Zorginstituut Nederland

Specialist medicinal products assessment procedure

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1 Introduction

1.1 Reason and objective

The National Health Care Institute advises the Minister for Medical Care on the quality, accessibility and affordability of the health care package. As a result, the National Health Care Institute issues publications on the working methods and developments within the specific elements of the package management. This report describes how the National Health Care Institute establishes the package management of specialist medicinal products. This will replace the 'Pakketbeheer specialistische geneesmiddelen' procedure (for package management of specialist medicinal products) from 2013[1]. The main adjustments to the assessment procedure are the introduction of the lock procedure and the inclusion of lock candidates using the Horizon Scan for Medicinal Products.

1.2 Specialist medicinal products

Specialist medicinal products are medicinal products that are part of the health care benefit, as defined in the Health Insurance Decision (Bzv) (Article 2.4, with the exception of substances mentioned in Art. 2.1, paragraph k of the Rzv (Health Insurance Regulation) and Annex 0 to the Rzv). Medical care includes, among other things, care such as medical specialists tend to provide. In practice, this means that medicinal products are used under the responsibility of a medical specialist and within the walls of an institution.

Specialist medicinal products are subject to an open system of insurance claims, unlike outpatient medicinal products where there is a closed system (Table 1). An open system of insurance claims means that specialist medicinal products are part of the health care package when they meet the established medical science and medical practice. The legislator does not have to explicitly include these medicinal products in the legislation and regulations first.

Table 1: System characteristics of specialist and outpatient medicinal products

	Specialist medicinal products	Outpatient medicinal products2
Claims system	Open inflow	Medication Reimbursement System (GVS: List 1A, 1B and 2, 3A and 3B of the Health Insurance Regulation)
Legal framework	Medical care, Article 2.4 Health Insurance Decision	Pharmaceutical care, Article 2.8 Health Insurance Decision, detailed in the Health Insurance Regulation
Funding	Diagnosis treatment combinations (DBC-system), add-on benefits	Claim as part of the 'transfer' benefit by a pharmacist

Within the open system, the National Health Care Institute assesses specialist medicinal products on the basis of the principle of risk-oriented package management. This means that only specialist medicinal products that pose such a high risk to the quality, accessibility and affordability of the insured package are assessed. In practice, these medicinal products can be classified into specialist medicinal products that are assessed in the context of the lock procedure and specialist medicinal products that are not placed in the lock but that nevertheless may entail risks according to stakeholders in the field.

Specialised medicinal products placed in the lock

Since 2015 (formalized in the Bzv in 2018), the Ministry of Health, Welfare and Sport (VWS)

[1] *Report 'Pakketbeheer specialistische geneesmiddelen', 2013.* *https://www.zorginstituutnederland.nl/publicaties/rapport/2013/12/03/pakketbeheer- specialty medicines*

[2] *Procedure for assessment of outpatient medicinal products, 2018.* *https://www.zorginstituutnederland.nl/publicaties/rapport/2016/09/09/procedure-beoordeling- extramural medicines*

has taken action allowing new (indications for) specialist medicinal products to be temporarily excluded from the health care package due to a high financial risk. This measure is called the lock procedure, or the lock. During the lock procedure, the National Health Care Institute can assess the medicinal product, after which any financial arrangements and/or other arrangements regarding appropriateness are determined. The lock procedure is further explained in Chapter 2.

'High-risk' specialised medicinal products not placed in the lock

For certain specialist medicinal products that are not assessed for the lock procedure, the stakeholders in the field predict risks with regard to the quality, accessibility and affordability of the health insurance package. For example, there may be doubts about the added effectiveness or affordability of a medicinal product that does not meet the criteria for entry into the lock. In such a case, the National Health Care Institute may decide to carry out an assessment for this specialist medicinal product. However, this is not yet very common in practice. In the coming period, the National Health Care Institute will further shape the 'triage' of medicinal products on the Horizon Scan for Medicinal Products, in cooperation with field parties. The aim is to formulate a uniform framework for the selection and evaluation of these medicinal products. The current report will not go into further detail about the assessment procedure for these non-lock specialised medicinal products.

