2011000490

*Report*

# Assessment of established medical science and medical practice

Approved by the Minister of Health, Welfare and Sport on 5th November 2007

***Publication number*** **254**


***Publication*** College voor zorgverzekeringen
P.O. Box 320
1110 AH Diemen
Fax +31 (0) 20 797 85 00
E-mail info@cvz.nl
Internet www.cvz.nl

***Series number*** 27071300
***Department*** PAKKET


***Authors*** Ms. Mr. P.C. Staal and Ms. Dr. G. Ligtenberg
***Direct line*** Tel. +31 (0) 20 797 87 33/87 95



***Orders*** Extra copies can be ordered via our website (www.cvz.nl) or by phoning the service desk, number +31 (0) 20 797 88 88.

## Contents:

## Establishing this report:

The report was drawn up by:
Ms. P.C. Staal
Ms. G. Ligtenberg
*in co-operation with:*
Ms. M. van Drooge-van Loon
Mr. A.R. van Halteren
Ms. J. Heymans, physician
Professional group of physicians within CVZ
Staff-members of the departments: Package, Disputes and Legal Affairs

A draft version of the report was sent for assessment to a number of external referees. We would like to take this opportunity of sincerely thanking them for their critical comments. These referees are as follows:
Prof. Dr. W.J.J. Assendelft, Public Health & Primary Medicine Dept. of the LUMC;
Prof. Dr. D.E. Grobbee, Head of the Julius Centre for Clinical Epidemiology and Primary Medicine;
Prof. G.R.J. de Groot, Special Professor in Health Insurance Law at the VU;
B.A.J. Jongejan, director of the Health Care Quality Institute, CBO;
Dr. H.M.J. Slot, paediatrician, Secretary of the Science and Education Board and the Quality Order of Medical Specialists.

## Summary

***Package manager***

***Definition of the package***

***General norm: established medical science and medical practice***

***As of 1st January 2006***

***Consistent framework of reference***

CVZ fulfils the function of package manager within the framework of the Health Care Insurance Act (*Zorgverzekeringswet,* Zvw) and the Exceptional Medical Expenses Act (*Algemene Wet Bijzondere Ziektekosten,* AWBZ). One of CVZ's tasks is to define the insurable package in accordance with current laws and legislation. Within this framework CVZ assesses what forms of care will be included in the basic package. One of the core aspects of the Zvw is that the question of which care is covered by the health insurance is determined in part by established medical science and medical practice. This criterion applies since the introduction of the Zvw (as of 1st January 2006) and it took the place of the Sickness Fund Act criterion of whether care is customary. The latter criterion only ever applied to G.P. care and care provided by medical specialists. Since the introduction of the Zvw, the criterion (currently: established medical science and medical practice) currently applies to all forms of care[1]. This requires an assessment framework that is consistent for all forms of care. In this connection, CVZ feels it is important to elaborate upon the way in which the criterion established medical science and medical practice will be verified. That is the purpose of this report.

***Principles of EBM***

***Core of the EBM-method***

CVZ follows the principles of evidence-based medicine (EBM) in order to determine whether care fulfils the criterion established medical science and medical practice. Determining factor for this choice is that it combines both elements that are included in this criterion, science and practice, and moulds them into an integrated statutory standard. Furthermore, it is important that, in addition to international literature, EBM takes published expert opinions into account.
The EBM method focuses on the "careful, explicit and judicious use of the best evidence". The evidence-based requirement does not imply that all medical interventions are expected to provide firm evidence or firm outcome indicators, but that the available evidence has been systematically selected, weighed up and put to use. Central to the method is that a level of

| | |
|---|---|
| | evidence is allocated to the medical-scientific information selected, thereby creating a hierarchy of evidence. Furthermore, the cardinal point of departure of EBM is that, in principle, strong evidence takes precedence over weaker evidence. |
| ***Steps in the EBM-method CVZ decision-making*** | When making an assessment, CVZ follows the steps involved in the EBM method. Important steps, as indicated above, are systematically searching for, assessing and classifying medical-scientific literature. CVZ subsequently adopts a standpoint over the question of whether the care fulfils the norm: established medical science and medical practice. The |
| ***Point of departure: High evidence*** | applicable point of departure for a positive decision is that medical-scientific data with the highest possible level of evidence must be available. Motivated deviation from this |
| ***Justified departure possible*** | requirement is possible. Particularly important is that CVZ justifies their reason for accepting a lower level of evidence. In the report CVZ describes a number of situations in which there is reason to regard medical-scientific data with a lower level of evidence as sufficient to conclude that the care is in accordance with established medical science and medical practice. |
| ***Knowledge and expertise*** | Carrying out the assessment requires adequate knowledge and expertise. CVZ has this, but where necessary they ask for input from external experts on specific matters (in particular the scientific associations of the various professional groups). |
| ***Experience, particularly with med. spec. care*** | The lengthy experience that CVZ already has in assessing medical-scientific research is mainly in the field of care provided by medical specialists. The introduction of the Zvw means that the criterion established medical science and medical practice now also applies to other forms of care. CVZ |
| ***Further development/completion of the assessment task*** | still has to obtain experience with certain interventions. CVZ has set itself the goal of developing and refining their assessment task even further. A transparent and verifiable method of work is vital to this. |

# 1. Introduction

***Package manager***

CVZ fulfils the function of package manager within the framework of the Health Care Insurance Act and the AWBZ. In brief, this means that CVZ assesses what is in the insured package, advises over the question of what should and should not be in the package (advice on additions and removals) and advises on the legislative system. In their report "Package management in practice"[2], sent to the Minister of VWS on 21st December 2006, CVZ elaborated upon how they would interpret their task as package manager.

***Clarification of the package***

***Monitoring adherence to legislation and regulations***

As mentioned earlier, part of the package management function is that CVZ assesses what will be covered by the Zvw. This activity is also referred to as "clarifying the package to be insured". In making this clarification, CVZ looks at current laws and legislation to examine whether a provision should be insured, i.e., whether it should be included in the basic package. Although CVZ's opinions regarding this clarification carry a lot of weight, strictly speaking they are not binding for parties in the field.

This clarification activity has been discussed on various occasions. Clarification always precedes advice on additions and removals. After all, only after determining whether care does or does not belong in the insured package is it possible to think about the question of whether its addition or removal is indicated. Furthermore, within the framework of issuing advice to the Complaints and Disputes Foundation (SKGZ) about disputes concerning insured provisions[3] and advice to health insurers and other interested parties, CVZ examines whether the provision should be included in the insured package. Furthermore, this examination is relevant to the assessment of innovative DBCs that CVZ carries out at the request of DBC Maintenance[4]. Although CVZ's opinion carries a lot of weight, strictly speaking it is not binding.

