

Drug prices

Considerations on the equitable management of expensive new medicines

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1. Introduction

The present Opinion on the equitable management of the (sometimes extremely) expensive new medicines which have been introduced in recent years, and are also expected to be developed in the coming years, was prepared in response to a letter received from the Federal Office of Public Health (FOPH). In this letter, the NCE was requested to comment, from an ethical perspective, on a number of complex questions which tend to be avoided. In view of the fact that health insurance premiums are rising year by year, and that patients justifiably expect these new medicines to be readily accessible, there is currently immense political pressure for action in this area.

Given that resources are limited, what form could and should the most equitable possible management of extremely expensive medicines take? To address this question, as well as consulting the relevant literature, the NCE held a series of hearings with experts and with representatives of various organisations (PD Dr Antonia Müller, consultant haematologist, USZ; Verena Nold, Mag. oec. HSG, Director of *santésuisse*; Dr Jörg Indermitte, Head of Authorisation of Pharmaceuticals, FOPH; Dr Heiner Sandmeier, Deputy Director of Interpharma; Dr Daniel Widrig, market access expert of Vifor Pharma). This question, of course, arises not only in Switzerland, but in all high-income countries worldwide, with discussions focusing in particular on the benefits or cost-effectiveness of new treatments, which are evaluated in HTA studies (cf. Box on p. 19). While the NCE takes the view that it is essential to determine the additional benefits offered by new medicines as precisely as possible, and to take the findings into account in decisions on equitable access to these products, it also emphasises the importance and priority of other ethical principles, first and foremost respect for human dignity, but also the principles of medical need, effectiveness and solidarity within society.

Below, an explanation of the subject matter and the current context (Chapter 2) is followed by a discussion of the legal framework (Chapter 3) and of the ethical justifiability of the sometimes extremely high prices charged for medicines (Chapter 4). Arguments and assessments are then presented on the question of how equitable access to expensive new medicines can be assured for everyone requiring treatment in Switzerland (Chapter 5). These are followed by final considerations (Chapter 6) and a number of recommendations for legislators and policymakers (Chapter 7).

2. Subject matter and current context

The content of the following discussion is based on a number of questions submitted to the NCE by the FOPH, and the attempt to respond to these from an ethical perspective. The questions concern the equitable management of the sometimes extremely expensive medicines which have become available in recent years, and which call into question established approaches to price-setting and financing. In its reflections, the NCE primarily considers *new* and *extremely expensive* medicines: examples, which have also been the subject of controversy in the media, include gene therapy products such as Zolgensma[®], used to treat spinal muscular atrophy; cell therapies such as the medicine¹ Kymriah[®], used to treat acute lymphoblastic leukaemia; monoclonal antibodies such as Ocrevus[®] for the treatment of multiple sclerosis; or medicines such as the HCV polymerase inhibitors Sovaldi[®], Harvoni[®] and Epclusa[®], which have been used for some years in the treatment of hepatitis C virus.²

Medicines such as those mentioned above only became available recently and, on account of the high prices charged, they raise a number of questions with regard to affordability and accessibility, including aspects of ethical relevance (equitability). Even though there would be good reason to consider, in the present document, the entire current pharmaceutical market, as well as the accessibility and appropriateness of *all* high-priced substances – according to the 2019 Helsana Drug Report, the most cost-intensive pharmaceutical product in Switzerland in 2018 was the antirheumatic Humira[®] (available since 2003), the active substance is adalimumab (Schneider et al. 2019, p. 19), which is also the top-selling drug world-

wide (Feldges 2018) – this would lie beyond the scope of these considerations. The same applies to any consideration – which might seem appropriate – of the financing and accessibility of generics. Of course, the fact that certain treatments and medicines are long established and that the (sometimes high) prices charged for them are accepted by society says nothing, in itself, about how the price-setting procedure and the regulation of access via the List of Pharmaceutical Specialties is to be ethically evaluated. However, consideration of this wide variety of costly medicines would result in inadequate attention being given to the specific current political pressure for action which prompted the questions submitted by the FOPH. This decision is also confirmed by the findings of the 2019 Helsana Drug Report. Although drug prices in Switzerland decreased overall in 2018 (compared to the previous year), total drug expenditures rose once again in 2018; according to the report, this was mainly attributable to the development of new treatments, primarily immunosuppressants and anticancer drugs (cf. Ludwig and Schildmann 2015): 22 new active substances entered the Swiss market in 2018, mainly anticancer drugs and immunosuppressants.³

Another factor increasingly shaping current developments in the drug market – in line with personalised medicine (cf. Box on p. 5) – are the frequent struggles to access *entirely new* drugs or drug combinations, for which an adequate evidence base is still lacking, under so-called off label use.

The costs for such treatments are only reimbursed by health insurers on the basis of individual guarantees

1 Strictly speaking, this is not a medicine but a gene therapy procedure, which was, however, patented as a medicine and is therefore treated as such.

2 In the text, trade names are used rather than the nonproprietary names of active substances, which are becoming increasingly complicated and thus less suitable for use in public discussion; for example, Zolgensma[®] contains the active substance onasemnogene abeparvovec; Kymriah[®] tisagenlecleucel; Ocrevus[®] ocrelizumab, Sovaldi[®] sofosbuvir; Harvoni[®] ledipasvir and sofosbuvir; Epclusa[®] sofosbuvir and velpatasvir.

3 A substantial proportion of the rise in immunosuppressant costs was due to a *single* new drug – i.e. the active substance ocrelizumab for the treatment of multiple sclerosis (Schneider et al. 2019, pp. 19 and 114). The Helsana report takes into account all services reimbursed by Helsana under compulsory health insurance between 2015 and 2018; as inpatient services are reimbursed on a flat-fee-per-case basis, the data analysed mainly relates to outpatient services (not only drug supplies but also surgical procedures and diagnostic tests).

of coverage. In the view of the NCE, this reality of *individual* guarantees – becoming increasingly important in everyday clinical practice, but not specifically addressed hereafter – is unsatisfactory: this is because, firstly, physicians' efforts to obtain such guarantees in individual cases take up valuable working time, which could otherwise be used for treating patients, and secondly, because the decision-making criteria applied by insurers' medical advisers are lacking in transparency and often lead to unsatisfactory results; from an external perspective, they appear to be not, or not fully, comprehensible. To date, little reliable knowledge is available concerning the actual accessibility, for patients in Switzerland, of such treatments and medicines under off-label use, which have become important particularly in the field of oncology and are also, for the most part, very expensive. In the medium to long term, this area will doubtless become more important; as a result, many of the procedures long established in Switzerland for the evaluation, recognition and public financing of new medicines will be called into question, necessitating the development

of adapted or wholly new price-setting procedures and methods. What form such adapted or new procedures could take lies beyond the scope of the NCE's considerations in the present Opinion; here, therefore, no comments are offered on this topic. What is clear from an ethical viewpoint is that access to new treatments and medicines should be made as equitable as possible also under off-label use, whatever form evaluation procedures for the recognition of new drugs or drug combinations may take; in other words, arbitrariness must be avoided, and decisions should be based on expertise and, as far as possible, be transparent, consistent and the same for everyone requiring treatment. In addition, those concerned should have the option of appealing against decisions.

In contrast to the current coronavirus-related health-care crisis, involving a risk of an acute shortage of ICU ventilator-equipped beds and staff, which in extreme cases may necessitate triage measures (Emanuel et al. 2020; SAMW 2020a), as in disaster medicine (Germy 2020; Lübke 2006)⁴, the questions concerning the

Personalised or precision medicine

When a person becomes ill, this is manifested in symptoms such as fever or pain; these symptoms are similar in most people. At the same time, however, a person who is ill also shows an individual disease pattern, defined by clinical and molecular profiles (e.g. laboratory results, gene sequence). Personalised or precision medicine is based on the idea that medical interventions, including drug treatments, will be more effective if they are tailored to the individual's disease profile, rather than being applied indiscriminately. In order to determine this individual profile and to respond with specific drugs or drug combinations, not only genetic data but also a variety of other patient data is taken into account. One important goal is to administer drugs in an individualised manner, tailored to individual patients or small groups of patients. This will lead to increasing stratification of patient populations; in other words, rather than large groups of patients (e.g. all those with a brain tumour) receiving the same therapy, each patient's treatment will be tailored as far as possible to the specific findings (SAMW 2019).

4 In disaster medicine, triage involves the division of those who require treatment into three groups, with the limited resources available only being used, in the first instance, for the middle group: the first group consists of those who are unlikely to survive even with comprehensive medical treatment; these people are not treated. The second group consists of those whose lives can only be saved if the available resources are devoted to them; they are accorded priority. The third group consists of those who will survive even without medical assistance; they are also, initially, left untreated.

equitable management of expensive new drugs are considered in the context of high-quality, universally accessible healthcare. Here, what is often at stake are improvements in patients' quality of life, rather than matters of life or death. In addition, the scarcity of resources available in this context is generally relative – being attributable to political decisions – rather than absolute, as in the case of a disaster or in transplantation medicine (Ubel 2000).