For the sake of completeness, in addition to specialist medicinal products, the National Health Care Institute also evaluates medicinal products that are entitled to reimbursement from the medicine reimbursement system (GVS; outpatient medicinal products[3]) and medicinal products that are assessed in an international context (EUnetHTA[4] and Beneluxa[5]).

1.3 Customised care through collaboration

Customised solutions are necessary for the package management of specialist medicinal products. That is why the stakeholders have an important role to play. Parties that can be involved in the assessment of specialist medicinal products are marketing authorisation holders, professional groups, health insurers, patient associations, hospitals and hospital pharmacists. During the assessment procedures, these stakeholders are explicitly involved in the composition of the files, the substantive assessments and the societal considerations.

[3] *Procedure for assessment of outpatient medicinal products, 2018.* *https://www.zorginstituutnederland.nl/publicaties/rapport/2016/09/09/procedure-beoordeling- extramural medicines*

[4] *European Network for Health Technology Assessment (EUnetHTA).* *https://www.eunethta.eu*

[5] *Beneluxa.* *https://beneluxa.org/*

2 Specialist medicinal products assessment procedure

This chapter describes the assessment procedure for specialist medicinal products to be assessed in the context of the lock procedure.

2.1 The objective of the lock procedure

From a societal point of view, it is important to make new effective medicinal products accessible to patients without putting an unnecessarily high burden on collective resources. To ensure accessibility for patients and the affordability of care in the long term, measures are needed to reduce expenditure on specialist medicinal products. The lock procedure[6] is a measure that was introduced to combat budgetary problems. The lock procedure allows specialist medicinal products that pose a financial risk to be (temporarily) excluded from the health care package. During the lock procedure, the National Health Care Institute assesses the possible inclusion of the medicinal product in the health care package. Depending on the advice of the National Health Care Institute to the Minister for Medical Care, financial arrangements (to reduce costs) by the Ministry of Health, Welfare and Sport may be part of the lock procedure. In addition, arrangements can be made about the appropriateness of the medicinal product. The lock procedure is concluded when the Minister decides to terminate the exclusion of the medicinal product and to either include the medicinal product in the package or not. The inclusion of a specialist medicinal product in the health care package may also be temporary or conditional.

2.2 Assessment agenda

2.2.1 By placement in the lock

The Ministry of Health, Welfare and Sport uses the Horizon Scan for Medicinal Products as a basis for the selection of lock candidates. The Horizon Scan for Medicinal Products monitors the arrival of new specialist medicinal products or indication extensions that are expected to be authorised for marketing in Europe within 2 years, together with the possible macro costs of this.[7] To get the best and most complete picture of the developments, the formation of the contents of the Horizon Scan Medicinal Products is a collaboration with medical specialists, (hospital) pharmacists, representatives of health insurers and patient representatives. Marketing authorisation holders are also given the opportunity to provide input on their own products. Twice a year (in June and December), the National Health Care Institute will publish this updated medicinal products review online.[8]

Based on the information from the Horizon Scan for Medicinal Products, the Minister for Medical Care carries out a risk analysis and determines which medicinal products are expected to meet the criteria for placement in the lock. These medicinal products are then considered 'lock candidates' in the lock candidate letters sent by the Minister to the Lower House of the Dutch Parliament in the spring and autumn. A medicinal product may be placed in the lock if one or more of the following conditions are met:

- The anticipated macro costs of providing the medicinal product for the treatment of one new indication or several new indications together amounts to €40 million or more per year. All new indications are placed in the lock;
- The expected cost of providing the medicinal product for the treatment of a new indication is €50,000 or more per year and the expected macro costs of such provisions is €10 million or more per year. This indication is also placed in the lock.

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[6] *Bulletin of Acts and Decrees 2018, 131.* https://zoek.officielebekendmakingen.nl/stb-2018-131.html

[7] *Previously, new specialist medicinal products or indication extensions of specialist medicinal products were brought into view through the so-called 'notification' by the marketing authorisation holder. Since 1 June 2019, the notification is no longer in force.*

[8] https://www.horizonscangeneesmiddelen.nl/

The macro costs mean the estimated total annual costs of the provision of the medicinal product for treatment in the context of medical care. This is an assessment of the absolute costs and not a cost increase compared to existing treatments. A new indication includes not only an indication for which a medicinal product is registered, but also off-label use of the medicinal product that is made protocol or standardized by the professional group. The placement in the lock is done within one month of market authorisation or the adoption of the protocol or the standard for the new indication, respectively. One condition for lock candidates is that the medicinal product is designated by the National Health Care Institute as a specialist medicinal product. However, this has not always been definitively established by the National Health Care Institute upon announcement that it has been placed in the lock.