***Norm: established***

One of the core aspects of the Zvw is that the question of

***medical science and medical practice***

whether care falls under health insurance cover is partly determined according to established medical science and medical practice. This criterion applies since the introduction of the Zvw (as of 1st January 2006) and it has taken the place of the Sickness Fund Act criterion of what is customary. CVZ already has years of experience in examining care according to that criterion. At the time emphasis was on assessing care provided by medical specialists. Since the introduction of the Zvw, the criterion (currently: established medical science and medical practice) also applies to other forms of care. This means that a consistent assessment framework needs to be applied to all forms of care. In connection with the desired transparency and verifiability, CVZ feels it is important to define how they will carry out verification of the criterion established medical science and medical practice. That is the purpose of this report.

***A great deal of experience with med. spec. care***

***New: package-wide***

***Consistent assessment framework***

***Relevant to health insurers***

***and for care-providers***

The method described here is also relevant to health insurers. After all, in individual cases they will have to make a decision, on the basis of a person's insurance, about the question of whether a form of care is covered by the insurance. As stated above, this will partly be determined by the criterion established medical science and medical practice. Health insurers will be able to use the method described here as guidance for their assessment. It is also important that care-providers clearly understand the verification method. It is they – particularly if they have been contracted to provide care by a health insurer – who have to inform patients/insured persons about whether an intervention being offered is in accordance with established medical science and medical practice (and therefore – as long as the other conditions have been fulfilled – covered by the insurance)[5].

***Treatment in CVZ committees***

***Comments from external referees***

A draft version of the report was discussed by the Pharmaceutic Products Reimbursement Committee (CFH) and CVZ's Insurance and Indication Disputes Committee. Comments made by these committees have been incorporated into the report. In addition to this, a draft version of the report was sent to a number of external experts for comments. The

comments received were incorporated into this report during its approval.

***Structure of the document***

The structure of the document is as follows. Section 2 discusses the relevant statutory framework. Section 3 discusses the introduction of the criterion established medical science and medical practice. This section also provides a short review of the Sickness Fund Act. Section 4 is about the difference between established medical science and medical practice and responsible and adequate care and services. Section 5 subsequently discusses the assessment of established medical science and medical practice. Section 6 contains a number of individual points for special attention. The document ends with a number of closing comments (section 7).

## 2. Statutory framework

***Risks to be insured***

Article10 of the Zvw contains a summary of the insurable risks. It is a rough profile of provisions, the right to which must be provided via health insurance[6]. These are the following insurable risks, in particular the need of:

a. medical care;
b. dental care;
c. pharmaceutic care;
d. medical aids;
e. nursing;
f. welfare;
g. residence in relation to medical care;
h. transport.

***Translation into insured provisions***

The insurable package is regulated in and by virtue of article 11 of the Zvw. That article regulates which provisions should be provided by health insurance and obliges health insurers to include these provisions in the health insurance/policy and to translate them into insured provisions. The health insurance agreement (policy) that insured persons take out with a health care insurer provides them either with the right to care or the right to the reimbursement of the costs of care.

***Bvz provides detailed regulation on content/quantity***

Article 11, third paragraph of the Zvw determines that the content and quantity of insurable provisions (which the health insurers must translate into insured provisions) are regulated in further detail by means of a governmental decree (Order in Council). The Health Insurance Decision (Bzv) is an elaboration of this Order in Council. Article 2.1, first paragraph of the Bzv, refers to articles 2.4 up to and including 2.15 for care to which insured persons have a right. These articles regulate successively medical care (including G.P. care, care by medical specialists, obstetric care, paramedical care and cure-oriented mental health care [GGZ][7]), dental care, pharmaceutic care, medical aids, nursing, welfare (including maternity care), residence and transport. The legislators define some forms of care in more general terms. This applies for example to G.P. care and care provided by medical specialists[8]. Other forms of

***General description***

***Detailed description***

care are regulated in more detail and sometimes one can even speak of a restrictive list[9]. This applies for example to medical aids and extramural pharmaceutic care. A restrictive list at category level applies to medical aids and a restrictive list at product level applies to extramural pharmaceutic care.

***Established medical science and medical practice applies to all forms of care***

For all forms of care – even for the forms of care that are regulated in (more) detail – the content and quantity of care is partly determined by established medical science and medical practice and – where there is no such criterion – by whatever is regarded in the relevant field as responsible and adequate care and services (article 2.1, second para, Bzv). For provisions defined at product level, which applies to extramural medicines, this verification with respect to established medical science and medical practice[10] has already taken place, i.e., before a medicine is included in the restrictive enumeration. In This means that if a medicine is indicated by the Minister (i.e., it has been included in the restricted list), then fulfilment of the norm of established medical science and medical practice has already been established[11].

## 3. Introduction of the criterion established medical science and medical practice

***As of 1st January 2006***

The criterion established medical science and medical practice was introduced on 1st January 2006 (when the Zvw came into force) and took the place of the Sickness Fund Act criterion of usual practice. That criterion, which at that time only applied to G.P. care and care provided by medical specialists, meant that the amount of care was determined by "whatever was usual in professional circles". In jurisprudence this criterion was defined as "sufficiently tested and regarded as reliable by the international world of medical science".[12] The Central Appeals Tribunal (CRvB) announced that, in order to determine this, all relevant data should be taken into account, including in particular literature, scientific research and authoritative opinions of specialists[13].

***Previously criterion of usual practice***

***Two criteria are not the same***

The criterion established medical science and medical practice replaced the usual practice criterion, but the two criteria are not the same, neither with respect to field of application nor with respect to content[14]. As stated previously the usual practice criterion applied only to G.P. care and care provided by medical specialists, whilst the criterion established medical science and medical practice applies to all forms of care. Furthermore another function of the usual practice criterion was as demarcation between G.P. care and the care provided by medical specialists; the criterion established medical science and medical practice does not have this function[15].

***Different field of application***

***Different content***

Furthermore, the criterion established medical science and medical practice is broader than the Sickness Fund Act usual practice criterion. In the first place there is the addition 'and medical practice'. The reason for this addition was to avoid narrowing the package down to only interventions for which scientific evidence was available[16]. In the second place there is the addition "that which is regarded in the professional field concerned as responsible and adequate care and services". According to the Bvz Explanatory Memorandum, the latter criterion involves care and services that have or require little or no scientific status. Under point 4 CVZ goes into more detail

about the criterion established medical science and medical practice and the above-mentioned addition.