In Switzerland at present, access to healthcare resources – at a high level – is essentially assured: affluence, social policy arrangements, compulsory health insurance for basic care, proximity to the pharmaceutical industry (of national economic importance), highly developed medical science and research, and political stability have all contributed to the development of high-quality healthcare in the recent past. Nonetheless, as in any functioning healthcare system, there exists in practice a mixture of over- and underprovision (Bisig and Gutzwiller 2004), so that Swiss healthcare must be said to be characterised both by waste and by the non delivery of useful services.⁵

In the view of the NCE, the ethical debates on distributive justice and equitable access with regard to expensive new medicines raise questions in two areas in particular: firstly, there are *procedural questions* which concern the ethical justification of decisions on access to new medicines and which – given the variety of (sometimes opposing) interests involved – are not easy to answer. Secondly, there are the efforts to define suitable and justifiable *substantive criteria* for the efficacy, appropriateness and cost-effectiveness (EAC) of medical interventions, i.e. the criteria which – though legally established and ethically relatively uncontroversial – frequently give rise to controversy when they have to be interpreted and applied in particular cases (Federal Health Insurance Act/KVG, Art. 32).

5 Since 2017, an association known as “Smarter medicine – Choosing Wisely Switzerland” has been seeking to raise awareness of the issue of over- and underprovision, and the avoidance of ineffective or counterproductive treatments, among physicians, members of other health professions and the public, as well as healthcare actors and policymakers, and to identify possible countermeasures.

3. Legal framework

3.1 Authorisation and reimbursement of medicinal products

Industrially manufactured medicinal products which are to be placed on the market in Switzerland require *authorisation from the Swiss Agency for Therapeutic Products (Swissmedic)*. The regulatory requirements for the authorisation of medicinal products are specified in the Therapeutic Products Act (TPA)⁶. Such products must be shown to be of high quality, safe and effective (Art. 10 para. 1 let. a TPA). A medicinal product is authorised for specific indications, which are listed in the product information approved by Swissmedic with the authorisation decision.

Mandatory authorisation of medicinal products is designed to protect human health. The federal authorities thereby fulfil their duty, in the medicinal products sector, to take the necessary measures to uphold the fundamental rights to life and to physical and mental integrity (Art. 10 FC⁷). To be distinguished from authorisation is the question of *reimbursement of medicinal products* under the compulsory health insurance scheme (OKP). Coverage of the costs of medicinal products by the OKP serves the constitutional goal of ensuring adequate provision of high-quality primary medical care that is accessible to all (Art. 117a para. 1 FC). This represents a social policy responsibility.

In principle, medicinal products are only reimbursed if they have been included in the *List of Pharmaceutical Specialties (SL)*⁸. Decisions on inclusion in the SL are made by the FOPH at the request of the authorisation

holder, although an expert opinion is to be obtained in advance from the Federal Medicines Commission (EAK) (Art. 52 para. 1 let. b KVG⁹ and Art. 37e KVV¹⁰). A medicinal product can only be included in the SL in accordance with the product information approved by Swissmedic (Art. 65 para. 1 and Art. 71a KVV). When a medicinal product is included in the SL, the FOPH also specifies the highest price to be reimbursed under the OKP. Medicinal product prices are thus not market prices, but officially set prices. *Every three years*, all medicinal products included in the SL are reviewed by the FOPH to determine whether they still meet the listing requirements (Art. 65d para. 1 KVV).

3.2 EAC criteria and medicinal product prices

The criteria applicable for the inclusion of a medicinal product in the SL are those which are legally specified for all services covered by compulsory health insurance, namely *efficacy, appropriateness and cost-effectiveness* (EAC criteria) (Art. 32 KVG and Art. 65 para. 3 KVV). According to the Federal Supreme Court's jurisprudence, a medical service is to be deemed *effective* "if it is objectively apt to bring about the desired diagnostic, therapeutic or nursing benefit"¹¹. While *efficacy* refers to the attainability of the treatment goal (medical outcome), *appropriateness* concerns the risk-benefit ratio of a medicinal product. Whether a medical treatment is appropriate is to be evaluated "according to the diagnostic or therapeutic benefit of its application in a particular case, taking the associated risks

6 Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA; SR 812.21).

7 Federal Constitution of the Swiss Confederation of 18 April 1999 (FC; SR 101).

8 The SL is available online at: <http://www.spezialitätenliste.ch>.

9 Federal Act of 18 March 1994 on Health Insurance (KVG; SR 832.10).

10 Ordinance of 27 June 1995 on Health Insurance (KVV; SR 832.102).

11 BGE 133 V 115 E 3.1.

into account”¹². Also of relevance here, apart from the adverse effects associated with a medicinal product, is the risk of misuse (Art. 33 para. 1 KLV¹³). A medicinal product is not to be included in the SL if the risks are disproportionate to the benefits. The criteria of efficacy and appropriateness thus relate to the medical indication, which is to be demonstrated using scientific methods (evidence-based). In contrast, the criterion of *cost-effectiveness* concerns the cost-benefit ratio of a medicinal product. In general, a medicinal product is considered to be cost-effective “if it assures the indicated therapeutic effect with the lowest possible financial costs” (Art. 65b para. 1 KVV).

Whether a medicinal product is cost-effective thus depends on the relationship between the medical benefits and the price. In the KVV, the evaluation of cost-effectiveness is operationalised by means of two comparisons (Art. 65b para. 2 KVV): firstly, the price is compared with the ex factory prices of the same medicinal product in the reference countries¹⁴ specified by the Federal Department of Home Affairs (FDHA); secondly, the efficacy and costs are assessed in relation to those of other medicinal products used to treat the same condition in Switzerland (Art. 65b para. 4^{bis} KVV). When the averages of the prices of the same product in reference countries and of comparators in this country have been determined, these so-called external and internal reference prices are each assigned a 50% weighting by the FOPH (Art. 65b para. 5 KVV).

In evaluating the cost-effectiveness of originator products, the FOPH takes into account not only the two comparisons mentioned above but also the costs of research and development, provided that the product represents a significant therapeutic advance (Art. 65b para. 6 KVV). If this is the case, an innovation premium is granted for a period of no longer than 15 years (Art. 65b para. 7 KVV).

3.3 Limitations

The FOPH can make the inclusion of a medicinal product in the SL subject to so-called limitations (Art. 73 KVV). It will then only be reimbursed under the OKP within the specified limitations. In particular, limitations may relate to the use of the medicinal product (medical indications), maximum amount or dosage, duration of treatment, treatment sequence, specialist qualifications required for prescription, or prior review of the EAC criteria by the health insurer’s medical adviser. Such limitations are means of ensuring the efficacy and appropriateness of treatment, or promoting the cost-effective use of a medicinal product. Limitations are thus directly *related to the EAC criteria*.

In recent years, however, the FOPH has also, in the case of expensive medicinal products, had recourse to limitations as a way of preventing *unacceptable impacts on the overall costs of the OKP*. Limitations ordered on economic grounds for the purpose of containing costs may amount, de facto, to the rationing of a medical service. Here, one could cite as an example limitations which, for reasons of cost, restrict reimbursement of a medicinal product to more severe forms of a disease, even though the product would also be effective and appropriate in milder forms. Such limitations have been ordered, particularly for an initial period, in relation to the highly effective medicinal products for the treatment of hepatitis C virus infection (Blach et al. 2019; Swiss Hepatitis 2019).

Whether limitations resulting in the exclusion of certain patient groups from effective and appropriate treatments are legally tenable is to be assessed with reference to the constitutional principles of the *rule of law* and *proportionality* (Art. 5 para. 1 and 2 FC). With regard to proportionality, the question arises whether limitations relating to disease severity are

12 BGE 127 V 138 E. 5; 130 V 299 E. 6.1.

13 Healthcare Benefits Ordinance of the EDI of 29 September 1995 (KLV; SR 832.112.31).

14 These are Germany, Denmark, the UK, the Netherlands, France, Austria, Belgium, Finland and Sweden (Art. 34a^{bis} para. 1 KLV). In principle, these provisions are important and to be welcomed; in practice, however, due to a lack of transparency, it is becoming increasingly difficult to obtain the relevant data.

actually conducive to the goal of cost containment in the longer term, or whether they are indeed counter-productive, particularly if the costs of non-treatment are taken into account (Rütsche and Wildi 2016, p. 210). With regard to *equality before the law* and *non-discrimination* (Art. 8 FC), it needs to be assessed whether the limitation-related distinctions between patient groups are materially justified and do not lead to discrimination, e.g. on the basis of patients' origin, gender, age, genetic constitution or social position.

3.4 Reimbursement of medicinal products in individual cases

The SL is essentially of a definitive and binding nature; accordingly, by law, coverage by the OKP of the costs of medicinal products not included in the SL is generally excluded.¹⁵ In special situations, however, the exclusion of reimbursement can lead to *undue hardship* for the patients concerned. A case in point is the use of medicinal products to treat conditions which are so rare that the authorisation procedure for the relevant indications is not worthwhile for manufacturers (*orphan diseases*).¹⁶ To make allowance for such cases, the Federal Council, in line with the Federal Supreme Court's jurisprudence, specified – in an amendment dated 2 February 2011 – criteria for the reimbursement of medicinal products outside the SL framework in exceptional cases. The provisions regulating reimbursement in individual cases (Art. 71a–71d KVV) relate to the following categories:

- reimbursement of a medicinal product included in the SL which is used outside the approved product information (*off-label use*);
- reimbursement of a medicinal product included in the SL which is used outside the specified limitations (*off-limitation use*);
- reimbursement of a ready-to-use medicinal product authorised by Swissmedic which is not included in the SL, for a use within or outside the product information (*off-list*);

- reimbursement of a medicinal product not authorised by Swissmedic which may be imported under the TPA and is authorised for the relevant indication in a country with an authorisation system recognised as equivalent by Swissmedic (*unlicensed use*).

