Economic considerations in psoriasis management
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Abstract With a prevalence of 2% to 3%, psoriasis is a very common chronic disease worldwide and generates therapy costs and continuing cost for health insurance and patients and their families. Cost-political changes in health care and the ever increasing health-economic demands in all areas of the health system make it necessary to differentiate between the two when recording the expenses for a disease. The main characteristics of the pharmacoeconomic evaluation are the record of costs, the cost-benefit and cost-effectiveness ratio, and efficiency of various treatment forms. Numerous publications discuss the cost of individual forms of therapy in the treatment of psoriasis, but there are fewer studies on the total cost of psoriasis therapy, especially studies that take both direct and indirect costs into account. The scientific articles on pharmacoeconomy and quality of life in psoriasis have proven (without a doubt) that, despite the lack of a vital threat, psoriasis is highly important to the national economy and to those who have the disease. This justifies appropriate monetary expenditure for treatment. Studies that address the cost of therapies (especially for chronic diseases) will be necessary in the future and will create the required transparency to guarantee reasonable medical care that takes the cost-benefit ratio and the best outcome for the patient’s quality of life into account.

Why do we formulate economic considerations?
Medical economy or health economy is an empirical and theoretical, interdisciplinary science that aims at recording the production and allocation of health services related to resource consumption and costs. The focus in this is a balanced use and distribution of goods, such as personnel, apparatus, medications, hospitals, and preventive and diagnostic measures, and the attendant efficiency, effectiveness, quality, and fairness in dealing with them. Pharmacoeconomy focuses especially on drugs and other forms of therapy.1-3

Cost-political changes in health care and the ever-increasing health-economic demands in all areas of our health system make it necessary to differentiate in recording the expenses for a disease. The cost of disease not only includes the costs for the direct therapy of the patient (“direct costs”) but also the secondary costs from the societal perspective (“indirect costs”). The disease burden to patients and their families is considered a cost factor by economists even if not directly accessible (“intangible costs”). Chronic diseases, for which therapy has no time limit and which are often coupled with considerable loss of quality of life for patients and their families, especially result in high direct and indirect costs for the health insurance, patient, and national economy.1-12

The extent to which the patient’s quality of life is affected in chronic skin diseases sometimes even exceeds the stress of chronic internal diseases and tumor diseases.13,14
Life-long therapy is necessary in a large number of cases and underlines the relevance of health-economic considerations. The formulation of economic considerations is important in weighing costs against benefits of treatment and in evaluating possible alternatives. The impetus for this is drastic budgeting in the health system on the one hand and the basic necessity of examining possible medical therapies with respect to their long-term costs and determining the resultant consequences for both the patient and the health system on the other.

Increasing health-economic limitations in therapy can mean in the long run that effective therapy concepts are abandoned in favor of therapies that appear at first glance to be less expensive but which finally are less cost-effective in long-term observation and when considering indirect and intangible costs. One such health-economic limitation, for example, is that nonprescription medications are excluded from reimbursement by state health insurances. Medications that can be obtained without prescription, thanks to their favorable side effect profiles, must be purchased by the patient himself or herself. The economic consequences depend on the degree of choice by the physician and the patient’s willingness to pay. The socioeconomic burden for the patient can become long-term. It consists of participation in prescriptions, in-hospital therapies, cures and the purchase of medications, and over-the-counter dermatologicals. Additional therapies, travel costs, loss of pay, and fewer professional chances add to the burden. These are important aspects that must be taken into account in the health-economic evaluation of therapies.

What are the characteristics of pharmacoeconomic evaluation?

The main characteristics of pharmacoeconomic evaluation are recording of costs, cost-benefit and cost-effectiveness ratio, and efficiency of the various treatment forms. The central questions here are, on the one hand, the allocation (the distribution of means according to need), and on the other hand, the efficiency with which a service is offered at guaranteed quality. The common goals of all studies are to weigh the costs and benefits and to evaluate possible alternatives. Pharmacoeconomy is thus a subarea of health economy. It examines the economic viability of drugs and therapeutic procedures. Economically viable are those procedures in which the costs accrued can be shown to stand in a reasonable ratio to the measured benefits. The “benefit” is determined in the form of medical parameters (such as skin severity score), monetary units (such as cost of disease), or intangible values (such as quality of life or satisfaction). Complex studies addressing specific questions and examining individual variables, on the basis of which treatment, medication, and services can be assessed, are the instruments for health-economic evaluation.