## 4. Established medical science and medical practice versus responsible and adequate health care and services

***Criterion adequate health care and services***

***Applies to: seated hospital transport***

***welfare-related medical aids***

To which aspects of the insurable provisions should the criterion established medical science and medical practice apply and to which aspects should the criterion of responsible and adequate care and services apply? As stated above, according to the Bvz Explanatory Memorandum, the latter criterion applies to care and services that neither have nor require a scientific status. This applies in any case to sedentary medical transport. The Bvz Explanatory Memorandum uses this as an example[17]. Furthermore, in their report dated 7th December 2006, CVZ states that no scientific status exists of is necessary for welfare-related aids[18]. Welfare-related aids are aids that promote participation in society, such as aids to communication and mobility and design elements for homes[19]. In general, these welfare-related aids are not worn on the body. The criterion responsible and adequate care and services applies to these aids too. Obviously, there must be a way of determining whether this criterion has been fulfilled. Not scientific evidence, but some other way of checking whether the care/service is capable of doing what it is intended to do and whether the safety and user-friendliness are guaranteed. For example, an answer can be provided by means of a practical evaluation and/or consumer research.

***Criterion established medical science and medical practice***

***Applies to all other forms of health***

The criterion established medical science and medical practice applies to the other forms of care[20]. These forms of care involve actions and forms of guidance that are intended to directly promote the health of individuals in the broadest sense, or to limit or mitigate any deterioration. The usefulness of these actions and guidance, because of their possible major impact on individual, must have been proven scientifically or there must be other grounds for being certain they are useful and will not cause any unwanted harm[21]. Forms of care that fall into this category are: medical care (including G.P. care, care provided by medical specialists, obstetric, paramedical care and GGZ that focuses on healing[22]), dental care, extramural pharmaceutic care, care involving health-related medical aids,

***care*** nursing and residence[23]. The criterion established medical science and medical practice applies to these forms of care[24].

## 5. Method for monitoring established medical science and medical practice

***Content of Section 5***

This section discusses the following aspects. In 5.a CVZ describes which method of assessment they use and their reason for choosing that method. CVZ subsequently describes the outlines of the chosen method (5.b). Next is a description of CVZ's chosen points of departure in applying the chosen method (5.c). Section 5.d. discusses CVZ's decision-making. 5.e discusses a number of special aspects.

### *5.a. Chosen method*

***Principles of EBM***

In determining what should be regarded as established medical science and medical practice, CVZ applies the principles of evidence-based medicine (EBM). The EBM-method originated in clinical practice and can be defined as follows:

***Definition EBM-method***

"Evidence-based medicine is the careful, explicit and judicious use of current evidence for making decisions for individual patients. The practice of evidence-based medicine implies the integration of individual clinical expertise with the best external evidence available from systematic research. The preferences, desires and expectations of patients play a central role in decision-making"[25]. External evidence refers to the results of valid and relevant clinical research.

***Guideline for practising physicians***

EBM was primarily developed as a guideline for practising doctors when making clinical decisions about individual patients. However, the method has found a wider application, for example, in the development of guidelines by professional associations of care-providers[26] and in policy development in the field of health care[27]. *Individual* patient preference, which is automatically involved in clinical decisions about individual patients, hardly plays any role at all in policy development.

***Currently a broader application***

***EBM useful for determining***

It is also easy to use the EBM-method in order to determine whether care fulfils the Zvw criterion of established medical science and medical practice. CVZ takes into account that the criterion established medical science and medical practice is a

***established medical science/medical practice***

single integrated statutory measure[28]. The EBM-method combines both elements. After all, it forms the integration of good medical practice and scientific insights. Furthermore, an important factor is that the EBM-method involves both the assessment of *international* literature and scientific research and information on published expert opinions[29]. By keeping to the EBM method of working, CVZ is also fulfilling the requirement laid down by the CRvB within the framework of the usual practice criterion in the days of the Sickness Fund Act, i.e., that in making their assessment, CVZ must take all relevant information into consideration, including, in particular, literature, scientific research and authoritative opinions of specialists[30] (see above, section 3).

## *5.b. Evidence-based medicine (EBM)*

***Making use of the best evidence***

As indicated, the EBM-method focuses on "the careful, explicit and judicious use of current best evidence". Evidence-based does not mean that firm evidence has to exist for all medical interventions, but it does mean that the available evidence has been systematically selected, weighed up and used. Furthermore, it is important to emphasise that EBM does not means that attention will be given only to 'hard' end-points , such as morbidity and mortality. More 'modest' end-points, such as quality of life, patient satisfaction and the experience of patients and care-providers, will also be included in the assessment. Obviously, here also, research and reports must have been carried out in a scientifically responsible manner. In this way experience-based practice is also involved in the assessment[31].

***Allocating "levels of evidence"***

The core of the EBM-method is that the selected medical-scientific information is allocated a cogency level (allocating "levels of evidence"), which results in a hierarchy of evidence. Making this hierarchy transparent is a transparent way of indicating the strength of the scientific evidence. Furthermore, the cardinal point of departure for EBM is that, in principle, strong evidence takes precedence over weaker evidence.

***EBM steps:*** The EBM follows these four steps :

***Formulating the question***

- ***Formulating the question to be answered.*** It must be formulated so that relevant literature can actually be found and irrelevant literature is ignored[32]. This is an initial selection, which can be further refined if necessary;

***Literature search***

- ***Structured search for literature.*** A large number of databases are available. Important ones are the databases of Medline/Pubmed and the Cochrane Library and EMbase[33]. In addition, it is relevant to be acquainted with national and international guidelines, such as those of the CBO or as found in the Guidelines International Network (GIN) and in the Guideline Clearing House of the Agency for Healthcare Research and Quality;

***Selecting literature***

- ***Selecting the literature found.*** A (detailed) selection of relevant studies takes place according to various criteria, which must have been properly and transparently defined prior to the selection. Examples of criteria are the follow-up duration, the degree of relevance of the end-points and the composition of the study population.

***Assessing literature***

- ***Assessing the selected literature****.* The assessment of the study described can be divided into:
  - the (internal) validity[34];
  - its importance (both the size and the relevance of the effect)[35];
  - its applicability[36];

***Classifying literature***

- ***Classifying the literature assessed..*** On the basis of the final assessment, each study is classified according to the level of evidence, using the following classification (reproduced here only for therapeutic interventions):

  A1: systematic review of at least two A2-level studies carried out independently of one another;
  A2: sufficiently large, high quality randomised double-blind comparative clinical study (RCT);

B : comparative study, though not with all A2 characteristics;
C : non-comparative study;
D : experts' opinion.

***Formulating conclusion(s)***

- ***Formulating one or more conclusions.*** This step is about having to determine which conclusion(s) can be drawn based on the literature that has been assessed and classified[37].
  The (methodological) quality of the studies was determined for all levels of evidence (from A1 up to and including D). This is weighed up in decision-making. It is also possible that more than one systematic review has been published for a given intervention, with differing conclusions. In that case the quality of the reviews will be the deciding factor[38].