For reimbursement in an individual case, at least one of the following conditions must be met (Art. 71a para. 1 KVV): either the use of the medicinal product is an indispensable prerequisite for the performance of another service covered by the OKP, which is unequivocally the prime concern (this is known as a *treatment complex*), or use of the medicinal product is expected to provide a *substantial therapeutic benefit* in a disease which could be fatal or lead to severe, chronic health impairments for the patient and – given a lack of therapeutic alternatives – no other effective and authorised treatment method is available.

Reimbursement of a medicinal product in an individual case is subject to a *guarantee of coverage* issued after consultation of the insurer's medical adviser (Art. 71d para. 1 KVV). The amount reimbursed must bear an appropriate relationship to the therapeutic benefits (Art. 71d para. 2 KVV) and is determined by the health insurer in consultation with the authorisation holder, i.e. the pharmaceutical company (Art. 71a para. 2 and Art. 71b para. 2 KVV). The price reimbursed must be below the maximum price specified in the SL (Art. 71a para. 2 KVV).

3.5 Absolute limits on costs in the Health Insurance Act?

With regard to the management of high-priced medicines, the question arises whether provision is made in the existing health insurance legislation for absolute limits on costs for the reimbursement of services, either in relation to overall costs or to the costs for the treatment of individual patients. This question has been addressed by the Federal Supreme Court on several occasions. Of fundamental importance are the three rulings from 2010, 2016 and 2019.

¹⁵ BGE 131 V 349 E. 2.2; 139 V 375 E. 4.2.

¹⁶ BGE 136 V 395 E. 5.2.

In the 2010 “*Myozyme I*” ruling¹⁷, the Federal Supreme Court had to decide whether the refusal, in a particular case, to cover the costs of an extremely expensive off-label treatment for an orphan disease was lawful. The condition in question was Pompe disease, an inherited metabolic disorder which is characterised by degeneration of muscle function and is associated with the risk of life-threatening deterioration of pulmonary function. The medicine at issue, Myozyme[®], was not included in the SL, and no alternative medicinal product was available to treat the disease. Continued treatment with Myozyme[®] would have led to costs of around CHF 500,000 per year. In its evaluation of mandatory reimbursement, the Federal Supreme Court invoked the constitutional principle of proportionality. On this basis, reimbursement under the OKP is to be rejected if the costs of a medicinal product are grossly disproportionate to the benefits in a particular case.¹⁸ If equality before the law is to be respected in the application of the proportionality principle, it argued, the level of services provided for individual patients must not exceed that which could also be provided, in a generalisable manner, for all other persons in a comparable situation: non generalisable service provision, it concluded, violates the principle of equality before the law.¹⁹ On this basis, the Federal Supreme Court ruled that, even if Myozyme[®] were proven to offer a high level of therapeutic benefits in the present case, mandatory reimbursement would have to be rejected on cost-effectiveness grounds, i.e. in the absence of an appropriate cost-benefit ratio.²⁰

In the 2016 “*Myozyme II*” ruling²¹, coverage of the costs of the same medicine was to be considered

once again. At issue were Myozyme[®] treatment costs of around CHF 370,000 for 11 months. Since the 2010 “*Myozyme I*” ruling, a decisive change had occurred in the legal position: with effect from 1 November 2011, the medicinal product Myozyme[®] had been included in the SL by the FOPH, with highly restrictive limitations and a substantially reduced price.²² The Federal Supreme Court noted that, on being included in the SL, a medicinal product is certified to be not only effective and appropriate but, in particular, also cost-effective.²³ Accordingly, there was no scope for further assessment by the Federal Supreme Court of the cost-effectiveness of the listed medicine Myozyme[®] in a particular case.²⁴ It can be concluded from the above that the general cost-effectiveness assessment of a medicine undertaken by the FOPH in accordance with the law is decisive even if the cost limits referred to by the Federal Supreme Court in the “*Myozyme I*” ruling are exceeded. From this, it follows that the FOPH is not bound by these cost limits.

Underlying the 2019 “*Knee operation*” ruling²⁵ were the following circumstances: in a 71 year-old patient, the treatment of serious complications following a partial knee replacement required hospitalisation for a total period of 421 days, with total costs amounting to CHF 2,410,744.45. The health insurer refused to pay its full share of the costs. The Federal Supreme Court emphasised that the evaluation of the cost-effectiveness of treatments is of a comparative nature. If in a particular case a number of diagnostic or therapeutic alternatives are appropriate, the cost-benefit ratio of each measure should be considered; however, the question of cost-effectiveness essentially does not

17 BGE 136 V 395.

18 BGE 136 V 395 E. 7.4.

19 BGE 136 V 395 E. 7.7.

20 BGE 136 V 395 E. 7.8.

21 BGE 142 V 478.

22 BGE 142 V 478 E. 6.3.

23 BGE 142 V 478 E. 6.2.

24 BGE 142 V 478 E. 6.4.

25 BGE 145 V 116.

arise in cases where only one treatment option, or no alternative treatment, is available.²⁶ The Federal Supreme Court had never set an absolute limit on the costs to be borne by the OKP; nor, therefore, could it be maintained that the Court had declared the QALY method (for explanations of QALYs see the Box on p. 15) to be of decisive importance.²⁷ One of the primary goals of the KVG, it noted, was “to ensure mandatory coverage by the OKP of the costs of inpatient treatment for an unlimited period”²⁸. There was no legal basis for the kind of proportionality-related rationing sought by the appellant, to the effect that necessary medical services should not be covered by the OKP for the purpose of overall cost containment.²⁹ It was thus also pointed out that legislators are responsible for deciding whether upper limits should be placed on costs in the OKP (Gächter 2019, pp. 212 f.). This does not, however, relieve the FOPH of its obligation, when deciding on the inclusion of medicinal products in the SL, to assess by means of comparisons (with the same product in other countries and with alternative treatments in this country) whether the products concerned are cost-effective, i.e. whether they “assure the indicated therapeutic effect with the lowest possible financial costs” (Art. 65b KVV). The evaluation of cost-effectiveness by the FOPH may lead to a comparatively overpriced medicinal product not being included in the SL, or only being included subject to limitations, even though its efficacy and appropriateness have been demonstrated. Given the outstanding importance of the SL in ensuring equal public access to medicinal products, it would, however, from a constitutional viewpoint, be appropriate to improve the democratic legitimation of the essential criteria for inclusion in the list and enshrine them in the legislation itself.

26 BGE 145 V 116 E.3.2.3.

27 BGE 145 V 116 E. 5.4.

28 BGE 145 V 116 E. 6.3.

29 BGE 145 V 116 E. 6.3. On the need for a legal basis for rationing measures cf. Rüttsche 2018, pp. 126 ff.

4. A fair price? Tensions between different justifications

Discussions concerning the allocation of healthcare resources are often based on the assumption that the prices of medicines, devices and interventions simply form part of the initial conditions. In fact, however, the justification of prices is the subject of sometimes tense political debates, and of competing accounts as to how these prices arise. The question of what makes a price fair, or equitable, is both an ethical and a political one, underpinned by questions about justice itself and about what is involved in making a price, as such, fair.

Justification of the prices of goods and services has a long history, considerably predating the existence of the pharmaceutical market. Various justifications of prices can be found in the literature.

The first is based on the value of work. Through our work, we create value and justify a recompense for this added value, which is essentially the value that we have added through our work. The costs of production (which must include the costs of research, development and placing on the market) constitute a first justification of the price of a medicine. The determination of these costs is therefore a matter of intense debate (Light and Warburton 2011).

The second justification is based on the market. Here, the expectation is that a price regulated by supply and demand in a competitive market will lead to optimisation of the quantity of the product available on the market, which will increase the benefits resulting from the product. From an ethical perspective, maximisation of benefits is one of the possible bases for an equitable distribution. However, it can be expected to be in tension with other principles of justice, such as equal distribution, priority to the worse off, or a decent minimum for all (Daniels 1994). In addition, the pharmaceutical market only rarely meets the conditions of

a market sufficiently ideal to ensure even the type of optimisation mentioned. Numerous drugs are in a monopoly position. Patients often do not have a choice as to whether or not to purchase the product, and in any case they do not choose it themselves. There is a significant number of market failures in this area.

This model also presupposes that the price, in this system, will reflect the value of the product, which is reflected by the price the customer is willing to pay. The value of the product, however, is only imperfectly represented by willingness to pay. The value of the product can obviously also be measured in various other ways, and constitutes the third justification of the price. Here, one finds the idea that the added value of a medicine in terms of health, its effect size, is the main justification of its price (ICER 2020).

Insofar as certain medicines may be vital for some patients, one also finds in the literature justifications of prices based on their ability to make the product accessible to the patients who need it.

A fair price is necessary to ensure that the transaction is not exploitative. As Matt Zwolinski and Alan Wertheimer (2017) point out, the problem with exploitation is not that it is harmful. It may be, but it is not necessarily so: a transaction which exploits one of the parties may also make him or her better off. It may even be consensual, and thus a lack of coercion does not indicate a lack of exploitation either. Exploitation is fundamentally a question of distributive justice. One person exploits another if their exchange grants the former an unfair share of the benefits compared to the associated burdens. Exploitation involves taking advantage of the other party's position of weakness to obtain an unfair economic exchange. Consequently, the fact that the price of a medicine is accepted by customers clearly provides no guarantee against

exploitation, any more than the fact that users benefit from the product. Justifying the price on the basis of customers' consent is thus not sufficient to demonstrate the absence of exploitation. At the same time, this understanding of exploitation makes it possible to define a different justification of the price. In practice, an exploitative transaction will be accepted if the parties do not have the same bargaining power, i.e. if one of the parties is in a position which allows him or her to take advantage of the other party's weakness. In theory, therefore, a consensual transaction between parties of equal power could not be exploitative. A price can thus be justified if it is that which would have resulted from mutual agreement in a fictitious situation where both parties had the same bargaining power (Wertheimer 1996).