The health goals in medicine include not only the length of life or the pathologic deviation of real values of physiologic variables from certain norm values but also the quality of life over time. The quality of life as a parameter in evaluating health goals in medicine has only gained importance during the past decade. Accordingly, reliable data, such as those available in many subareas of medicine, are still being developed. The quality of life in health economy and health politics is important as a decisional parameter to distribute the limited resources in the health system as fairly as possible according to need. It is a declared health-political goal in Germany and also in many other countries to use the required financial resources to maintain or reinstate the quality of life for chronically ill patients. To do this, in the future, we will need reliable data on which the so-called cost allocation can be based. The quality of life as an intangible cost factor needs to be recorded here, which can serve to check the therapy goals, to justify the necessity of the dermatologic therapy, and to depict the economic viability of a therapy. The economic viability of a therapy is measured, among other things, on the extent of improved quality of life and on the extent of reduced continuing costs in relation to the generated costs.

The principle of economic viability is divided into 2 basic principles:

(a) Act so that a maximum benefit (such as patient’s state of health) is achieved with the available means (maximal principle).
(b) Act so that an achievable benefit (such as desired state of health for the patient) is attained with the least possible cost (minimal principle).

What do we know about the economic importance of psoriasis?

With a prevalence of 2% to 3%, psoriasis is a very common chronic disease worldwide, which generates high therapy costs and continuing costs for both the health insurance and the patients and their families. A growing number of studies have addressed the health-economic and pharmacoeconomic aspects for psoriasis in the past years.

A cost-of-illness study published in 2005 in Germany determined average costs for the health system of €864 per patient per year; 60% of the costs were attributable to reimbursable preparations and 22% to in-hospital treatments. The costs that patients had to pay themselves for supplies and nonprescription medications amounted to €596 per year. Indirect costs were cited at €1440 per year, whereby total costs per patient of €2866 accrued. The total costs for patients treated with systemic therapy were €4985. Another study performed in Germany divided the patients into 3 therapy groups (topical therapy, systemic therapy, and high need) and calculated for these patients mean total costs of €6709 per patient per year, of which €2299 were paid for...
In-hospital treatment, €2014 for medication costs, €1039 for indirect costs, and €794 for out-of-pocket expenses. There were considerable differences between the 3 subgroups. Subgroup 1 (topical therapy) generated costs of €4088, subgroup 2 (systemic therapy) generated costs of €7148, and the high-need group of patients generated total costs per year of €8831.19

Similar data are found in Italy. Within the Interdisciplinary Association for the Study of Psoriasis study performed there on about 8000 patients with psoriasis, annual total costs per patient of €904.51 were calculated, whereby in Germany, the largest part (83.9%) was generated by direct costs for hospitalization, and the cost for systemic therapy only accounted for 10.9% (€99.01).18 It is agreed that the 20% most severely affected patients generate the greatest percentage of costs in psoriasis therapy.27

In the Netherlands, the annual expenditures for patients with psoriasis amount to €25 million or a total of 1% of health costs in the country. A total of €644,366 accrued alone from costs resulting from absenteeism from the workplace.28 Comparing these data with data from the United States, it quickly becomes clear that the ways of determining the costs are different; but, regardless of how calculated, psoriasis accounts for a significant percentage of health costs in the country.29 In 1997, a total of US$649.6 million were spent in the United States for 1.4 million patients with psoriasis; 4.7% (US$30.5 million) accrued from hospitalization, 13.3% (US$86.6 million) for outpatient visits to the physician, and 22.7% (US$147.9 million) for prescription medications. The percentage of over-the-counter drugs was cited at 54.9% (US$357.2 million). Thus, more than 50% of the treatment costs were paid, at least in part, by patients themselves.

The differences in therapy costs between the United States, the United Arab Emirates, and Italy were examined in a further study, and it was determined that the costs for topical therapy differ markedly between countries. As an example, the cost for 1 g of calcipotriol in the United States is US$2.00; in Italy, €0.45; and in the United Arab Emirates, US$0.60. The situation is similar for systemic immunosuppressives, where 100 mg of cyclosporin A costs US$4.99 in the United States, US$4.50 in the United Arab Emirates, and US$9.12 in Italy. Methotrexate costs more than double in the United States than in the United Arab Emirates (US$4.99-US$7.59 vs US$2.60). In general, the costs for psoriasis therapeutics in the United States for example are higher than in Italy. The costs for medication and external therapeutics have a marked effect on the overall proportion of direct costs in psoriasis therapy. International differences affect total costs to a large degree.25

Comorbidity is an important factor influencing the cost of disease. In a cohort study, it has been demonstrated that patients with psoriasis, treated with systemic therapeutics, have significantly higher comorbidity, associated with markedly higher expense for the health system, than patients without psoriasis but the same comorbidity.30 In this study, data of 2489 patients with psoriasis in a cohort study were compared with data of 7467 patients without psoriasis and assessed over a period from 1996 to 1999. The mean direct costs for the cohort of patients with psoriasis amounted to US$7778 per year. For patients with psoriasis receiving systemic therapy, the expenses were on average US$4000 higher than for patients without psoriasis. The comorbidity was coupled with significantly higher costs for patients with psoriasis than for patients without psoriasis.