## *5.c. CVZ's points of departure for assessments*

***Points of departure when following EBM-steps***

In determining whether care fulfils the established medical science and medical practice criterion, CVZ keeps to the steps described in brief above. CVZ takes the following points of departure into account:

***Comparing standard/usual treatment***

- CVZ assesses the intervention to be examined in comparison with the standard or usual treatment[39], including both efficacy, effectiveness, and side effects or other undesired effects in the comparison. Experience, applicability and ease of use can also be included in the assessment[40].

***Systematic reviews***

- Where possible CVZ will use or expand upon qualitatively good systematic reviews of randomised studies on the subject. Such reviews have the highest level of evidence. If a systematic review is available that fulfils the quality requirements, then it is sufficient to check whether other

additional studies have appeared since carrying out the literature search for the review. The studies included in the review and the additional studies are then assessed jointly.

***Peer-reviewed publications***

- In principle, for their assessment of established medical science and medical practice, CVZ uses only published and peer-reviewed literature[41].

***Specific regulations for assessing medicines***

- The Health Insurance Regulation includes rules for the assessment of medicines (assessment of mutual replaceability and therapeutic value). For example, article 2.39 of the Health Insurance Regulation provides a summary of the data to which attention will exclusively be given when indicating medicines. This is explained in more detail in the brochure "Procedures for the assessment of extramural medicines"[42]. For example, it indicates that in principle, when assessing medicines, no attention will be given to: 1) opinions of experts consulted by the registration-holder and 2) "expert reports" used during registration, unless no EPAR/NPAR is available[43]. This involves a special circumstance for the assessment of medicines.

***EBM-guidelines***

- Where possible, CVZ makes us of existing (international) EBM-guidelines. It is important to determine the quality, the possibility of being outdated and the independence of these guidelines.

***Insurance status abroad***

- Where possible, CVZ considers the insurance status abroad of the care being assessed[44]. After all, in legal decisions about the usual practice criterion (current criterion: established medical science and medical practice), the question of whether the form of care is included in other member states' social insurance package is significant. See also point 5.d.2.
  Decision-making on the package will always be based on current Dutch legislation. Extensive additional legislation applies to forms of care with a positive list, such as, for example, pharmaceutic care. This does not call for

comparison with the situation abroad.

## 5.d. CVZ's decision-making over established medical science and medical practice

***Health care provisions based on established medical science/medical practice***

CVZ gives its opinion on the question of whether care (for certain indications) is part of established medical science and medical practice. The answer is either positive or negative. Unlike when designing guidelines, CVZ does not make any recommendations.

***Equivalence or added value***

The intervention that is to be assessed should be equivalent to the standard or usual treatment or it should have added value. This applies both to efficacy and to undesired effects. If the conclusion of "equivalence" or "added value" is based on the data assessed, then the care is in accordance with established medical science and medical practice. If the conclusion is that the assessed intervention is not at least equivalent, then the standpoint is that the care does not fulfil the established medical science and medical practice requirement.

***Higher evidence takes precedence over lower evidence Lower evidence should not be ignored (due to side effects)***

If studies have the same outcome indicators, in principle evidence of a higher level takes precedence over lower level evidence. However: reports of severe side effects in particular may have a low level of evidence (case reports). This (low level) evidence must not be ignored, but included in weighing up whether there is a proper balance between efficacy and side effect.

CVZ's approach can be described as follows:

***Concordance outcomes: unequivocal decision***

- The availability of one A1-level[45] study or at least two A2-level studies with concordant results is, in principle, sufficient for an unambiguous decision (conformity/non-conformity with established medical science and medical practice). One should always check for the presence of conflicting evidence of a lower order and the possible reasons for this. This is particularly important for severe side effects.

***Not in the event of discordant outcomes***

If several equivalent systematic reviews or RCTs with discordant results are available, then an unambiguous decision cannot be taken. In this case the presence of lower order evidence that supports the results of one or more of the discordant reviews/RCTs may form the deciding factor.

***Involve lower evidence in assessment***

- Where no A1 level study or (completed) studies A2-level studies have been published, CVZ will include evidence of a lower order (B, C and D-level studies) in their assessment. As indicated above, EBM is not limited to randomised trials, meta-analyses or systematic reviews; a positive decision can also be made based on lower evidence. In that case a number of conditions/comments apply:

***Conditions***

- the results of relevant studies and sources must be consistent and up-to-date;
- it is important to find out why no higher level evidence is available;
- there must be plausible, important reasons why there is no evidence of the highest level. Only then can a conclusion based on lower evidence be drawn, that this is a case of care that conforms with established medical science and medical practice. Below CVZ goes into more detail about the arguments that can be brought forward.

***No arguments for lack of RCTs***

An illustrative example:

In 2006 CVZ assessed the intervention "endovenous laser treatment of varicose veins"[46]. At that moment there were no RCTs comparing the efficacy of this intervention with the standard treatment over a long-term period. Nevertheless, the intervention was already being used on a large scale, partly due to more rapid recovery and cosmetically improved results for patients. CVZ was unable to find any arguments as to why RCTs should not be demanded in this case, and for this reason

they decided that this intervention does not yet fulfil the norm established medical science and medical practice. The results of an RCT are currently expected. As soon as they have been published in a peer-reviewed journal, CVZ will re-assess the intervention.

*5.d.1. Lower evidence*

***Positive decision on grounds of lower evidence***

In the following situations, a positive decision can be made on the grounds of lower evidence. These are situations in which it has been established that no (additional) RCTs can be demanded and for which the lower evidence is so convincing (consistent and up-to-date) that the conclusion can be drawn that the care being assessed fulfils the established medical science and medical practice requirement.

***RCT requirement: non-ethical***

These are the following situations:

- interventions whereby it would not be ethically responsible to carry out (randomised) research. This applies to interventions involving persons unable to give their informed consent (children, people suffering from dementia, the mentally handicapped) and for interventions that have to be carried out in ICs and in acute life-threatening situations. Exceptions to this are therapeutic research whereby the study can benefit the trial subjects themselves and non-therapeutic group-related study. This is where a study cannot be carried out without the participation of the group to which the trial subjects belong, the burden is acceptable and the risks for the trial subjects are negligible.

***Rare disorder: RCTs not required***

An illustrative example:

In 2006 CVZ assessed the intervention "early intensive neurorevalidation in children with a vegetative or low level of consciousness"[47]. This was a relatively short-term intervention both diagnostically and therapeutically. Due to the small number of patients (± 40 per year), the fact that they were unable to give consent and the fact that this was an extremely serious disorder, CVZ decided that no randomised studies

could be demanded. Descriptive studies were available over a cohort of patients, and comparison took place with historic controls. CVZ deemed this sufficient to decide that this care conformed with established medical science and medical practice.