2.3 Assessment process

The assessment process for specialist medicinal products consists of an optional preliminary process, followed by the assessment and a possible appraisal. Figure 1 shows a simplified diagram of the assessment procedure for specialist medicinal products.

2.3.1 Preliminary process

In the preliminary process, marketing authorisation holders can request a preliminary consultation. For this purpose, the marketing authorisation holder must submit a preliminary dossier prior to the start of the assessment. The submission of a preliminary dossier does not require a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA). During the preliminary consultation with the marketing authorisation holder, the preliminary dossier is discussed so that any ambiguities, flaws and problem areas in the dossier are detected early. This enables the marketing authorisation holder to align the dossier to the dossier requirements and other concerns of the National Health Care Institute at an early stage. The submission of a preliminary dossier is therefore highly recommended. No rights can be derived from a preliminary consultation.

The National Health Care Institute can initiate a scoping consultation with field parties if there are substantive questions about the medicinal product within the treatment of the disease. During this consultation, (oral or written) input from relevant parties is requested about ambiguities that the National Health Care Institute identifies in the assessment. Examples of subjects that may be covered during a scoping session are questions about relevant outcome measures, clinical relevance limits, the placement of the medicinal product in the treatment algorithm, the estimation of the number of patients in the Netherlands, the expected market penetration or appropriateness agreements, such as start and stop criteria. Who the relevant parties are and what the scoping is about depends on the dossier/medicinal product. Parties participating in a scoping include the professional groups, patient associations and health insurers. Marketing authorisation holders are not involved in the scoping consultation, as opposed to the preliminary consultation.

Finally, the marketing authorisation holder can apply for scientific advice from the National Health Care Institute at any time. This may include anything that is unclear about the approach of the (preliminary) dossier. Scientific advice is usually provided early in the assessment process, always prior to any preliminary consultation. The scientific advice may be provided orally or in writing[9].