In summary, there are numerous publications dealing with the costs of individual forms of therapy in the treatment of psoriasis, but there are fewer studies on the total costs of psoriasis therapy, especially taking both direct and indirect costs into account. The relatively high average annual costs per patient underline the necessity of an effective control of psoriasis. The results of the cost-of-disease studies can be used for health-economic assessment of innovative pharmaceuticals in psoriasis therapy. In an international comparison for in-hospital treatment, outpatient visits to the physician and over-the-counter preparations vary in international comparison. Clear discrepancies can be observed with respect to treatment costs between the individual studies, which can be explained both by the different methodical approaches and by the differences in health care habits. Hospitalization time for psoriasis has decreased significantly in the past decade, which can be ascribed to both increased use of treatment in day clinics and new medication therapy options, which can be applied safely and less expensively on an outpatient basis. In comparing the costs of in-hospital and day clinical treatment, it was found that day clinic treatment is less expensive with respect to direct costs but requires considerably more time than in-hospital treatment.31 Taking the time factor into consideration is especially important in the calculation of indirect costs, which might arise, for example, from work disability. Quality of life can also be involved as a characteristic of intangible costs. Early success in patients treated in a day clinic requires high compliance in applying treatment and continuity of the patient’s own individual therapy.

Quality of life occupies a decisive key position as a so-called intangible cost factor. The burdens observed individually are different and range from a search for a partner, through sex life, and on to a loss of ability to work. Social life is decisively influenced by the disease and may lead to severe detriment to the development of personality. The severity of the disease course correlates with the length of treatment and the risk of losing one’s job. Agreement also exists concerning the relevance of the cost factors that arise. The finding of reduced quality of life is confirmed by many authors, especially in psoriasis.32-77

What do we know about the economic viability of psoriasis therapy?

The main characteristics of pharmacoeconomic assessment are the recording of costs, the cost-benefit ratio, the cost-effectiveness, and the cost-efficiency of the various forms of
care, especially therapies. There are a number of publications on the therapy of psoriasis that deal with and assess the cost-effectiveness of individual therapies.

**Special pharmacoeconomy of topical therapy**

Numerous studies confirm that a combination therapy with topically applied glucocorticoids and calcipotriol is more cost-effective than therapy with topical steroids alone.75-80 The advantage lies in the possibility of reducing the steroid as soon as a stable skin finding is achieved and in the long-term reduction of rebound phenomena by avoiding continuous application of glucocorticoids alone. Even with initially higher costs of topical therapy with calcipotriol, a greater frequency of visits to the physician is observed in purely steroid treatment, which generates a considerable additional cost factor. The reasons could lie in the higher recurrence rate after withdrawal of monotherapy with steroids.81,82 Topical treatment with one-time daily application of a fix combination of calcipotriol and betamethasone is more cost-effective than the use of the single substances once daily.83 Compared with topical monotherapy with tazaroten, the combination of betamethasone and calcipotriol is nearly twice as cost-effective, with initially comparable costs.84 Advantageous is the once-daily application, which enables a considerable savings in time for the patients. A study showed that patients spend up to 26 minutes daily in applying topical preparations.84 A reduction of treatment time per day to a single application would lead to an increase in quality of life and an additional saving in indirect costs or direct costs for the patient (“time-earnings-lost”). Increased compliance could be expected, which increases with each reduction in treatment units. In combination with a UVB treatment, topical therapy with calcipotriol also results in a reduction of radiation units and more rapid response with comparative cost neutrality.28 In summary, it can be stated that the medication price per gram is not an adequate predictor for the calculation of therapy costs given that a combination of medications can lead to a reduction in overall costs.