***Blind study not possible***

- interventions whereby blinding is impossible. This is often the case for surgical interventions. For medical aids also, it is not always possible to fulfil all the requirements of an RCT. In particular the "double blinding" requirement is often not feasible. In that case, the following characteristics of an RCT are feasible: control group that undergoes the standard treatment, randomising test persons over the intervention group and the control group, sufficient test persons, sufficiently long study period and relevant outcome indicators.

***Low prevalence***

- interventions involving an indication group with an extremely low prevalence (rare disorders).

***Starting RCT outdated***

- interventions for which it is too late to start an RCT. This is the case, for example, when an intervention has already become well established, so that patients can be expected to refuse to co-operate in randomisation. In such cases neither will researchers generally be motivated to start up (an) RCT/RCTs.

***Interventions that have existed for longer***

- interventions that have been in use for a long period of time and for which international consensus exists about their efficacy, but for which no randomised study has been done in the past. The said international consensus is based on lower evidence.

An illustrative example:

***Intervention established: starting RCT unrealistic***

In 2007 CVZ assessed the metal-on-metal hip resurfacing arthroplasty (MoM HRA hip prosthesis)[48]. This hip replacement method has been applied widely during recent years. In spite of the fact that only 1 RCT has been published, CVZ decided

that this intervention fulfils the criterion established medical science and medical practice. They had two reasons for this: a plethora of other studies were available, in particular non-randomised comparative studies and large cohort studies with a long follow-up. On the grounds of this evidence, the professional groups, both national and international, had started placing such prostheses on a large scale. On the grounds of these data, CVZ assessed that to initiate an RCT would be an unrealistic demand.

***Necessity of good arguments***

For the record, CVZ comments that the point of departure is that a positive decision demands medical-scientific data with the highest possible cogency, but a defended departure from this requirement is possible. In particular it is important that CVZ explains their grounds for accepting evidence of a lower level.

*5.d.2. Comparison with foreign social insurance systems*

***Insurance situation abroad***

CVZ indicated above that, where possible, their assessment will involve the care form's insurance status in other countries. In such a case, CVZ's fixed standpoint is that the mere fact that a (new) treatment was provided in accordance with the legislation of the country where the treatment in question took place, without any evidence, is insufficient to reach the standpoint that the care fulfils the established medical science and medical practice requirement.

***Often no decisive role***

As some other social health insurance systems also use (among other things) established medical science and medical practice as a factor to determine the content and size of the package, in a specific case it may be important to investigate which (medical) considerations played a role in the package decision in the country concerned. This could be relevant in situations in which, though evidence was available, it was not of the highest level.

***Considerations abroad sometimes relevant***

*5.d.3. Relevant knowledge and expertise*

***Not a form-filling***

The examples provided show that the assessment of whether a care intervention conforms with established medical science and medical practice is not a simple form-filling exercise but

***exercise***

must be assessed on its merits and this demands sufficient relevant knowledge and expertise. This is in particular care-related expertise and insight into clinical epidemiology. CVZ has this knowledge and expertise and is continually working towards further improvements[49]. This does nothing to diminish the desirability of asking for external input, in particular from experts on specific subjects. CVZ discusses this in more detail below.

***Care-related knowledge and expertise required***

*5.d.4. Consultation experts*

***For the benefit of quality and basis of support***

In order to promote the quality of CVZ's assessment, and also to create a broad basis of support in practice, it can be desirable to obtain relevant and practical knowledge from the relevant Dutch scientific associations. Due to their specific expertise and experience in practice, they are able to supplement any relevant information and literature that may be missing or assist in the technical interpretation of data. Furthermore, where applicable, they can provide (additional) information about (reasons for) the absence of scientific evidence at the highest level. This can also help overcome possible publication-bias (the circumstance that negative results of a study are not always published). After all, the professional group will usually be aware if publication bias is involved.

***Seeking knowledge among professional groups***

In particular CVZ will approach the scientific associations with this type of question, rather than individual experts. After all, this will help realise input that is broadly supported. CVZ comments that their interest is of course in the input of an association from a scientific perspective. Comments relating to the promotion of professional interests – another task fulfilled by scientific associations – should therefore be excluded from consideration.

*5.d.5. Transparent and verifiable decision-making*

***Substantiation of***

CVZ will substantiate their standpoint in relation to established

***standpoint***

medical science and medical practice.

***Verification/ evaluation of method***

In brief, the following matters will be included in that substantiation:

- the question posed;
- the criteria that play a role in the literature search and selection (outcome indicators, follow-up, patient population), followed by the results;
- the criteria that play a role in the assessment (efficacy, cost-effectiveness, side effects/undesired effects) followed by the results (quantitative and qualitative);
- the grounds for the conclusion based on the above-described approach.

This working method will obviously be examined and assessed regularly.

## *5.e. Specific matters for (possible) discussion during assessment*

*5.e.1. Technical variant or innovation*

***Technical variant/innovation***

***Ruling on medical science/medical practice necessary?***

CVZ is sometimes faced with the question of whether there is or is not any reason to make a statement on established medical science and medical practice. This happens in cases of a technical variation as part of care that has already been included in the package, for example, an implant in back surgery which has been altered (in details), or a new type of hip prosthesis. A new treatment technique may also be involved. For example, the recent introduction of endoscopic surgery.

***Assessment per case***

***Assessment necessary in case of relevant***

CVZ determines per case whether assessment of the intervention, including the technical variant/innovation is required or not. The standpoint adopted by CVZ is that if the alteration can be assumed to have (possible) consequences for the efficacy, effectiveness, safety or general applicability of the intervention, there is reason to assess the altered intervention and make a statement about established medical science and

***consequences***

medical practice. Indications of the involvement of one or more of the said consequences are:

- the professional group is researching or has already researched the matter involved;
- a current guideline is paying particular attention to the technical variant/innovation and expressed considerations in relation thereto;
- the technical variation/innovation has financial consequences or could form a reason for determining a separate tariff.

***Consultation professional group***

Here also, consultation with the professional group can lead to clarity regarding the above-mentioned points.

For the rest, this could occur for any forms of care and each time CVZ will have to answer the question of whether it really is an innovation or just an inconsequential variation. Drawing up the package agenda also involves such questions. CVZ is currently busy elaborating upon the points of departure for determining agenda points and priorities.

*5.e.2. Technical variation in medical aids (me-too products)*

***No central assessment***

CVZ does not carry out a (central) assessment for so-called me-too products. Me-too products are products with the same working mechanism and the same treatment goal as products that fall under the medical aids category mentioned in the Health Insurance Regulation and which fulfil the criterion established medical science and medical practice. As the working mechanisms and treatment goals of these new products are (largely) comparable with products already included in health insurance, they are not subjected to a separate, central assessment by CVZ. It is then up to the health insurers to determine whether they will supply or reimburse these newer versions. Where there is doubt as to whether a me-too product is involved, the manufacturer can contact CVZ and/or the health insurer can consult CVZ by submitting an application for advice. CVZ will then issue a statement on the question of whether a me-too product is involved[50].