In the light of the above, we should not expect a fair price to emerge from market processes. Nor can prices negotiated by parties of unequal power provide a sufficient basis for an idea of what the price should be if it is to be fair. At the same time, defining how a fair price is to be justified remains a difficult task. What are we entitled to expect of a price? It should permit access to medicines – at the very least, to essential medicines. It should cover the costs of development, production and placing on the market. It should reward innovation, the value added by the manufacturer, and provide the manufacturer with an incentive to take risks. It should reflect the value attached to the product. It should be the result of an intelligible and reasonable process, based on justifications acceptable to “fair minded people – those who seek mutually justifiable grounds for cooperation” (Daniels 2000, 1301). The tensions between these various parameters contribute to the difficulty of the debate.³⁰

30 To illustrate the difficulty, reference can be made here to remdesivir, which since February 2020 has been undergoing clinical testing as a treatment for COVID-19 and is the first product to be approved for the treatment of this disease. For the US market, a price of USD 2,340 per patient (treatment course) has already been set for Medicaid/Medicare, although it is not clear how this was arrived at: <https://www.aerzteblatt.de/nachrichten/114280/Hersteller-nennt-Preise-fuer-Remdesivir-in-den-USA> (accessed 9 July 2020).

5. Ethical considerations – Responses to the questions submitted by the FOPH

Questions submitted to the NCE by the FOPH

(in a letter from Pascal Strupler dated 23 December 2019)

“In the area of medicinal products, the following specific questions arise:

1. Is it ethically legitimate, in the area of medicinal products, to set limits (e.g. financial, or based on patient groups, age, prognosis, benefit)?
2. Who is to set these limits, and what ethical aspects are of particular importance for the discussion on the setting of limits?
3. Is it ethically acceptable that the treatment provided for an individual should generate very high costs for society?
4. Is it justifiable to restrict, for the benefit of the public, an individual’s right to receive an effective treatment?
5. In Switzerland, is it ethically acceptable to exclude, on economic grounds, an effective medicinal product from reimbursement in spite of proven efficacy, or to restrict reimbursement e.g. to patient groups who would benefit most? Is a different view to be taken if no reasonable therapeutic alternatives are available?”

Question 1: Is it ethically legitimate, in the area of medicinal products, to set limits (e.g. financial, or based on patient groups, age, prognosis, benefit)?

As is already apparent from the wording of the second question below (“Who is to set these limits...?”), the setting of limits is indispensable in the area of healthcare. There is no health system in which unlimited resources are available and no limits exist; this is true both in general and specifically in relation to medicines. The crucial point from an ethical perspective is thus not whether such limits are, or may be, set, but whether the way in which they are set is fair or unfair, just or unjust (Daniels and Sabin 2002; Hurst and Danis 2007; Marckmann 2010; Zimmermann-Acklin 2011, 2013). The importance to be attached to the efficacy,

appropriateness and cost-effectiveness of treatments or medicines when limits are set is enshrined in current legislation and is also, ethically, largely uncontroversial, although both the interpretation of these criteria and the possible need for additional criteria continue to be debated. Depending on the ethical approach adopted, different views are taken as regards the extent to which, when limits are set, consideration may or should also be given to questions of benefit maximisation above the individual level (i.e. in relation to subgroups of society). While some authors see this as an ethical principle, according to which the scarce resources available should be allocated in such a way as to obtain the greatest possible health benefits (Marckmann 2009), others are fundamentally opposed to benefit maximisation, invoking the right to

equal treatment for all, based on human dignity (Klonschinski 2016; Lübke 2011). As soon as attention is focused, not on individual patients, with their rights and obligations, but – as suggested in the question – on specific patient or age groups, the idea of supra individual benefit maximisation comes into play, i.e. pursuit of the greatest possible benefit for the largest possible number of people. If the available resources (funding, medicines, treatment personnel, etc.) were deployed where they produced the greatest possible health benefits for the largest possible number of people, the right to receive decent treatment would fall by the wayside for those groups where no further significant benefits could be attained – at least compared to the output attainable with the same resources in other groups – for example, those who are very elderly or at the end of life. The widely used health-economic instrument of QALYs (based on the calculation of quality-adjusted life years) is designed to provide a generic unit of measurement for valuing health outcomes, permitting comparison of the benefits attained in different areas.

Apart from the rather difficult question of how exactly quality of life is to be determined when the QALY model is used, it is clear that the basic idea of benefit

maximisation is in opposition to the idea that, based on human dignity, everyone has a right to medical treatment, irrespective of the benefits attained as a result. If available resources were allocated in such a way as to yield the greatest possible health benefits for society, certain patients for whom the benefits of treatment would be limited would lose out – e.g. those at the end of life, persons with disabilities and chronic health impairments, or the very elderly. An ethically acceptable position, as formulated below, involves taking benefit maximisation into account merely as one criterion among other, overarching principles.

The ethically problematic nature of a strong emphasis on benefit maximisation can be illustrated by considering two extreme situations: in a *disaster situation*, attention is focused on the overall benefits which can be achieved by the deployment of extremely scarce resources, generally measured in human lives saved. In contrast, in a situation where – for example, after an accident in the mountains or in a mine – *individuals* are in danger, every possible effort is usually made to rescue the victims; this is normally also attempted in cases where the resources required are disproportionately high, compared to the benefits attainable. In situations where individual lives are endangered,

QALYs

Quality-adjusted life years are a unit used in health economics to assess the value of an intervention firstly in terms of the life years gained as a result and secondly according to the quality of life. To account for quality of life, a life year gained is assigned a value between 0 (death) and 1 (perfect health): for example, if it is possible to cure a hepatitis C virus infection in an otherwise healthy young patient by means of treatment with sofosbuvir, many additional life years in perfect health (i.e. QALYs with a value of 1) will be gained. Even if the price of the substance may be high, the price per QALY gained as a result would be fairly low compared to other treatments, given the large number of QALYs attainable in a young patient with this treatment – compared to non-treatment or to the formerly established alternative treatment (prior to 2014). On this basis, the benefits of use of this medicine can be compared with the benefits attainable with all other possible interventions – e.g. the employment of additional healthcare professionals, architectural modifications (renovation) of a hospital, a particular method of ventilation in extremely premature infants, measures for the prevention of obesity or diabetes, etc. (Breyer et al. 2013, pp. 26-33).

people usually respond according to the Rule of Rescue – i.e., they do everything possible to help those at risk, even if the costs are irrationally high (Cohen et al. 2015; Hurst 2016; Lübke 2017; Zimmermann 2017). While the ethical problem in the first type of case lies in the unequal treatment of those involved, in the second type of case it stems from the fact that resources are deployed which would in fact be more urgently required elsewhere and may then possibly be lacking (Bohmeier and Schmitz-Luhn 2013; Schöne-Seifert and Friedrich 2013).

All that emerges initially from this observation on the Rule of Rescue is that direct confrontation with people in need generally leads to them being helped – even if this requires the use of all currently available resources. What at the micro level of an encounter between a physician and a person in need is indisputably also part of professional ethics, and, more generally, is ethically cogent on a human-rights basis, becomes more controversial at the macro level, in health policy decision-making. Here, assistance for specific groups of patients may need to be weighed against the protection of so-called statistical lives, which are also at risk. In both cases, lives are to be rescued – in the first case, the persons concerned are already known (identified, for example, as persons with a particular disease for which an expensive new treatment is offered), in the second case (for example, in preventive measures such as population screening, which may also be very costly), they are not. How equitable decisions are to be made here is a matter of intense debate (Cohen et al. 2015).

Everyday situations, for example in geriatric or oncological practice, will probably lie somewhere between the above-mentioned extremes. Accordingly, in each case, if access to expensive new medicines is to be restricted, it will need to be ethically evaluated what weight is to be given to the criterion of benefit maximisation and what to the right to equal treatment for all – in other words, how, if at all, benefit maximisation is to be weighted when setting treatment limits. In

particular cases, this is likely to depend, for example, not only on the question of the urgency of treatment and the severity of disease, but also on how high the absolute costs of introducing a new medicine for *all* those requiring treatment would be (number of treatment candidates) and on the ratio of the expected benefits to the costs (cost effectiveness of a new medicine). As noted above, the question of whether it is possible to take into account the number of people requiring treatment when treatments are limited is also a matter of legal controversy. Nonetheless, in recent years, this challenge appears in certain cases to have prompted the introduction of limitations, particularly in the above-mentioned cases of the two substances sofosbuvir (Sovaldi®) and alglucosidase alfa (Myozyme®).

In the case of Sovaldi®, for example, with around 40,000 people infected with the hepatitis C virus (HCV) in Switzerland³¹ at the time the medicine was introduced (over 100 million worldwide), a large number of people were affected, whereas in the case of Myozyme® only 16-20 people in Switzerland were affected at the time of the Federal Supreme Court decision. In economic terms, irrespective of the potential benefits of the medicines concerned, the disparity in the number of people affected makes a huge difference. This, *de facto*, also probably contributed to the fact that Myozyme® was made accessible to all people requiring treatment in Switzerland, even though its cost effectiveness was highly controversial, while Sovaldi® was initially only made accessible to a small proportion of those requiring treatment in Switzerland, even though prescription of this medicine for all HCV patients would presumably have been highly beneficial (in most cases, the infection would have been cleared as a result, thus preventing the development of serious complications). From an ethical perspective, it seems initially clear that, in a situation of considerable affluence such as that prevailing in Switzerland, economic challenges are only of limited significance, given the substantial financial resources which can be made available in such a prosperous country.