The treatment costs were analyzed in another study based on a validated decisional model for analysis of the cost-effectiveness of calcipotriol and tazaroten. The data were collected from a meta-analysis of available literature. Particular attention was paid to the clinical response and remission times, from which symptom-free days were calculated. The costs for visits to the physician, treatment preparations, laboratory examinations, and the treatment of adverse effects were integrated into the decisional model. Cost-effectiveness was expressed as the costs anticipated in a reduction of the radiation units with consistent therapeutic success. The direct costs for a UVB radiation unit were €8.67 per treatment. Indirect costs in the study consisted of travel expenses and loss of income. The time for a radiation unit including travel, waiting time, and treatment time was 110 minutes, which resulted in a loss of income of €27.38. In addition to the direct costs of
treatment, the total cost amounted to €36.05 per treatment unit. The cost for 1 g of calcipotriol was set at €0.38. In a 20-week combination therapy, the expenses were thus €1175.90 for the combination therapy with calcipotriol and UVB (direct and indirect costs). The costs for the combination therapy of UVB and bland care amounted to €1212.14. The cost savings from the reduction of UVB radiation units were nearly offset by the costs of the calcipotriol, but the combination therapy with calcipotriol 3% was less expensive and radiation units could be saved.

Another cost analysis was performed among other things on the costs for phototherapy (psoralen-UVA, UVB broadband, UVB narrowband, and retinoid PUVA). The therapy costs were analyzed in comparison with costs for corresponding therapy monitoring and the costs of therapy for adverse events. In addition to the total cost, differentiation was made between annual costs after PASI reduction of 50% and 75%. Psoralen-UVA therapy was the most cost-effective among the different phototherapies. A 75% reduction in PASI generated annual costs of $3111. These costs for UVB broadband therapy were between $4233 and $7472. UVB narrowband therapy costs $4811 annually for a PASI reduction of 75%. It also became clear that the least costs were generated in phototherapy for “therapy monitoring.” Only the combination therapy of UVB and internal retinoids generated annual monitoring costs of $618 compared with $106 for all other phototherapies.87

Another multicenter study of UV-brine therapy in 2000 determined that 50% of 690 outpatients with psoriasis had a relapse after 6 months, and 68% after 12 months.88 Overall, however, it is agreed that balneophototherapy offers a cost-effective alternative in the treatment of psoriasis and keeps especially the indirect costs in a considerably lower range than other therapy concepts.

Special pharmacoeconomy of systemic therapy

As early as 1993, annual costs of systemic psoriasis therapy were examined in a retrospective study in the United States.89 Data collected over a period of 8 years (1983-1991) was evaluated, wherein patients who had undergone monotherapy were especially selected. The therapies were examined with respect to their costs and the clinical response rate. Among others, therapy concepts using methotrexate, cyclosporine, and etretinate were compared. Over the period of 1 year, therapy with methotrexate caused direct costs of US$1381 (801-2293); etretinate, US$1995 (1363-2927); and cyclosporine, US$6648 (5453-7750). The direct costs were also broken down according to their individual components. Visits to the physician caused costs of US$243, US$261, and US$649. Laboratory tests cost US$470, US$465, and US$1021. The expenses for medication amounted to US$458, US$1267, and US$4119. Had a liver biopsy been performed in all patients treated with methotrexate, there would have been additional costs of US$490 annually. Methotrexate and etretinate had the highest response rate in the retrospective analysis. The high costs of cyclosporine medication and the costs for the attendant laboratory monitoring were noted.

In 1998, a study of the cost-benefit ratio for methotrexate compared with a combination treatment of UV and tar in mild, moderate, and severe psoriasis was performed in a model analysis. The conclusion was that methotrexate has higher cost-effectiveness in serious psoriasis.90

Ellis et al91 used a computer-supported decision model of cost-effectiveness to test methotrexate compared with a rotation scheme between methotrexate and cyclosporine in serious psoriasis. The direct costs, including the treatment of side effects, were calculated. In a 10-year treatment period, the costs of the methotrexate treatment were US$33,000 with a symptom-free interval of 2 years, whereas the rotation scheme generated costs of US$38,000 with 4 years of freedom from symptoms.