***Up to the health insurers***

*5.e.3. Difference in level of evidence with a patient group with the same diagnosis*

***Lack of cost-effectiveness data***

If there are (as yet) no – or relatively few – data on long(er)-term cost-effectiveness data for a given intervention, then this will generally result in the conclusion that the intervention cannot be regarded as at least equivalent with the standard treatment. However, it may be the case that an intervention is conform established medical science and medical practice for a sub-group of patients with the same diagnosis. This could be the case for a sub-group of patients who do not benefit from the standard treatment (contraindication) and for whom nothing else is available except the intervention concerned. The limited efficacy evidence will be deemed acceptable for that sub-group. There must be sufficient grounds for the difference in approach within the patient group, for example, using arguments (provided by the professional group) based on the pathophysiology of the disorder.

***Health care according to status quo re medical science/medical practice for sub-group***

***Motivate difference in approach***

An illustrative example:

***Implantable insulin pump only health care in accordance with medical science/medical practice for diabetes sub-group***

Insulin can be administered to diabetes patients intraperitoneally instead of subcutaneously, using implanted insulin pumps. Limited research has been carried out with this method of administration: in short-term studies it proved capable of regulating the diabetes properly. However, there are no long-term studies to prove that this method of administration is just as effective as the usual one in respect of prevention/delaying the complications of diabetes mellitus. Furthermore, there are reports of complications, such as infections and material failure. For this reason CVZ has concluded that intraperitoneal administration by means of an implanted pump is an insured provisions only for patients for whom subcutaneous administration of insulin is no longer possible. In this case, therefore, data with a lower level of evidence are considered sufficient because these are patients for whom there is no other means for administering insulin[51].

*5.e.4. Cost-effectiveness data*

***Cost-effectiveness data***

In principle, cost-effectiveness data do not play a role in assessing established medical science and medical practice. For example, two interventions may exist for a single disorder.

***Purchasing by health insurers***

***Supply by care-providers***

If both are just as effective, then both fulfil the norm established medical science and medical practice. In principle, it is up to the health insurer to purchase the most effective care (the Zvw is designed so that health insurers can make such a selection, thereby encouraging care-providers to work as efficiently as possible). If proper cost-efficacy analyses are carried out, then care-providers themselves will probably make a choice, and the intervention with the least favourable cost-efficacy ratio will eventually become obsolete. Over the course of time, that care will eventually no longer fulfil the norm established medical science and medical practice.

***Percutaneous angioplasty versus bypass operation***

An illustrative example:

In the general population, due to efficacy and cost-effectiveness aspects, percutaneous angioplasty (PTCA) is preferred to a bypass operation for certain forms of coronary disease. However, in the long term percutaneous angioplasty is less effective for patients who suffer from coronary disease and diabetes, and a bypass operation is recommended. In other words, a generally less effective intervention can be indicated for a sub-group of patients. Preferably, this should be substantiated by pathophysiological mechanisms.

*5.e.5. Organisational aspects of health care*

***Organisational aspects***

***Sometimes integrated in medical science/practice***

In principle, assessing the criterion established medical science and medical practice does not involve organisational aspects of care (such as, e.g., logistics in operating theatres). Improved logistics in operating theatres can increase efficiency in the deployment of personnel, funds, etc., but they will generally have no effect on the prognosis for the patient. However, situations are imaginable in which this is the case. For example, setting up an acute stroke unit in a hospital. Improved procedures for patients with a CVA can lead to improved prognosis, fewer admissions to nursing homes, etc. Demonstrating this with proper comparative study is a reason to regard such organisational aspects as established medical science and medical practice. After all, in this case the maximum efficacy of treatment is inextricably linked to an optimal procedures set-up.

# 6. Other points for attention interest

## *6.a. What is the definitive moment?*

***Definitive moment is the moment at which treatment is undergone***

Under the Zvw, which involves property insurance subject to public law, the moment at which an insured person undergoes medical treatment is the definitive moment. If at that moment the treatment is in accordance with established medical science and medical practice, then the treatment falls under the person's health insurance cover[52] – as long as any other stipulations have been fulfilled, and in as far as the care is otherwise regarded as an insured provision[53].

***Moment of publication is the definitive moment***

Furthermore, there is the question at which moment care initially fulfils the criterion established medical science and medical practice (and therefore the moment at which the care initially falls under the cover of the insurance). According to a ruling of the CRvB, the definitive moment is when the results of the scientific research relevant to the reversal were made known to the professional group by publication[54]. There will not always be immediate recognition that a given publication has consequences for assessing established medical science and medical practice. The fact that the form of care being assessed now fulfils the criterion established medical science and medical practice will often only become clear at a later date, when there is a reason for carrying out a (new/additional) literature search. The turning point may therefore be in the past and the form of care being assessed had become subject to insurance cover at an earlier date. This could mean that an insured person who objected to the refusal of a provision or its reimbursement, may eventually become eligible, retrospectively, for that care or its reimbursement.

***Turning point sometimes in the past***

## *6.b. General statutory indication requirement*

***General assessment***

Established medical science and medical practice requires a general assessment of the care form. If the conclusion is that the care form fulfils this criterion, then it should be included in

| | |
|---|---|
| ***Assessment of circumstances (indication-requirement)*** | the insured provisions (unless the legislator explicitly excluded the care or failed to explicitly indicate it[55]). This does not automatically mean that an insured person actually has a right to the provision. Article 2.1, third paragraph of the Bzv determines that an insured person only has a right to a form of care or service in as far as he can reasonably be said to rely upon a given amount of that care. This means that attention must be paid to the individual circumstances of a case. Is the requested care indicated in a given case[56]? The costs of the requested treatment can be weighed up against the added value of specific treatment for the insured person in comparison with other possible treatments. |

### *6.c. AWBZ*

| | |
|---|---|
| ***Established medical science/medical practice does not apply for the AWBZ*** | The criterion established medical science and medical practice is incorporated as such in the Bzv (which is dependent upon the Zvw). This does not apply to insurance regulated in the AWBZ. Nevertheless, this criterion also applies in the AWBZ for the function treatment and activating guidance. CVZ advice on disputes over AWBZ indications often involve the extent to which an intervention is evidence-based. |
| ***Sometimes applicable*** | |

An illustrative example:

| | |
|---|---|
| ***Insufficient evidence for dolphin therapy*** | In 2006 CVZ assessed whether the so-called dolphin therapy is sufficiently evidence-based. CVZ adopted the standpoint that this is not the case. According to CVZ, because the efficacy of dolphin-therapy does not seem to have been sufficiently demonstrated, the professional group has not assessed this method as effective. For the moment, within the framework of the AWBZ, the interpretation is that this is not an effective form of care[57]. |
| ***Broader application needed*** | The established medical science and medical practice criterion should also be used for other AWBZ functions than treatment and activating guidance. This need is all the more imperative, due AWBZ-care being transferred to the Zvw as of 1st January |

2008[58]. We need to marshal our thoughts on the meaning and the consequences of applying the established medical science and medical practice criterion to (what is currently still) AWBZ-care[59].