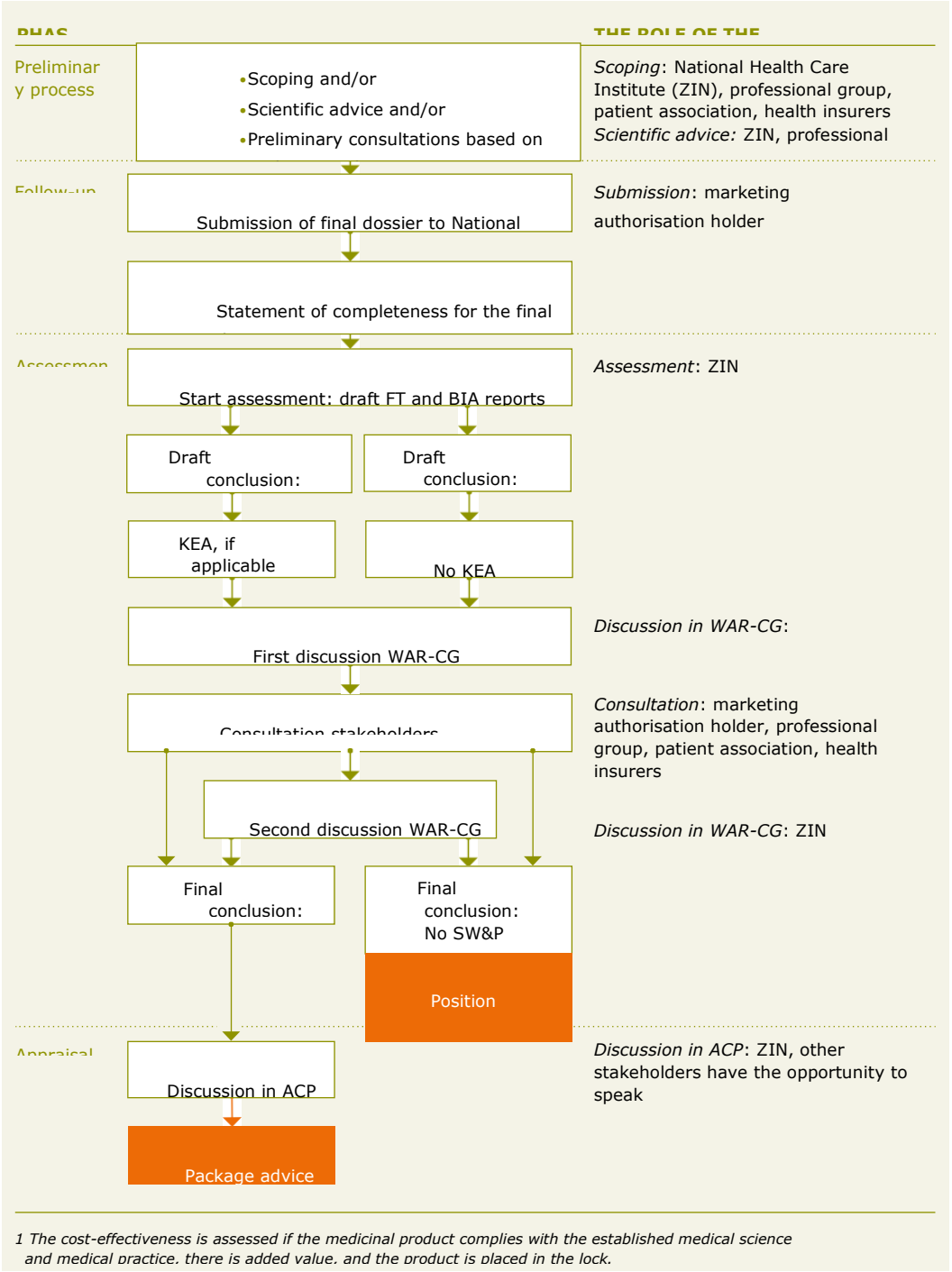
2.3.2 Assessment

The assessment will be based on a scientific evaluation of the specialised medicinal product. The assessment consists of the following components: a pharmaco-therapeutic assessment, a

[9] *Scientific advice procedure.* https://www.zorginstituutnederland.nl/over-ons/werkwijzen-en-procedures/adviseren-over-en-verduidelijken-van-het-basis- package-to-care/evaluation-of-medicinal products/scientific-advisory-for-delivery-case-gvs

budget impact analysis and, where appropriate, a cost-effectiveness analysis (including the disease burden calculation). This results in the pharmaco-therapeutic report, the budget impact analysis and the pharmaco-economic report (see 2.3.2.1 through 2.3.2.3). The assessment is carried out in stages: depending on the outcome of the pharmaco-therapeutic assessment, a cost-effectiveness analysis may or may not be carried out. Ultimately, the assessment leads to a conclusion on the established medical science and medical practice, the expected budget impact and possibly the cost-effectiveness and burden of disease. The assessment is thus the basis for a position by the National Health Care Institute (in case of an explanation) or for a weighting by the Package Advisory Committee (ACP; in case of package advice; see 2.3.3 Appraisal and 2.3.4 Decision-making by the National Health Care Institute).

Figure 1: Diagram of the assessment process for specialist medicinal products



1 The cost-effectiveness is assessed if the medicinal product complies with the established medical science and medical practice, there is added value, and the product is placed in the lock.

ACP: Package Advisory Committee, BIA: Budget impact analysis, FT: Pharmaco-therapeutic, KEA: Cost-effectiveness analysis, SW&P: Established medical science and medical practice, WAR- CG: Scientific Advisory Council – committee on Medicinal Products, ZIN: National Health Care Institute.