Based on literature data, the costs of “therapy failures” under individual systemic therapeutics were examined in a model analysis for a 12-week treatment period. Correspondingly, the costs for methotrexate were US$623; acitretin, US $2729; cyclosporine, US$2969; narrow-band UVB, US$3692; PUVA, US$4668; etanercept, US$16,312; and efalizumab, US $17,196. The costs for therapy failures, in relation to successfully treated patients, were US$187 for methotrexate, US$505 for cyclosporine, US$767 for PUVA, US$1034 for nUVB, US$1310 for acitretin, US$8319 for etanercept, and US$12,897 for efalizumab.92

Special pharmacoeconomy of biologicals therapy

Modern biologicals are especially effective in patients with serious forms of psoriasis and offer a considerable improvement in quality of life. An article published in 2005, in which various systemic therapies were compared with respect to costs and cost-effectiveness, included biologicals for the first time.87 The therapy costs of infliximab, etanercept, efalizumab, and alefacept were recorded. Annual costs of US$26,436 were found for infliximab. This included monitoring costs of US$116 yearly. In considering cost-effectiveness, a PASI reduction of 75% results in costs of US$23,946. Compared with the annual therapy costs of US$21,158 for etanercept, it is found in the cost-effectiveness analysis, taking annual PASI −75% costs into account, that therapy with infliximab is the most cost-effective (US$23,946 vs US$24,717) for therapy with etanercept 50 mg twice weekly). Even systemic therapy with efalizumab, which appears considerably more cost-effective in looking only at the annual therapy costs of US$17,836 is found to be clearly inferior in the analysis of cost-effectiveness. A PASI −75 reduction generates therapy costs of US$25,960. Alefacept, which is still not authorized in the Federal Republic of Germany, is far lower in the effectiveness analysis ($45,163 per year/PASI −75).
To improve the skin findings by a PASI value of 1%, US$319 must be spent annually for infliximab, US$330 for etanercept 50 mg, US$346 for efalizumab, and US$602 for alefacept.

The costs of the classic immunosuppressives (cyclosporine, methotrexate) are considerably lower. For a PASI reduction by 75%, US$10,600 must be spent for cyclosporine annually and US$2491 for methotrexate 15 mg. It became clear that the costs for therapy monitoring and the treatment of adverse side effects were considerably higher than in the biologicals. For therapy monitoring in methotrexate, the annual costs are US$1188 and for cyclosporine US$1794.

There are presently few articles dealing with the special pharmacoeconomy of biologicals. There is a great need in the coming years for cost-effectiveness analyses to evaluate these therapies, which are very cost-intensive in the initial phase and over a longer period when one takes indirect costs into account.

Conclusions and perspectives

The scientific articles on pharmacoeconomy and on quality of life in psoriasis have proven without a doubt that despite a lack of vital threat, the disease is of high importance in the national economy, as well as of great importance for those who have it, and justifies appropriate monetary expenditure for treatment.\(^3\) The costs of developing and producing innovative, highly effective medications are immense. It can be expected on the benefit side that modern pharmaceutical and immunotherapeutic therapy developments will result in considerable and long-lasting improvement in the quality of life of those affected. It can be expected that modern medication therapy will lead in the future to reduced continuing costs of disease because therapies will probably be more effective, act longer, and with fewer side effects.

The beneficial effects of this refer especially to the indirect and the intangible costs of each therapy. From a health-political point of view, the question arises as to the extent to which cost providers are willing to spend high additional (incremental) costs for new therapy procedures, when the monetary benefits of these are enjoyed more by the national economy and the resultant intangible benefits (quality of life) by the patients. Overall, the wide-reaching socioeconomic consequences of psoriasis as a chronic skin disease make the high expenditure for research and therapy appear justified. Supplying patients with skin diseases with the necessary modern drugs must remain guaranteed in the future. From a health-economic point of view, quality of life takes precedence over costs. In light of the current health economic situation and the still-increasing research activity in the area of quality of life research and pharmacoeconomy, it can be assumed that these areas will gain in importance in the coming years.\(^1,2,93-95\)

Meanwhile, efforts are apparent in Germany and internationally to harmonize methods for recording quality of life and recording pharmacoeconomic aspects to reach a consensus on the procedures for dermatologic studies. A corresponding Guideline for Recording Quality of Life has already been adopted by the German Dermatological Society. Based on the reached consensus, recording of quality of life and also of continuing costs will probably become an integral part of good clinical studies (Good Clinic Retrospective) and possibly find application in national law in the authorization of drugs.

Studies that address the costs of therapies, especially of chronic diseases, will be necessary in the future and thus will create the required transparency to guarantee reasonable medical care, taking the cost-benefit ratio and the best possible outcome in the patient’s quality of life into account. Consensus is needed about the relevant end points of psoriasis in clinical studies. There is no adequate pharmacoeconomic overview article as a decisional basis for practice. In particular, additional studies are required especially on the high-price therapies (biologicals, systemic therapies) to enable better pharmacoeconomic assessment. The health system is facing decisive changes, whereby the principle of solidarity must be revised taking into account the demographic development in the population and the ever-increasing range of medical diagnostics and therapies.

References