## *6.d. The package principle effectiveness*

***Package principles***

In drawing up our advice on additions (e.g., of new forms of care) and removals from the package of care, CVZ applies four package principles: necessity, efficacy, cost-effectiveness and feasibility. These principles are described in the report "Package management in practice", which CVZ published and sent to the Minister of VWS on 21st December 2006[60]. In order to assess the effectiveness of a form of care, CVZ sets to work in the same way as when assessing established medical science and medical practice. Therefore, the assessment framework described in this report also applies to assessments of the package principle efficacy.

***Comparable method***

# 7. Closing comments

***Statutory task***

As package supervisor, it is CVZ's task to assess whether care fulfils the statutory norm established medical science and medical practice. CVZ has years of experience examining care in relation to this criterion (previously: the criterion of usual practice). As stated above, in the past the emphasis was on assessing medical-specialist care. New aspects are that the introduction of the Zvw means that the criterion applies to the entire package and also, therefore, that the assessment method (that had already been developed) has to be used for the entire package. The fairly recent expansion to include all forms of care means that CVZ will have to gain experience with certain interventions and develop and refine its assessment task. In this respect the increased attention currently paid to experience-based practice is rather interesting. The process of development and refinement will involve a regular examination and evaluation of the working method and the points of departure. Only by presenting itself as an organisation that is continually learning and that is open to verification will CVZ be able to optimise its role as package supervisor even further.

***A great deal of experience with med. spec. care***

***New: package-wide***

***Further development/completion***

**Health Care Insurance Board**
**[*College voor zorgverzekeringen*]**

*Chairman of the Board of Directors*

Dr. P.C. Hermans

References and notes:

[1] There are two exceptions. The criterion established medical science and medical practice does not apply to seated medical transport or welfare-related aids. See also section 4.
[2] Report on package supervision in practice. Diemen: CVZ, 2006. Publication no. 245 [in Dutch].
[3] See article 114 Zvw.
[4] Fixed method for the DBC-assessment is that if CVZ establishes that a new care form (for which a DBC has been drawn up) fulfils the criterion established medical science and medical practice (i.e., it is effective), CVZ goes on to assess whether it also fulfil the other package principles. Depending on the results of this assessment, CVZ could advise the Minister to exclude a care form or limit its application.
[5] See the explanation of articles included in article 2.1 of the Health Insurance Decree (Bull. Acts & Decrees. 2005, 389).
[6] See note 6 of the article by Groot GRJ de. Established medical science and medical practice. Tijdschr Gezondheidsrecht 2006; 30(5): 326-50 [in Dutch].
[7] The GGZ, which focuses on healing, will be transferred from the AWBZ to the Zvw as of 1st January 2008.
[8] One can also refer to an open definition of the provision to be insured. This means, for example, that a new care form which is effective (fulfils the established medical science and medical practice criterion) and which is care as normally provided by medical-specialists (and which is not explicitly excluded), should, in principle, be included among the provisions to be insured. In other words, new care forms, as long as they fulfil the statutory requirements, are automatically included in the package. Treatments that have clearly become obsolete will automatically be dropped from the package.
[9] In that case one can also speak of a closed system of provisions to be insured.
[10] When assessing pharmaceutic care, this is also referred to as: testing the therapeutic value.
[11] See the pleading notes of Prof. G.R.J. de Groot dated 4th July 2007 (cause list no. 2007/01755) concerning CVZ/NESS Nederland B.V. : "If provisions are defined at product level, as in the case of medicines, there is no room for application of the established medical science and medical practice criterion. A medicine is either included on the limited list of insured medicines, or it is not."
[12] See HvJ EG 12th June 2001, C-157/99, RZA 2001/115 (Peerbooms-Smits ruling).
[13] See CRvB 30th September 2004, RZA 2004/179. Here, the concept of "specialists" is wider than medical specialists.
[14] This means that the terms "customariness criterion" and "usual care" should no longer be used. The criterion established medical science and medical practice etc. is the current statutory criterion and is therefore the only criterion that should be used.
[15] See the explanation of articles in article 2.1 of the Health Insurance Decree (Bull. Acts & Decrees. 2005, 389).
[16] Bull. Acts & Decrees. 2005, 389, p.36.
[17] See the explanation of articles in article 2.1 of the Health Insurance Decree (Bull. Acts & Decrees 2005, 389).
[18] Ness Handmaster Report. Diemen: CVZ, 2006. Publication no. 246 [in Dutch].
[19] Aids to communication are summarised and defined in article 2.26 of the Health Insurance Regulation. This covers computers, typewriters, telephones etc. Aids to mobility are summarised and defined in article 2.17 of the Health Insurance Regulation. These include, for example, crutches, rollators and mobility chairs. Design elements for homes are summarised in article 2.33 of the Health Insurance Regulation. Examples are tables and chairs that are adapted to functions limitations.
[20] The Health Insurance Decree regulates many forms of care by referring to "care as normally provided by ….. ". This phrase is usually related to established medical science

and medical practice. The idea is – or so it is claimed – that this criterion does not apply in combination with "normally provided". However, this is an incorrect interpretation of the law. The choice for the phrase "normally provided" is prompted on the one hand by the desire to provide a function-oriented definition, whereby the legislator does not impose compelling instructions per care form as to which care provider is allowed to carry out which form of insured care. However, on the other hand, the choice is prompted by the desire to give greater clarity about the content of the insured care, by referring to certain types of care-providers in the definition. There is nothing implying that the choice for this phrase is prompted by the idea that this would limit the application of the criterion established medical science and medical practice to those case in which the legislator has used the words "normally provided" in the description of the provision to be insured. See the defence on appeal dated 27th February 2007 from Prof. G.R.J. de Groot (cause list no. 2007/01755) concerning CVZ/NESS Nederland B.V. See also the ruling of the Appeals Court in Amsterdam dated 11th October 2007, concerning CVZ/NESS Nederland B.V. (cause list no. 175/07 SKG).

[21] Blood transfusions form an example of the latter (established beyond doubt). There is a lack of scientific studies showing that a blood transfusion is an effective treatment in certain situations. However, medical practice has demonstrated sufficiently that administering blood is useful in certain situations. Consensus exists on this matter within the international world.