Note: This is a simplified view of the assessment of specialist medicinal products. However, there is always a tailor-made solution for each medicinal product. The current state of affairs per medicinal product is published in the work agenda on the site of the National Health Care Institute.[10]

[10] *National Health Care Institute work page.* https://www.zorginstituutnederland.nl/werkagenda

The final dossier of the marketing authorisation holder is an important part of the assessment. This allows the marketing authorisation holder to submit their justification for their claim. In case of a positive CHMP advice, a final dossier (with the draft European Public Assessment Report (EPAR)) can be submitted (see the website of the National Health Care Institute for the dossier requirements and formats).[11] The marketing authorisation holder determines when a final dossier is submitted.
Once the final dossier has been received, the National Health Care Institute will check whether the dossier is complete (target period: within 2 weeks). The final dossier must meet the required dossier requirements. In the event of a preliminary consultation, it must also be checked whether the observations of the National Health Care Institute about the preliminary dossier have been sufficiently processed. The lead time of the assessment starts from the moment that a dossier has been declared complete. For specialist medicinal products, a target period of 4 months applies.

Placement of the specialist medicinal product on the agenda for the Scientific Advisory Council – Committee on Medicinal Products (WAR-CG) can take place if the final EPAR has been published by the EMA and the final dossier has been declared complete by the National Health Care Institute. The National Health Care Institute is advised by the WAR-CG during monthly closed meetings. In principle, there are two WAR-CG meetings per specialist medicinal product. During the first meeting, the draft reports are determined on the basis of the advice of the WAR-CG. After this first discussion, the National Health Care Institute sends the draft reports to the stakeholders for consultation. The stakeholders differ for each dossier. Parties that are almost always consulted are the marketing authorisation holder, the professional group, the patient association and the health insurers. The objective of the consultation round is to verify that all available scientific evidence has been taken into account and properly weighted (response time of stakeholders: 5 days). During the second meeting, the WAR-CG advises the National Health Care Institute on the final reports that include the comments of the stakeholders. If the National Health Care Institute subsequently approves, the final reports will be adopted. The National Health Care Institute sends these to the stakeholders to inform them.

2.3.2.1 Pharmaco-therapeutic assessment

In the pharmaco-therapeutic report, the National Health Care Institute assesses whether a specialist medicinal product meets the established medical science and medical practice. The established medical science and medical practice is a relative measure. When registering a medicinal product, the EMA assessed the medicinal product for efficacy and safety. However, package admission centralises on a different question: does the treatment with the medicinal product, given its effectiveness and safety, lead to a relevant (additional) value for the patient compared to the standard treatment or the usual treatment?[12] This means that a specialist medicinal product admitted to the market does not necessarily have to meet the requirements of the established medical science and medical practice. In addition to effectiveness and safety, the pharmaco-therapeutic report also describes the experience, applicability and ease of use.

The pharmaco-therapeutic report ends with a conclusion on the established medical science and medical practice. Depending on the outcome of the pharmaco-therapeutic assessment, a budget impact analysis and/or cost-effectiveness analysis may or may not be carried out. The possible outcomes of the pharmaco-therapeutic assessment with the corresponding follow-up process are shown below. These are indicative because custom-made solutions are needed for each medicinal product. More information on the principles of package management can be

[11] *Summary of dossier requirements for medicinal product assessments.* https://www.zorginstituutnederland.nl/over-ons/werkwijzen-en-procedures/adviseren-over-en- clarify-of-the-basic package-to-care/assessment-of-drugs/summary-file requirements-at-drug assessments

[12] *Report 'Therapeutic Value Assessment Criteria', 2014.* https://www.zorginstituutnederland.nl/over-ons/publicaties/publicatie/2014/07/01/criteria-for-assessment-therapeutic-value

found in various National Health Care Institute publications.[13] [14]

Established medical science and medical practice

- Added value
  If, following the advice from the WAR-CG, the National Health Care Institute concludes that the specialist medicinal product has added value compared to the standard treatment or the usual treatment, this means that the medicinal product meets the legal criterion of established medical science and medical practice, and it is in principle insurable care. Furthermore, the National Health Care Institute calculates the budget impact and determines whether the performance of the cost-effectiveness analysis, which is mandatory in the event of added value, is of sufficient methodological quality. In the case of added value, the ACP appraisal, in which the package criteria are weighed in full, is standard (see paragraph 2.3.3 Appraisal)
- Equal value
  If the National Health Care Institute concludes that the specialist medicinal product has added value compared to the standard treatment or the usual treatment, the medicinal product meets the legal criterion of established medical science and medical practice, and it is in principle insurable care. If the value is equal, a budget impact analysis is sufficient to identify the difference in costs between the two medicinal products. The performance of a cost-effectiveness analysis usually has no added value in such a situation, as it is implicitly assumed that in case of equal value there will be no difference in quality of life. If the value is equal, the ACP performs an appraisal to weigh the package criteria.

