed at optimising enforcement practice by exploiting potential synergies between the Confederation and the cantons, and considering certain amendments at ordinance level. Since magistral medicinal products play a significant role in the supply of medications to patients, better data are needed in order to increase transparency in this area.

Key Words

Therapeutic Products Act, TPA (HMG), Medicinal Products Ordinance, MPO (VAM), Ordinance on Establishment Licences, OEL (AMBV), medications, medicinal products, pharmacy preparations, medicinal products, manufacturing licence, risk assessment, enforcement

Summary

Background and objectives

The TPA aims to ensure quality, safety and security of supply

The Swiss Federal Law on Medicinal Products and Medical Devices, (Heilmittelgesetz SR 812.21 HMG; Therapeutic Products Act TPA), has been in force since 1 January 2002. The aim of the TPA is to ensure that only high-quality, safe and effective medicinal products are brought to the market. To ensure this, finished medicinal products are required to be authorised in Switzerland. Exceptions to this policy of obligatory authorisation are provided for. These include pharmacy preparations also known as unlicensed pharmaceutical preparations, which may be produced by establishments with a manufacturing licence. In practice, magistral medicinal products (magistral MPs) should ensure the supply of a specific clientele if for example no authorised medicinal product (or suitable form of administration of such a product) is available for treatment.

Supply bottlenecks after the TPA took effect in 2002

After the TPA took effect in 2002, it became clear that with the new legislation, the supply of medicinal products was not always sufficient for the requirements of patients. Hospitals were particularly affected by serious shortages of medicinal products that were not available as authorised products.

Early revision of the TPA: expansion of production options while maintaining quality and safety

'Early revision' of the TPA was initiated as a result of these demands. The principal subject of this revision was expansion of production options for magistral MPs. In order to meet these requirements and maintain a balance between product safety and security of supply, as well as complying with the principle of authorisation, a concept was developed for the revision based on the following four aspects:

(1) Quality and safety

(2) Rational sharing of responsibilities in enforcement

(3) Flexibility (greater operational scope by using the skills of experts)

(4) Transparency

Main issues of the evaluation

The evaluation is planned to show what contribution magistral MPs make to the supply of medicinal products, and to what extent existing legislation plays a constructive role with regard to the supply of magistral MPs to the Swiss population. In addition, implementation of amendments to the legislation will be examined at federal and cantonal levels. The views of target groups affected by the revision will also be sought. With regard to future revisions, it needs to be shown how the TPA and the associated regulations can be developed further so that magistral MPs can make an optimal contribution to the supply of medicinal products while maintaining their product safety.

Evaluation design

Various methods for obtaining information

The predominant methods of gathering information for the evaluation were the following:

- Structured interviews with representatives of the Cantonal Pharmacists Association (KAV), the Swiss Druggists Association (SDV), the Swiss Association of Public Health Administration and Hospital Pharmacists (GSASA), the Interest Group for Pharmaceutical, Cosmetic and Related Products (IKP) as well as Swissmedic and pharmaSuisse.
- Online survey of 50 hospital pharmacies in Switzerland. This consisted of a questionnaire with 32 questions (response rate: 62 %) as well as an Excel file for the declaration of manufactured or dispensed magistral MPs (response rate: 42 %).
- Focus group with five representatives of the Cantonal Pharmacists Association (KAV) from the Cantons of Bern, Fribourg, Lucerne, Neuchâtel and Zurich.
- Secondary analysis of data collected by the Cantons of Fribourg, Geneva and Zurich. Data were available for all groups of magistral MPs from the Canton of Zurich, while the Cantons of Fribourg and Geneva only had data on Formula propria [not subject to medical prescription].

Findings

Legislation consistent with the need for certain amendments – enforcement in progress

The objective of the early revision of the TPA was to improve the balance between security of supply and product safety for magistral MPs. Based on the findings of the present evaluation, we are making good progress towards this objective. The legislation is largely appropriate for achievement of this goal, and the proposals for legislative amendments are mainly concerned with enforcement practice. Enforcement, for which the Cantons are primarily responsible, is underway. However, it will still take some time to complete widespread implementation.

Magistral MPs play a significant role in the supply of MPs, which will continue to increase

Magistral MPs play an important role in the supply of medications to patients. The first steps of this evaluation have been made towards an overview of the production of magistral MPs in Switzerland. Twenty hospital pharmacies have reported over 2,700 magistral MPs with over 400 active substances, which were manufactured and/or dispensed in 2013. Stakeholders are agreed that the requirement for magistral MPs will continue to increase in future. The main reasons for this are the withdrawal of authorised medications that are no longer profitable, as well as the increasing demand for niche products such as those in the field of complementary medicine.

Demarcation issues regarding authorisation of products and circumvention of authorisation are minor issues

Demarcation issues related to authorisation of medications and problems regarding the circumvention of authorisation are of minor importance. Most magistral MPs are produced by hospital pharmacies and other pharmacies (both dispensing and non-dispensing) for provision to their own clientele. This usually involves relatively small quantities. Since an

authorisation requires substantial time and effort, this issue only arises in individual cases for contract manufacturers without a retail licence.