[22] The GGZ, which focuses on healing, will be transferred from the AWBZ to the Zvw as of 1st January 2008.

[23] Where the question arises of whether a stay in a hospital or another care institution is medically necessary, it will have to be answered on the basis of scientific literature. Is clinical treatment, i.e., treatment accompanied by an admission, medically indicated according to established medical science and medical practice?

[24] Care and admission also involve non-medical aspects. Admission to a hospital for treatment by a medical-specialist automatically involves being provided with food and beverages. Furthermore, there will have to be provisions for staying in a hospital. This means there will have to be a bed, a toilet, a cupboard, etc.

[25] Offringa M, Assendelft WJJ van, Scholten RJPM. Introduction to evidence-based medicine. 2nd revision. Dr. Houten: Bohn Stafleu van Loghum, 2007.

[26] Such as doctors, paramedics and nurses.

[27] Examples are: expanding the vaccination programme and the question of whether screening for diabetes among the general population makes sense.

[28] In other words, these are not two separate criteria, science and practice.

[29] See also point 5.c.

[30] See also point 5.c.

[31] The CBO has started structured patient participation in the development of guidelines. See the CBO website.

[32] An aid to translating the question in a method for searching international literature is the PICO-method. This stands for:
P = patient population
I = Intervention or diagnostic test
C = control intervention or reference test
O= outcome.
In addition to the PICO, filters can be used: for example, the year from which the search applies (if an addition is required to a systematic review that is several years old). Both free text words and controlled thesaurus terms are possible (e.g. MeSH = Medical Subject Headings, Medline's thesaurus with controlled terminology).

[33] The most frequently used databases for literature searches are: Medline via Pubmed, the Cochrane Library, Embase drugs and pharmacology, INAHTA, CBO and Clinical Evidence.

For information on current trials one tends to use: Clinicaltrials.gov. Sites for information in the field of foreign policy are: NICE, AETNA, CIGNA, Regence Group and Medicaid (CMS).

[34] *Validity* means that the study actually did measure the effect of the intervention. Did randomisation take place, and if so, did it go well, was it a blind study and if so, who was blind (patient, treating physician, person assessing the effects?), who complete was the follow-up, was (in cases of controlled studies) the intervention the only variable in the study legs?

[35] The *importance* of a study is reflected by the size and the relevance of the effect and the precision of the estimation of the effect (e.g. a difference score, the relative risk [RR], the odds-ratio [OR], and the reliability interval). In assessing diagnostic tests, the terms used are sensitivity and specificity.

[36] The *applicability* of study results depend on the similarities between the study population and the patient population, the advantages and disadvantages of treatment for the patient and medical ethical aspects.

[37] For an extensive description of the EBM method, CVZ suggests the EBRO-instructions (Evidence-Based Guideline Development, Manual for members of working groups, November 2006). This manual can be found on www.cbo.nl. CVZ also suggests the book written by M. Offringa, W.J.J. Assendelft en R.J.P.M. Scholten. Introduction to evidence-based medicine. 2nd revision, Dr. Houten: Bohn Stafleu van Loghum, 2007.

[38] See, for example Jadad AR, Cook DJ, Browman GP. A guide to interpreting discordant systematic reviews. CMAJ 1997; 156: 1411-6.

[39] Standard treatment is the treatment that is regarded in daily practice as first choice treatment, the efficacy of which has been established. Usual treatment exists when it is used in practice on a substantial number of patients with the indication concerned (taken from: *Farmacotherapeutisch Kompas* 2007).

[40] See the *Farmacotherapeutisch Kompas* 2007. Diemen: CVZ, 2007.

[41] This relates to literature that has only been accepted by a scientific journal after a critical assessment by peers.

[42] This concerns a joint publication by the Ministry of VWS and CVZ. It can be found on CVZ's website.

[43] See paragraph 12 of the Procedures for assessing extramural medicines.

[44] Places for finding information in the field of foreign policy include the following sites: NICE, AETNA, CIGNA, Regence Group and Medicaid (CMS).

[45] The qualification A1 can also be sub-divided into A1+ and A1-. The reference indicates that the internal validity of a systematic review is acceptable, for example, if publication bias has been taken into account by also involving unpublished data in the review.

[46] CVZ 20th November 2006, no. 26073455, RZA 2007/12.

[47] Appendix 1.k. of the Package Advice 2007. Diemen, CVZ, 2007: 61-3. Publication no. 248.

[48] CVZ 23rd July 2007, no. 27024808 and no. 27041039.

[49] CVZ provides regular (refresher) courses for their employees who test interventions according to the criterion established medical science and medical practice and those who are involved with the development of the framework for assessment. If first-class specialist knowledge is required, such as for example HTA-expertise, CVZ purchases it.

[50] The term me-too also exists in pharmaceutic care. A me-too medicine is a medicine that is chemically as good as identical to the first product from a given group, but which only differs in one or more chemical sub-groups. Me-too medicines are also assessed by CVZ. Furthermore, such a product is only subject to the insurance if the Minister has designated the product as such.

[51] CVZ 21st May 2007, no. 27013933.

[52] Groot GRJ de. The established medical science and medical practice. Tijdschr Gezondheidsrecht 2006; 30(5): 326-50 [in Dutch].

[53] As indicated previously, a (more) closed system applies for a number of care forms. For example, for medical aids, one can only speak of an insurable provision if the category concerned is designated as a medical aid in the Health Insurance Regulation. A medical aid that is regarded as care in accordance with established medical science and medical practice, is nevertheless not included among the provisions to be insured if the category to which the medical aid belongs is not designated as a medical aid in the said regulation.

[54] CRvB 19th January 2006, RZA 2006/80.

[55] For example, a limited list applies to medical aids and pharmaceutic care. Only designated medical aids and medicines are covered.

[56] Established medical science and medical practice is also the determining factor for the question of whether a patient has an indication for a given care form. This is apparent from the mere fact that medical-scientific research normally provides an answer to the question of whether intervention X is effective on indication Y. In medical-scientific research, an immediate answer can usually be found to the question regarding indication.

[57] CVZ 21st February 2006, RZA 2006/36. See also appendix 1.n. regarding interventions in mentally handicapped children in the Package Advice 2007. Diemen: CVZ, 2007: 81-4. Publication no. 248.

[58] The GGZ, which focuses on healing, will be transferred from the AWBZ to the Zvw.

[59] This discussion is in line with the discussions surrounding the assessment of the package principle "effectiveness" in the AWBZ. See section 4.c. of the Package Advice 2007. Diemen: CVZ, 2007: 22-4. Publication no. 248

[60] Report on package management in practice. Diemen: CVZ, 2006. Publication no. 245.