No established medical science and medical practice

A specialist medicinal product that has no proven added value or equal value, or for which the available scientific evidence is not sufficient to draw conclusions on its value, does not comply with the established medical science and medical practice. This medicinal product is therefore not insurable care. In this case, the National Health Care Institute will issue a negative advice. The calculation of the budget impact and the assessment of cost-effectiveness are not discussed. There is also no appraisal.

The National Health Care Institute has a number of arrangements for medicinal products that seem promising, but that have not yet been sufficiently demonstrated to be established medical science and medical practice for reimbursement. The Promising Care Arrangement (Regeling Veelbelovende Zorg)[15] and the recently started Conditional inclusion of orphan drugs, conditionals and exceptionals[16] are examples of this.

2.3.2.2 Budget impact analysis

By means of a budget impact analysis, the National Health Care Institute makes an estimate of the costs associated with the use of the medicinal product in the first three years after inclusion in the health insurance package[12]. The National Health Care Institute bases its estimation on the costs incurred when all patients with the indication for which the National Health Care Institute has established that the medicinal product complies with the established medical science and medical practice are actually treated with this medicinal product. Where relevant, the National Health Care Institute also takes into account the (expected) market penetration and possible cost savings as a result of substitution of current treatments (medicinal products only). If there are substantial costs and/or savings associated with the

[13] *Report 'Established medical science and medical practice', 2015. https://www.zorginstituutnederland.nl/publicaties/rapport/2015/01/15/beoordeling-stand-van-de- science and practice*

[14] *Package management in practice (part 3), 2013. https://www.zorginstituutnederland.nl/publicaties/rapport/2013/10/18/pakketbeheer-in-de-praktijk-deel-3*

[15] *Promising Care Arrangement. https://www.zorginstituutnederland.nl/werkagenda/veelbelovende-zorg*

[16] *Orphan medicinal products, 'conditionals' and 'exceptions' can be conditionally admitted, among other things following a negative advice (as well as earlier in the evaluation process) by the National Health Care Institute. More information on this new arrangement, which came into effect in early 2020, can be found at: https://www.zorginstituutnederland.nl/werkagenda/voorwaardelijke-toelating-weesgeneesmiddelen-conditionals-en-exceptionals*

administering of the medicinal product, such as hospitalisation, surgery, or infusions, the National Health Care Institute may also include these costs in the calculation.

2.3.2.3 Cost-effectiveness analysis

Using the pharmaco-economic part of the reimbursement dossier, the National Health Care Institute determines whether sufficient insight has been given into the relationship between costs and effects in relation to comparative treatment and whether the cost-effectiveness of the medicinal product is favourable compared to the current reference value.

The reference value depends on the calculation of the burden of disease. The marketing authorisation holder provides a cost-effectiveness analysis with burden of disease calculation. It consists of an economic model that calculates the cost-effectiveness based on the available data on effectiveness (both clinical and quality of life) and cost data that are representative of the Dutch treatment practice. In the cost-effectiveness analysis, the National Health Care Institute bases its evaluation on the social perspective. This means that all relevant social costs and benefits are included in the evaluation. Information on the design of these economic evaluations can be found in the Economic Evaluations in Health Service guideline and its cost manual.[17] [18]

By definition, for both the budget impact analysis and the cost-effectiveness analysis, centralised or decentralised price agreements are not taken into account. These agreements are almost always confidential and may, in the case of decentralised agreements, for example, differ between health insurers. That is why the National Health Care Institute uniformly applies the list prices. If relevant to the assessment, at most, price agreements can be mentioned in the conclusions of the reports.