31 According to Swiss Hepatitis, cf. <https://www.hepatitis-schweiz.ch/en/hepatitis-c> (accessed 18 March 2020).

However, Sovaldi[®], at the price of approx. CHF 70,000 per patient charged by the manufacturer in Switzerland in 2015, would have generated additional one-time costs of CHF 2.8 bn for health insurers, on the theoretical assumption that all 40,000 people had been treated. Theoretically, it would have been possible to shoulder this amount, particularly since, in all probability – so far as this could be known on the basis of the evidence then available (results of long-term studies will not be available for some years) – the costs for alternative HCV treatment options and for the treatment of sometimes serious complications such as cirrhosis and liver cancer would no longer have arisen. However, one undesired and politically delicate consequence would have been a marked increase in the following year's health insurance premiums.

What is crucial from a political/ethical viewpoint is the fact that considerations regarding the affordability of Sovaldi[®] are to be seen in a context in which a whole series of expensive new, and in some cases highly effective, medicines have been – and in the short and medium term will probably continue to be – authorised by Swissmedic. Financing these *in the aggregate* could certainly become a significant problem for the health insurers and cantons, even if savings on certain other treatment costs will generally be possible as a result of the introduction of new medicines. As well as Sovaldi[®], the substance ocrelizumab (Ocrevus[®]), approved in Switzerland since 2017 for the continuous treatment of multiple sclerosis, offers an example of what is at stake: annual treatment costs amount to CHF 33,000 per patient, compared to annual costs of only CHF 3,000 per patient with the previously established treatment rituximab (MabThera[®] or Rituxan[®]), although not officially approved for the treatment of multiple sclerosis. Since approx. 15,000 people are currently affected by multiple sclerosis in Switzerland, this innovation – on the assumption that all patients

will switch from the old to the new treatment – will involve additional costs of CHF 450 m per year for health insurers. With de facto annual costs of CHF 35.4 million, ocrelizumab was the treatment with the highest costs of all the new medicines launched in Switzerland in 2018 (Schneider et al. 2019, 58).

At this point, it becomes clear that health policy decisions on restricted access to expensive medicines are to be seen in the context of wider decisions on resource allocation, also requiring ethical evaluation: if additional financial resources are needed for healthcare, they will no longer be available in other sectors. This is otherwise known as the problem of opportunity costs – i.e. the costs arising when other opportunities cannot be realised. If, for example, at the political macro level, investments in the education or security sector are forgone so that resources can be deployed in healthcare, this can be expected to have not only desirable effects (e.g. financing of new medicines for everyone requiring treatment) but also undesirable consequences (e.g. cancellation of school renovation projects or planned armed forces reforms). Similar mechanisms are applicable for individuals or families: if monthly health insurance premiums rise, money is no longer available for other expenditures.

Health policy decisions to finance expensive new medicines which, like Sovaldi[®] or Ocrevus[®], are needed by many people in Switzerland may thus lead to losses or funding gaps in other sectors. Such savings or opportunity costs may not only have undesirable effects on the overall situation of a society but also have consequences for public health. There is clearly an association between educational level, an intact labour market, opportunities for political participation and life expectancy in a society (Anand et al. 2004; Marmot 2005).³² In other words, even if it is argued that health is to be accorded greater weight than other

32 Of relevance here is, firstly, the finding that, even in high-income countries, there is a marked gradient in morbidity and mortality between the lowest and highest income groups, and that education, as well as being strongly correlated with income, has an independent influence on morbidity and mortality. As a result, depending on income distribution and the degree of profit maximisation in the health system, with increasing divergence from universal health coverage as defined by the WHO, there is a risk of reinforcement of the so called inverse care law (originally formulated by Julian Tudor Hart (1971)), which states that, as profit maximisation increases, those most in need receive the least care.

goods such as social security, education or employment, it does not automatically follow that the financing of expensive medicines should be prioritised in resource allocation decisions. For this reason, taking public health findings into account, even in macro level decisions where a certain priority is accorded to public health as a transcendental good (cf. Box on p. 18) over the promotion of other fundamental goods, healthcare is not always or unequivocally to be favoured. Rather, the various causes of morbidity and mortality in the population – including social factors – should be considered, so that, with an eye to the consequences, reasonable and equitable deliberations can take place as to where available resources should be deployed in order to safeguard or improve public health.

In the light of these reflections, there emerges once again the above-mentioned dilemma involving, on the one hand, consideration of the *urgency of treatment* with a particular medicine (the Rule of Rescue) and, on the other, insights into the *protection of public health* expressed in statistical terms. Put starkly, and with regard to preventive measures, in particular, the question to be answered is: should priority be given to saving identified or statistical lives? Ethicists' views on this matter differ; accordingly, political decisions in a pluralistic society should seek as far as possible to consider both perspectives and to reconcile them in particular cases through special regulations (Cohen et al. 2015).

From the above considerations, it is clear how challenging it is likely to be to make equitable political decisions in the near future, on the assumption that increasing numbers of extremely expensive (and at the same time effective) medicines will be placed on the market, as is already foreseeable, particularly in the area of oncology but also in the area of immunosuppressants or antiviral agents.³³

Question 2: Who is to set these limits, and what ethical aspects are of particular importance for the discussion on the setting of limits?

This question highlights the two ethically significant issues relating to the setting of limits in an equitable manner: firstly, the “who question” and hence the political and ethical legitimation of decisions; of relevance here are procedural criteria and questions of political participation. Secondly, there is the question of the substantive criteria to be considered from an ethical perspective when such decisions are made.

First, a number of considerations concerning procedural aspects and thus the “who question”: Who sets the limits, or who should do so? What is problematic about decision-making is clearly not any failure to follow democratic pathways and processes: if decisions are examined by the Federal Supreme Court and made by the competent political institutions, then they undoubtedly have *political/democratic*

Health: a special type of good

Health is conceived as a *transcendental* or *conditional good* because the presence of health is a condition for the possibility of realising many other goods in life (Kersting 2000, pp. 481-490). This means that, in the hierarchy of goods to be promoted through political efforts, health should be accorded a special status for reasons of consistency. This becomes particularly clear during a pandemic, for example, when even the temporary curtailment of fundamental rights is considered politically acceptable in the interests of safeguarding public health.

³³ These problems, arising from welcome advances in medical research, have been frequently discussed, and analysed with reference to numerous concrete examples, in the publications of Leonard M. Fleck (cf. Fleck 2009).

legitimation. Problematic, rather, is the almost complete lack of public attention to and debate on decision-making practice with regard to the restriction of access to expensive new medicines. From an ethical viewpoint, it is important that there should be an open political discourse on the setting of limits or priorities for health services, which should include access to the justification of decisions and opportunities for participation and appeal (Marckmann 2010). The stakeholders to be involved in such a process should include not only those directly concerned by a disease or treatment, but also the medical profession, health insurers, product manufacturers and the public. Only when these procedural conditions are fulfilled can controversial political decisions be said to have *ethical* legitimation.

The problems can be illustrated by the decisions on the availability of Myozyme® and Sovaldi®: in the first of these cases, a landmark Federal Supreme Court

decision³⁴ on an appeal by a health insurer was adopted in 2010. A few months after this ruling, the FOPH decided to include Myozyme® in the SL, thus making it available to patients under precisely defined conditions. A postulate on this topic was also submitted to the National Council.³⁵ In the case of access to Sovaldi®, limitations (see Section 3.3) were specified by the FOPH for several years; however, these were progressively eased in response to the relevant pharmaceutical company willingness to grant price reductions, but also as a result of growing public pressure³⁶. The question of the limitations specified for Sovaldi® was addressed in a newspaper article written by the Director of the FOPH, which explained the criteria underlying the controversial decisions on restricted access.³⁷ Both of these cases evidently involved health policy decisions of a certain significance for the Swiss population. The fact that there was virtually no public debate on the underlying criteria is thus ethically questionable.

Health Technology Assessment (HTA)

HTA involves the systematic evaluation of medical interventions for the purpose of providing scientific policy advice. The medical, social, economic, legal and ethical implications of the use of medical procedures and products are systematically and transparently assessed. The goal of HTA is to help improve the quality and increase the cost-effectiveness of healthcare. Typical characteristics are a multidisciplinary approach and a systematic evaluation of the benefits of medical interventions. In many countries around the world, HTA organisations have been established to develop recommendations for policymakers (Schlander et al. 2011, p. 4).

34 BGE 9C_334/2010; cf. Wasserfallen & Junod (2011) and the Swiss Journal of Biomedical Ethics issue devoted to resource allocation in health care: Bioethica Forum (2011) Vol. 4 No. 3.

35 Postulate 11.3218 was submitted on 17 March 2011 by the then National Councillor (now Federal Councillor) Ignazio Cassis: the postulate, which refers to the Myozyme® ruling, notes that the lack of rationing criteria gives rise to *legal uncertainty* and *inequality before the law* in Switzerland; in its response, the Federal Council indicates that, while the establishment of an HTA agency is under consideration, it sees no other need for action with regard to rationing criteria.