No evidence of safety issues with magistral MPs

Any person who manufactures and sells medications or applies or dispenses them to humans or animals for commercial gain must notify Swissmedic of serious or previously unknown adverse reactions and events, as well as quality defects. Swissmedic receives approximately 450 notifications per year, but has received no such notifications for magistral MPs in recent years. There is no evidence that major problems with product safety have arisen since the early revision of the TPA. Many factors contribute to this situation, such as the expertise and responsibility of the stakeholders, the legislative basis (such as risk assessment, requirements in accordance with GMP regarding small amounts, listing of authorised active substances) and enforcement.

The cantons are primarily responsible for enforcement

The main responsibility for enforcement of the new legislation lies with the cantons according to Article 5, TPA. They are responsible for granting manufacturing licences and the associated monitoring procedures for dispensing and non-dispensing pharmacies and other retail businesses that manufacture medicinal products. The Confederation (Swissmedic) is only responsible for monitoring manufacturers with a retail licence who manufacture magistral MPs with risk scores of at least 100 points, as well as manufacturers without a retail licence. These circumstances are rare in practice. Swissmedic is also responsible for monitoring the safety of therapeutic products (including magistral MPs) according to Article 59 of the TPA, as well as for further development of the Swiss Pharmacopoeia according to Article 52 of the TPA.

Situation with enforcement differs between the cantons, primarily due to lack of resources

Enforcement in the cantons is expensive and time consuming, due to the wide range of manufacturing operations and the large number of magistral MPs manufactured. The evaluation has shown that enforcement in the cantons is underway, but full implementation will still take some time to complete. A major reason is the lack of resources on the part of the responsible cantonal pharmacists and the inspection intervals, which are often quite long as a result.

Differences in enforcement – progress towards increased coordination

There are differences in enforcement between the cantons, related to issues such as inspection routines, notifications and incorporation of Federal law into cantonal legislation. Efforts to coordinate and harmonise enforcement between the cantons are based primarily on the initiative of the Cantonal Pharmacists Association and will continue in the future.

Cantons need on-going support from the Confederation.

The cantons would like to have continuing support from the Confederation. This primarily involves instruments for harmonising and increasing the efficiency of enforcement, as expressed in the guidelines for Good Manufacturing Practice (GMP). These include further development of the Swiss Pharmacopoeia for the preparation of product monographs on officinal medicinal products, which is required particularly by the hospital

pharmacies. The cantons also believe that it would be useful to have an efficient instrument for clarification of permissible active substances in Switzerland and abroad, or support for raising the awareness of [pharmaceutical] operations with aids such as information materials.

Legislation has proven successful – consider detailed amendments

At legislative and regulatory levels, the amendments in the early revision of the TPA have generally been successful. They provide a good basis for the safe and orderly supply of patients with magistral MPs. Certain amendments and clarifications at ordinance level have been proposed by stakeholders.

Recommendations

Improve data availability to increase transparency

The availability of data regarding the type and quantity of magistral MPs produced and dispensed is still poor. An important first step towards improving this situation has been made as part of the evaluation. However, all stakeholders should be involved in considering how data availability can be significantly improved, for example with an online database in which magistral MPs that are produced can be listed. A sound database increases transparency and makes it easier to update the legal framework appropriately in future. It is also easier to carry out a specific intervention if this is necessitated by issues such as quality problems.

Review current practice of risk assessment

The practice based on the Pharmacopoea Helvetica (Supplement 11.1 from September 1st 2013) that Swissmedic is currently responsible for granting manufacturing licences with a risk score at least 100 points, and assesses small amounts according to GMP but with stricter conditions in accordance with GMP similar to the requirements for authorised medicinal products cannot be justified and needs to be reconsidered.

Compile further product monographs rapidly

Further development of the Swiss Pharmacopoeia should be expedited. In particular, further product monographs should be prepared as rapidly as possible for commonly used magistral MPs. This would increase the number of officinal MPs.

Selectively expand range of permitted substances and make corresponding information easily accessible

Authorised active substances are a central element of the legislation concerning magistral MPs. The range of active substances should be systematically expanded in coordination with the relevant stakeholders, particularly in the area of magistral MPs. Active substances that are contained in authorised medicinal products and taken off the market for reasons of profitability must continue to be available for the manufacture of magistral MPs. It should also be determined whether the preparation and gradual updating of a negative list would be useful (e.g. products for fresh cell therapy from cell extracts). To facilitate enforcement, a database of all active substances that could be queried by all stakeholders is recommended, possibly in the form of a web application.

Exploit potential synergies in enforcement

For enforcement, the potential of synergies at the cantonal level needs to be exploited as far as possible. This would allow rapid progress to be made with enforcement even if resources are scarce. In some cantons, resources

for enforcement should be increased in any case in order to ensure enforcement that is objective and as consistent as possible. Highly consistent enforcement is also desirable from the perspective of many businesses that operate across cantonal borders.

Review proposals for amendment at ordinance level

In addition to the recommendations already mentioned for amendments at the level of laws, acts or ordinances (active substances, risk assessment), the proposed amendments listed above in relation to quantitative restrictions (Article 19c VAM, Medicinal Products Ordinance) and the information on packaging (Art. 19e VAM) should be reviewed in consultation with the stakeholders. Furthermore, current European developments in the area of magistral MPs must be taken into account in the drafting of any amendments of ordinances.

Need for regulation of radiopharmaceuticals

Radiopharmaceuticals need to be regulated, but this issue should be addressed outside the legislative framework for magistral MPs. Legislation dealing with radiation protection is most important here.