2.3.3 Appraisal

The appraisal is a social weighting and an integral assessment of the four package criteria: effectiveness, cost-effectiveness, necessity and feasibility. On the basis of these criteria, it is considered, for reasons of fairness and solidarity, whether the reimbursement of the medicinal product is also appropriate from a societal point of view. The appraisal takes place after it has been concluded that a medicinal product complies with the established medical science and medical practice, i.e. when it has added value or equal value. In the case of the appraisal, the National Health Care Institute consults the ACP, which meets in public every month. The ACP advises the Executive Board of the National Health Care Institute whether a specialist medicinal product should be included in the health care package. The public meeting of the ACP also allows participation of stakeholders (usually the marketing authorisation holder, the professional group and/or the patient association).

Information on the package criteria and their justification were evaluated during the assessment and are the starting point for the appraisal. The appraisal answers the question as to whether the relationship between effectiveness and costs is acceptable from a societal perspective. In the case of specialist medicinal products, the package criterion 'necessity' includes the burden of disease as determined during the assessment[19]. The package criterion 'feasibility' answers the question as to whether the inclusion of the medicinal product in the package can be achieved in practice, also taking into account the expected budget impact.

2.3.3.1 Appraisal results

In the case of lock medicinal products, the ACP advises the Executive Board of the National

[17] *Guideline for economic evaluations in health service, 2016 (Richtlijn voor het uitvoeren van economische evaluaties in de gezondheidszorg). https://www.zorginstituutnederland.nl/over-ons/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-gezondheidszorg*

[18] *Cost-effectiveness in practice. 2015 (Kosteneffectiviteit in de praktijk). https://www.zorginstituutnederland.nl/publicaties/rapport/2015/06/26/kosteneffectiviteit-in-de-praktijk*

[19] *In the case of the package criterion of necessity, this also includes the ability of the individual to pay for a treatment. Since the cost of specialist medicinal products is generally high, this aspect does not apply here.*

Health Care Institute to either include the medicinal product in the health insurance package or not. Often conditions are imposed on the possible inclusion of the medicinal product in the health insurance package, such as price negotiations and/or arrangements regarding appropriateness. The advice of the ACP to the Executive Board carries a lot of weight, but is not binding for the final package advice.

2.3.4 Decision-making by the National Health Care Institute

Package advice

The National Health Care Institute will issue a package advice if the assessed specialist medicinal product needs to be included (or excluded) from the health insurance package. The legislation and regulations, in this case the Rzv (Health Insurance Regulation), must be adapted for this purpose.

The package advice includes the result of the integral weighting of the four package criteria. The National Health Care Institute takes into account the advice of the WAR-CG, the ACP and all the reactions of the stakeholders. The package advice also includes the appropriateness of the medicinal product in practice. The National Health Care Institute evaluates the (appropriate) use and cost (effectiveness) of all lock medicinal products. The National Health Care Institute can advise the Minister for Medical Care to negotiate the price if the results of the appraisal warrant this. In a package advice, the decision to reimburse the medicinal product through the basic health insurance is made by the Minister for Medical Care.

Position

In the case of an explanation, the National Health Care Institute tests whether a medicinal product is covered by the basic health care insurance. In the case of an explanation, there is no amendment to the legislation and regulations, but a finding as to whether a medicinal product is part of the health insurance package or not. This is a conclusion (position) as to whether or not the specialist medicinal product meets the legal criterion of established medical science and medical practice. In view of the open nature of the basic health care insurance, compliance with this criterion means that a medicinal product is eligible for reimbursement. This finding is relevant for health insurers in the implementation of the Zvw (Health Insurance Act).

An explanation consists of a pharmaco-therapeutic assessment, possibly complemented by a budget impact analysis. During an explanation, the WAR-CG is asked for advice and stakeholders are consulted. During an explanation, a cost-effectiveness analysis and an appraisal by the ACP are not requested. The Minister for Medical Care cannot include a specialist medicinal product in the health insurance package after the National Health Care Institute has given a negative advice.

3 Conclusion

The introduction of the lock procedure for expensive specialist medicinal products and the placement on the Horizon Scan for Medicinal Products agenda are measures that make it possible to keep insured care accessible and affordable in the longer term, while also keeping an eye on the patient's interest. Through this report, the National Health Care Institute provides insight into the assessment procedure for specialist medicinal products. This assessment process focuses on collaboration with stakeholders in order to create customised solutions for each specialist medicinal product.