36 The pressure came, firstly, from the Swiss Hepatitis Strategy group (<https://www.hepatitis-schweiz.ch/>), which is partly sponsored by the pharmaceutical industry, but was intensified by reports in the media providing information on the prices charged for Sovaldi® in other countries and suggesting that the drug could, for example, be cheaply imported from Australia for patients in Switzerland.

37 Cf. Strupler 2014. He writes: "We all enjoy unrestricted access to the complete list of services covered by health insurance and to the full range of high-quality medical treatments. Switzerland is a prosperous country and can afford this." However, he goes on to say: "Scarce resources need to be deployed where they provide the greatest benefits. This is also the reason why the FOPH, supported by Federal Medicines Commission experts and in agreement with other European regulatory authorities, has specified so-called limitations (i.e. restrictions on use) for around a quarter of all the medicinal products included in the List of Pharmaceutical Specialties. The newer drugs for chronic hepatitis C such as Sovaldi have been limited in such a way as to ensure expert, high-quality treatment of hepatitis C by experienced physicians. Medicinal products are to be used in an effective, appropriate and cost-effective way. Restriction of the reimbursement of medicinal products is thus based on criteria of medical rationality."

An approach aimed at ensuring that political decision-making is informed by engagement with the perspectives of various stakeholders is exemplified by the Swiss Medical Board (SMB)³⁸. This institution, established through a private initiative in the canton of Zurich in 2008, is now a centre of competence in health technology assessment (HTA), with a broad range of sponsoring organisations. Part of its mission is to develop recommendations concerning procedures and medicines for policymakers, medical professionals and other service providers. The SMB adopts a multidisciplinary approach: taken into consideration in the overall assessment of services are not only medical and economic, but also ethical and legal aspects, including quality of life and the wishes and values of patients and society. The FOPH is not represented in the SMB; instead – as part of the “Health 2020” strategy adopted in 2013 – it launched, in 2015, its own HTA programme for the re-evaluation of services/items already reimbursed by the compulsory health insurance scheme (OKP). This programme is to be gradually expanded over the coming years.³⁹ The use of synergies with the Federal Programme proposed by SMB did not materialise.⁴⁰ There is no point in maintaining two parallel structures in a comparatively small area of care provision such as Switzerland, the Executive Committee of the SMB has decided to discontinue the operations at the end of 2021.⁴¹ From an ethical viewpoint, it remains to be assessed whether an institution that produces HTA reports or has them produced and develops recommendations for legislators on this basis, albeit with the involvement of an extra-parliamentary commission, should not operate more independently than is currently the case with the federal HTA strategy. As long as HTA recommendations

are prepared by the same political actor that is also responsible for decision-making, the procedure will be suboptimal due to the lack of separation of responsibilities (Schlander et al. 2011, pp. 26 f.).

The importance of public debate on decisions concerning the setting of limits or priorities is emphasised – and justified in terms of the ethics of equity – by US ethicists such as Norman Daniels, James Sabin and Leonard Fleck (Daniels 2000; Daniels & Sabin 2002; Fleck 2009). The authors stress that, in order to make a just and caring society possible, it is essential to establish rational and fair processes to ensure the legitimacy of decisions on setting limits in healthcare. What they have in mind are real⁴² processes of democratic deliberation, based on the fundamental insight that only limited resources are available to meet virtually unlimited needs. In Leonard Fleck’s view, while the results of public deliberative processes may not be entirely just, they are far better than existing decision-making processes in the US, which he considers to be non-transparent, arbitrary, subjective and ultimately irresponsible (Fleck 2011, p. 168).

Sweden, for example, has a national model for transparent prioritisation in healthcare (Broqvist et al. 2011). The centre responsible is based at Linköping University; its goals include the promotion of public debate on ethical principles and criteria for priority setting (cf. Box p. 21).

38 <https://www.swissmedicalboard.ch> (accessed 18 March 2020).

39 <https://www.bag.admin.ch/bag/en/home/versicherungen/krankenversicherung/krankenversicherung-bezeichnung-der-leistungen/re-evaluation-hta-html> (accessed 10 May 2020). Further information on the HTA programme is available in French https://www.g2020-info.admin.ch/fr/create-pdf/?project_id=53 or German https://www.g2020-info.admin.ch/de/create-pdf/?project_id=53 (accessed 10 May 2020). Nantermod interpellation https://www.parlament.ch/fr/ratsbetrieb/suche-curia-vista/geschaeft?AffairId=20204081&mc_phishing_protection_id=28632-btgpuplse2iqnjuueb60 (23.09.2020).

40 See Humbel interpellation <https://www.parlament.ch/de/ratsbetrieb/suche-curia-vista/geschaeft?AffairId=20204188> (24.09.2020)

41 https://www.swissmedicalboard.ch/index.php?id=69&L=2%27&tx_news_pi1%5Bnews%5D=132&cHash=a57c106eee87b101f9b2f275aac19874 (25.09.2020); <https://www.nzz.ch/wissenschaft/smb-der-angekueandigte-tod-einer-verdienten-institution-ld.1577110?reduced=true> (21.09.2020)

42 *Real* as opposed to *hypothetical discourse*, also proposed by Norman Daniels – following John Rawls’s idea of discourse behind a “veil of ignorance” – for healthcare ethics.

National model for open priority setting in healthcare in Sweden

"The purpose of the national model is to:

- help create a national consensus on what criteria should be included in priority setting,
- help create improved conditions for communicating priority setting and its principles to different professions, various care levels, between county council and municipality, to different parts of the country as well as organisations and authorities,
- help create improved systematic application of the governmental guidelines for priority setting, and thus create conditions for proportionately more resources to be allocated for use in appropriate and effective care for those people in greatest need,
- help improve conditions for open priority setting, its principles and consequences.

Our objective is that the national model for open priority setting should be understood and accepted by all actors within health care, i.e. health care staff, administrators and politicians, and in the long run the general public."⁴³

The NCE recommends that experience in Sweden should be explored, and that it should be considered whether similar initiatives would also be conceivable and practicable in Switzerland. Public debate on the processes whereby decisions are made and how they are justified should be promoted, so that broader public engagement is possible, with the involvement of a variety of stakeholders (Hochuli 2019; Scheidegger 2019). The fact that the SL is publicly accessible and decision-making processes are clearly regulated is to be welcomed; however, this is no substitute for public debate. Given the enormous costs arising from new medicines, the NCE believes that there is a need to raise public awareness of the fact that not everything that comes onto the market can automatically be financed without giving rise to opportunity costs or gaps in other budgets – be it at the political macro-level or the private micro-level.⁴⁴

When resources are to be limited, apart from the question of who is to set the limits and should there-

fore be involved in the decision-making process, the following substantive criteria of ethical relevance are also to be considered: the principle of human dignity requires that all people should be granted the same access to medical treatments, and that their fundamental moral rights should be respected. This principle overrides all other principles. Further principles which are important in decisions on limiting access to expensive medicines are those of medical need, solidarity, effectiveness and benefit. Conflicts may arise between these principles, necessitating the weighing of obligations or goods; here, the principles of medical need and solidarity should take precedence over the benefit principle (Broqvist et al. 2011).

Human dignity

Human dignity is the characteristic common to all people which underlies respect for freedom and also the need to protect the lives of particularly vulnerable individuals such as children or people with dementia. In the context of access to expensive new medicines,

43 <https://liu.se/en/article/national-model-for-open-priority-setting-within-health-care> (accessed 17 March 2020).

44 Two documentaries broadcast on Swiss television in 2018 pursued the aims espoused here, namely creating public awareness of the limits to available resources: "Combien pour une année de vie de plus?" (<https://www.rts.ch/play/tv/temps-present/video/combien-pour-une-annee-de-vie-de-plus-?id=8938005&station=a9e7621504c6959e35c3ecbe7f6bed0446cdf8da>); "Wie viel ist uns ein Menschenleben wert?" (<https://www.srf.ch/sendungen/dok/wie-viel-ist-uns-ein-menschenleben-wert-2>).

respect for the principle of human dignity has two implications: firstly, the prohibition of any unjustified unequal treatment or any form of discrimination, e.g. on the basis of gender, age, origin or religion; secondly, in order to promote equal opportunities, the obligation to compensate for differences for which individuals cannot be held responsible – particularly important in relation to access to medicines are the consequences of the “natural lottery” (e.g. a person’s genetic endowment). If a child is born with spinal muscular atrophy and a drug treatment is available for this genetic disorder, then respect for human dignity requires that the treatment should be made available to the child.⁴⁵

Medical need

In relation to the allocation of scarce resources, particular importance attaches to the degree of medical need in a particular case. This is measured, on the one hand, by the severity of disease and, on the other, by the urgency of treatment (Marckmann 2009). Another factor intuitively recognised as relevant by many people is whether an individual’s condition involves a mild or severe disability, or is life-threatening. This criterion (known as *need or priority to the worst off*) is not taken into account in the above-mentioned QALY model, which is ethically problematic: if a person’s state is improved by drug treatment from fairly good to excellent, this counts just as much in the QALY model as the improvement in the state of an extremely ill patient whose suffering is somewhat alleviated by treatment. While the total benefit obtained in both cases may be the same, the severity of disease and urgency of medical assistance are not.

Solidarity

While the interpretation of the solidarity principle may be far from clear in historical, cultural and ethical terms, its basic meaning in the case of the financing of expensive new medicines is evident: it concerns

the essential willingness of the public to make a contribution to the treatment of those who are severely ill. This willingness is not, however, unlimited and is likely to rest on the following three foundations: firstly, uncertainty as to whether individuals or their close relatives or friends may themselves require treatment in the foreseeable future (substantial symmetry of risk); secondly, the intuitive inclination to provide certain services for the benefit of the worst off in society, especially when they cannot be held responsible for their plight (altruism, fellow-feeling, caring); thirdly, the willingness to promote the common good, on the grounds that people prefer to live in a society where assistance is provided for those in need on the basis of social insurance schemes, rather than in a society where those in need are left to fend for themselves or to rely on the charity of the generous, as stated in the Preamble to the Federal Constitution: “[...] that the strength of a people is measured by the well-being of its weakest members” (welfarism).

Medical effectiveness

In the current context, the principle of effectiveness of interventions involves two elements: firstly, the requirement that the administration of a medicine actually helps to alleviate a particular condition; secondly, that the use of a medicine in a given situation is appropriate or proportionate. Attention is thus focused on the desired results of treatment, which must be demonstrably attributable to the use of a medicine and appropriate to the patient’s situation (or, in medical terms, indicated). The assessment of medical effectiveness is based on experience and evidence; the assessment of whether an intervention is appropriate or indicated is, however, based on both objective (diagnosis) and subjective aspects (the physician’s evaluation and the patient’s values and attitudes) and is therefore less clear-cut and should be undertaken on a case-by-case basis.

⁴⁵ It would be interesting to investigate the question of whether the offer made by Novartis to distribute 100 doses of Zolgensma® free of charge globally by means of a lottery runs counter to respect for the principle of human dignity. A crucial consideration here is the fact that the substance is still very new, little tested and therefore not yet approved by Swissmedic. As soon as the medicine is authorised in Switzerland, access should be regulated *in the same way for everyone* by virtue of the principle of human dignity. Based on the principles of need and benefit, in particular, the costs should be reimbursed for all those requiring treatment.

Benefit

In the context of the financing of expensive new medicines, the benefit principle attracts particular attention, although because of the high costs what is at issue is always the ratio of the expected benefit to the costs involved – i.e. the cost effectiveness of a medicine. While from an ethical perspective, in the interests of fair resource allocation, it is always to be welcomed that, when choosing between a more and a less cost-effective medicine to treat the same condition, preference is given to the former, it may be problematic, for the reasons mentioned above, if benefit maximisation is made a decision-making principle. Priority is to be accorded to respect for the fundamental rights which follow not only from respect for human dignity but also from consideration of the principles of need, solidarity and effectiveness. If these principles are assured, subsidiary consideration of cost effectiveness is important so as to avoid waste and to enable scarce resources to be used in such a way as to provide the greatest possible benefit for the largest possible number of people.

Question 3: Is it ethically acceptable that the treatment provided for an individual should generate very high costs for society?

This question concerns the general social framework which must be in place to permit the operation of solidarity-based financing for (possibly) extremely expensive treatments in healthcare (Friedrich 2018). In particular, the question seeks to determine what degree of inequality in the treatment of individuals is ethically acceptable, thereby implicitly also referring to the unequal distribution of healthcare costs overall. De facto, a small proportion of patients in Switzerland account for a large proportion of treatment costs, with by far the highest costs arising at the end of life (Beck et al. 2016; Felder et al. 2000; von Wyl et al. 2018). The need for extremely expensive treatments for individual patients could be intensified in the future, as a result of progress in the area of personalised (biomarker-based) medicine. Here, in contrast to established medicine, the stratification of patient populations is more fine-grained; this means that, rather than large groups of patients (e.g. those with a brain tumour) all

receiving the same therapy, ultimately each individual will receive a treatment tailored as far as possible to their specific findings.

In addition, what is striking about the particularly high end-of-life costs is that they decrease as the age at death increases, that they are generally especially high in the case of cancer treatment, and that, finally, the willingness of the public to assume these end-of-life costs in Switzerland is very high (Zimmermann et al. 2019, Chapter 6). These empirical facts do not in themselves say anything about the normative question of whether or not the high end-of-life costs are ethically justified (Duttge & Zimmermann-Acklin 2013). One practical difficulty which should not be underestimated in the evaluation of this controversial question is that we rarely know in advance whether, and if so when, a patient will die. This is particularly true in the case of intensive care medicine, as is confirmed by current experience in the treatment of COVID-19. If it were clear, *ex ante*, who would survive intensive care, then of course only those individuals would be subjected to such treatment – this is required by respect for the principle of non-maleficence alone.

The question of an ethically acceptable distribution of costs concerns the willingness of the public to display solidarity and thus the fundamental principle of social health insurance. The only reason why this system works – and for this reason the introduction of the Health Insurance Act (KVG) was approved by a majority of voters in the 1994 referendum – is that everyone lives with the uncertainty of not knowing whether or not they may themselves at some point require an extremely expensive treatment. High-priced medicines and treatments are now in some cases so costly that only a very small proportion of the population would be able to meet these expenses out of their own pocket. This positive attitude towards social health insurance has also been expressed in public surveys on Switzerland's health system in recent years (Interpharma 2019, pp. 32-37).

The concern expressed in the question raised by the FOPH relates to the sustainability of society's solidarity in the area of healthcare. Given the emergence of

high-priced medicines, this concern is doubtless justified. The fact that many households do not pay their health insurance premiums is a sign of the limits to solidarity (SAMW 2020b). The NCE takes the view that a strengthening of the sense of solidarity is to be achieved primarily by means of the public engagement efforts called for above – in particular, through closer involvement of the public in the background to decision-making processes and the justification of the setting of limits.

Question 4: Is it justifiable to restrict, for the benefit of the public, an individual's right to receive an effective treatment?

From an ethical perspective, this question is to be answered in the negative as long as it is clear that a treatment is medically effective, i.e. that the administration of an expensive new medicine, for example, can be assumed to provide a medical benefit. If the net medical benefit – i.e. the benefit net of possible adverse effects (Raspe 2013; Schöne-Seifert & Friedrich 2013) – or the expected clinical effectiveness of a new medicine is likely to be only marginal, or if its cost-benefit ratio is poor – i.e. a new medicine is extremely expensive but provides very limited additional medical benefit (which is likely to be the case today for many me-too products, pseudo-innovations or cancer drugs offering only minimal survival benefit) – then it may be fairer not to make this medicine available, so as to have the resources available elsewhere in the health system. Under these circumstances, however, it would be essential that such a limit should be *applicable equally for all those requiring treatment*, rather than for an individual person, as suggested in the question (Buyx et al. 2011). In other words, such a decision can only be ethically justifiable at the macro-level – not at the micro level (the patient's bedside)

or the meso-level (within a single healthcare organisation). With regard to extremely expensive new medicines, this can only be the case if the product offers only a marginal medical benefit, and at the same time shows low cost-effectiveness, and if on this basis a political decision is made not to make the product available to any patients in Switzerland.

This is not applicable in the case of the above-mentioned examples Ocrevus[®] and Sovaldi[®], as these expensive new medicines have been shown to offer clear medical benefits and are also cost-effective⁴⁶ (for Ocrevus[®] see Frasco et al. 2017; Graf et al. 2020; McCool et al. 2019; Zimmermann et al. 2018; for Sovaldi[®] see Jakobsen et al. 2017 ; Pfeil et al. 2015 ; Stahmeyer et al. 2017 ; Wei et al. 2018). But there are also expensive new procedures – likewise the focus of media attention – such as Kymriah[®] and Zolgensma[®], which have not yet been evaluated, and the benefits of which are therefore not yet known. However, based on initial trials with Kymriah[®] and Zolgensma[®], they are widely believed to offer medical benefits even though these are not beyond dispute (for Kymriah[®] see Malone et al. 2019; Shahryari et al. 2019; Zavras et al. 2019; for Zolgensma[®] see: Ribera Santasusana et al. 2020; Shahryari et al. 2019).⁴⁷

Question 5: In Switzerland, is it ethically acceptable to exclude, on economic grounds, an effective medicinal product from reimbursement in spite of proven efficacy, or to restrict reimbursement e.g. to patient groups who would benefit most? Is a different view to be taken if no reasonable therapeutic alternatives are available?

If this question is to be answered, the criterion of “economic grounds” first needs to be clarified: essentially, it is not acceptable from an ethical viewpoint to

⁴⁶ Conclusions concerning cost effectiveness are based, for example, on the costs per QALY associated with the use of a new medicine: if these fall below a certain threshold, then a medicine is said to be cost-effective. Specified thresholds vary and they are generally not expressed as a fixed value, but guidance can be obtained from the NICE thresholds (UK) or earlier studies by the SMB, which has now, however, switched from QALYs to the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation). The fact that ranges are indicated, rather than clearly defined thresholds, is designed to permit a certain political flexibility (Marckmann 2009).

⁴⁷ As an alternative to commercial products, Heidelberg University Hospital has established its own production centre for CAR T-cell therapies, which is designed to ensure the provision of treatment for patients and also to reduce costs (<https://www.tagesanzeiger.ch/uenstig-und-selbst-gemacht-342374177937> (accessed 8 July 2020)).

exclude from reimbursement – i.e. to explicitly ration – a medicine of proven efficacy with a clear net benefit. In the context of a highly prosperous country such as Switzerland, the “economic grounds” mentioned in the FOPH’s question could refer to two types of case: firstly, that of a medicine which, though effective, is not cost-effective (or is of limited cost-effectiveness) and whose reimbursement under the OKP is therefore called into question because the EAC criteria are not fulfilled; a case in point was the Federal Supreme Court’s assessment of Myozyme® in 2010. The second type of case would be that of a medicine which, though effective, appropriate and cost-effective (i.e. clearly fulfilling the EAC criteria), is extremely expensive and is required for the treatment of large numbers of patients – as in the case of Sovaldi®, for which limitations were applicable from 2014 to 2018.

Ethical comments on cases of both types have already been given above: if a medicine is effective, but clearly not cost effective, then the legislators are ethically and indeed legally obliged to negotiate with the manufacturer so as to obtain more favourable financial conditions, which could make the product cost effective. Here, in retrospect, the case of Myozyme® is not particularly suitable, as this is a medicine for a disease which is extremely rare worldwide; accordingly, in this case, for reasons of justice, other, more generous standards need to be applied than in the case of conventional medicines in order to assess cost effectiveness.

In the second type of case, the evaluation is less clear. Essentially, a medicine should be reimbursed if it fulfils the EAC criteria. This was already (more or less unquestionably) true of Sovaldi® in 2014. However, if the reimbursement of such a product generates a level of economic costs which would be problematic for reasons of health protection, limits may or – depending on the extent of the opportunity costs – must, from an ethical perspective, also be set. Whether this was the case for sofosbuvir during the period when reimbursement was subject to limitations is a matter of dispute; in retrospect, following the decision to reimburse sofosbuvir for all those requiring treatment, irrespective

of the severity of their condition, it has become apparent that treatment with Sovaldi® (or other medicines with the same active substance) is not sought by anything like all 40,000 HCV patients and that, as a result, the additional burden placed on health insurers does not appear to be as significant as had been assumed; in addition, the price per treatment has dropped substantially since 2014.

With regard to the ethical evaluation of restricting reimbursement of effective medicines to patient groups who would benefit most, further distinctions need to be made: if it can be shown in an evidence-based manner that a medicine is particularly effective in a specific patient group (assuming that cost effectiveness is also demonstrated), then this case is ethically trivial: the medicine should be reimbursed. Likewise trivial is the case in which it can be shown that the medicine is not (or is scarcely) effective for certain patients: it should not then be reimbursed for this group; one example – in this case, an expensive medicine already established – would be Herceptin® (active substance: trastuzumab), which is used to treat breast cancer in patients with HER2 overexpression. Treatment with Herceptin® is only indicated for HER2-positive tumours (only found in one in five patients). Lying between these two clear-cut situations is a grey area where assessment is required in each particular case. However, in the debate on the restriction of Sovaldi® to specific patient groups where severe symptoms had already developed, the ethically required clarity was called into question, as it was pointed out that patients in earlier disease stages would also have benefited considerably from treatment with the active substance sofosbuvir.

Finally, it is asked whether the ethical assessment is affected by the existence (or absence) of therapeutic alternatives in the scenario considered here. This case appears to be clear: if a medicine unequivocally offers a substantial benefit and if it is cost effective (i.e. it fulfils the EAC criteria), then it should be reimbursed regardless of whether an alternative treatment is available or not. But here, too, two further conditions should be added: if an alternative treatment is

available which is equally effective – according to all available evidence-based information – but less costly, then a decision (based on the EAC criteria) should be made in favour of the existing medicine – i.e. the new product should not be reimbursed. If the situation is comparable to the case of Sovaldi[®], where an alternative treatment was available – namely, interferon (at that time combined with the active substance ribavirin), established since the 2000s (Rosien et al. 2017) – but it was much less effective, also expensive, and furthermore was only clinically effective in half of all cases and was associated with serious adverse effects (e.g. autoimmune reactions, anaemia and depression), then both the expected savings and the reduction in adverse effects are to be taken into account in the overall evaluation. In the case of the limitations specified by the FOPH for Sovaldi[®], the fact that these aspects were not given due consideration was rightly criticised.

6. Final considerations

The above discussion has shown that, in recent years, the introduction of extremely expensive new medicines in Switzerland has created a challenging situation. Decisions on the management of the latest developments in the area of medicinal products not only have major practical implications for the public but are also of particular relevance for the ethics of equity. It has become apparent that, in future, the application of the legally specified criteria – efficacy, appropriateness and cost-effectiveness (AAC) – will in itself scarcely be sufficient to ensure that the costs, reflected in steadily rising health insurance premiums, are kept within the bounds of an acceptable budget. This is due not only to the high prices which are charged for medicines, and which appear at least in some cases to be justified, but also to advances in research, particularly in the field of oncology and in the treatment of autoimmune and viral diseases. If expenditures on extremely expensive new medicines continue to rise, the resources deployed will then not be available elsewhere in the health system or in other policy sectors; likewise, at the private household level, the additional money spent on health insurance premiums will mean that less is available for other items. If – as is the case in Switzerland at least to a certain extent – healthcare is regarded as a priority goal by a large proportion of the population, it does not immediately follow that ever-increasing resources should be allocated to healthcare in the narrow sense. As the health of the population is also determined by a number of other factors, it can be concluded from a public health perspective that the (always limited) resources available should not be invested exclusively in the area of direct healthcare – e.g. for expensive medicines – but also in other areas of social policy.

In other words, in view of the sometimes extremely high prices of new medicines, it is now becoming quite clear that, in healthcare, limits have to be set. The NCE takes the view that such limits, or limitations, should be made as equitable as possible. If this is to be assured and implemented in a way that is widely comprehensible, it is crucial that public awareness of the scarcity of resources should be promoted, not only so as to make restrictions and the underlying political justifications transparent, visible and understandable, but also to give the various stakeholders – ultimately all those who pay health insurance premiums – the opportunity to participate appropriately in the decision-making processes.

7. Recommendations

Based on the above considerations, the NCE offers the following recommendations for legislators and other policymakers:

With regard to the improvement of decision-making processes:

- Given the significance for society of decisions on access to expensive new medicines, *fact-based public debate on the decision-making processes and justifications* should be encouraged and established. This is the only way not only to raise awareness of the reality of scarce resources but also to enable society to address this issue with the involvement of various stakeholders.
- Given the challenges involved in the management of expensive new medicines, it is important to support *solidarity-based awareness and action in society*. This can be achieved, in particular, through greater involvement of the public in decision-making processes and plausible justifications for the setting of limits.
- In view of the outstanding importance of the SL in ensuring that public access to medicinal products involves equality before the law, it would be appropriate to *seek more comprehensive democratic legitimation for, and to enshrine in legislation, the criteria used for the inclusion of medicinal products in the list, and in particular for price-setting by the authorities*.
- The establishment of an *independent HTA institution outside the FOPH* is to be pursued, so as to permit consistent separation of HTA studies and associated recommendations on the one hand and political decisions on the other. HTA studies and recommendations should not be elaborated by the same actor that is subsequently responsible for making decisions.
- Access to expensive new medicines is also to be made equitable in the area of off-label use, i.e. in cases where access to medicines is not (yet) regulated by the SL: decisions should be based on

expertise and should as far as possible be transparent, consistent and the same for all those requiring treatment.

With regard to the substantive criteria to be used in decision-making:

- From the viewpoint of *equality before the law and non-discrimination*, it should always be assessed whether, when access to expensive new medicines is restricted, distinctions made between patient groups are justified and do not lead to discrimination, e.g. on the basis of patients' origin, gender, age, social position or genetic constitution.
- Fundamental criteria and ethical considerations for decisions on access to expensive new medicines are *non-discrimination, equal treatment for all, urgency of treatment, severity of disease and appropriate consideration of the principle of benefit maximisation*. When arrangements are established for access to expensive new medicines, apart from considerations of benefit (cost effectiveness, additional benefit, recommendations from HTA studies), the overriding ethical principle of human dignity must always be respected, as well as the principles of need, effectiveness and solidarity.
- The health of the population depends on various factors, with healthcare – including pharmacotherapy – representing just one, albeit important, area. *If it becomes necessary, for the purpose of introducing extremely expensive medicines, to cut expenditures in other social policy sectors, then it should be examined, from a public health perspective, what implications such cuts in other areas could have for the health of the population*. This is the only way to ensure that, in the long term, the goal of protecting public health is not undermined as a result of the financing of extremely expensive new medicines.
- *Defining a fair price is a difficult exercise*. We should not expect a fair price to emerge from market processes, or from negotiations between parties of unequal power. We are entitled to expect that a price

should permit access to medicines; cover the costs of development, production and placing on the market; reflect the benefits associated with the product; reward innovation and the risks involved in product development; and be the result of an intelligible and reasonable process. The tensions between these various parameters contribute to the difficulty of the debate. Resolving these tensions will require public debate based on serious argumentation.

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9. List of abbreviations

BGE	Federal Supreme Court decision
CAR T cells	Chimeric antigen receptor T cells
COVID-19	Coronavirus disease 2019
EAC	Efficacy, appropriateness, cost-effectiveness
FC	Federal Constitution
FDHA	Federal Department of Home Affairs
FOPH	Federal Office of Public Health
HCV	Hepatitis C virus
HER2	Human epidermal growth factor receptor 2
HTA	Health technology assessment
KLV	Healthcare Benefits Ordinance (SR 832.112.31)
KVG	Federal Health Insurance Act (SR 832.10)
KVV	Health Insurance Ordinance (SR 832.102)
NCE	National Advisory Commission on Biomedical Ethics
OKP	Compulsory health insurance scheme
QALY	Quality-adjusted life year
SAMS	Swiss Academy of Medical Sciences
SL	List of Pharmaceutical Specialties
TPA	Federal Act on Medicinal Products and Medical Devices (Therapeutic Products Act)
USZ	University Hospital Zurich

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