2 Definitions

Package Advisory Committee (ACP)	Advisory committee that advises the Executive Board of the National Health Care Institute from a social perspective. The ACP consists of external members with different fields of expertise. The advisory committee avoids any conflicts of interest. The ACP conducts monthly public meetings where the stakeholders can have their say.
Appraisal	Societal weighting as to whether a medicinal product should be reimbursed from the point of view of a fair distribution of resources. This will take into account the package criteria: effectiveness, cost-effectiveness, necessity and feasibility. In the case of an appraisal, the National Health Care Institute consults the ACP.
Assessment	A scientific substantive assessment of medicinal products based on the four package criteria. The assessment includes the therapeutic value, budget impact and, where appropriate, the burden of disease and cost-effectiveness. In the case of an assessment, the National Health Care Institute consults the Scientific Advisory Board's Committee on Medicinal Products (WAR-CG).
Assessment procedure	The assessment process for specialist medicinal products consists of an optional preliminary process, followed by the assessment and, if indicated, an appraisal. The assessment procedure will be completed in the form of a package advice to the Minister for Medical Care or a position.
Explanation	Testing whether the care meets the mandatory legal criteria. In the context of the specialist medicinal products assessment procedure, the established medical science and medical practice is the applicable legal criterion. An explanation results in a position on whether a specialist medicinal product meets the established medical science and medical practice.
Appropriateness	Care that is necessary, effective and efficient.
Horizon Scan for Medicinal Products	The Horizon Scan for Medicinal Products is an integral, public and an as objectively as possible overview of innovative medicinal products (specialist and outpatient) or indication extensions for medicinal products that are expected to be introduced to the market over the next two years.
Cost-effectiveness	The ratio between the difference in cost and the effectiveness of two or more treatments.
Registered medicinal product/ registered indication	A medicinal product / medicinal product indication for which a commission decision or parallel commission decision has been granted under the Dutch Medicines Act.
Open inflow	Medical care, which includes specialist medicinal products, is covered by the open system of the health care package. This means that when care is effective, it automatically flows into the health care package, without any changes to the legislation and regulations. This does not require a decision by the Minister for Medical Care. The lock procedure is an exception to the open inflow.
Risk-oriented package management	The selective assessment of medicinal products that identifies risks regarding the affordability, accessibility or quality of the package. This includes both the assessment of lock medicinal products (high financial risk) and certain specialist medicinal products, which are not in the lock, but for which risks are nevertheless foreseen by the parties in the field.

Scoping	An oral or written consultation with relevant parties prior to the assessment. The objective of a scoping is, among other things, to define the patient population, the comparative treatment(s) and the relevant outcome measures.
Lock procedure / lock	Since 2015, the Ministry of Health, Welfare and Sport (VWS) has introduced a 'lock' for certain medicinal products with a financial risk. This was formally established in 2018 by means of Article 2.4a of the Health Insurance Decision (Bzv). Normally, there is an open inflow of inpatient medicines in the health insurance package, provided that the care meets the established medical science and medical practice. With the lock, the Minister of Health, Welfare and Sport can deviate from the principle of open inflow for medicinal products with a high financial risk. During the lock procedure, the medicinal product is excluded from reimbursement and the Minister for Medical Care asks the National Health Care Institute to carry out an assessment. In addition, the Ministry of Health, Welfare and Sport can agree a financial arrangement with the marketing authorisation holder. Finally, stakeholders can reach agreements on the appropriateness of the relevant medicinal product. The National Health Care Institute monitors and evaluates these agreements.
Specialist medicinal product	A specialist medicinal product is part of the health care benefit. Medical care includes, among other things, care such as medical specialists tend to provide. In practice, this means that medicinal products are used under the responsibility of a medical specialist and within the walls of an institution.
Established medical science and medical practice	The main criterion from the Bzv (Article 2.1, second paragraph) and one of the basic principles of the explanation. The 'established medical science and medical practice' determines the relative effectiveness of an intervention: to what extent does the (new) intervention contribute to the intended objective of the intervention, in comparison with the care that is already being offered for this disease in Dutch practice? To avoid a deterioration in the health insurance package, the starting point is that the outcome of the assessment must be positive (i.e. added or equal value in relation to the comparative treatment(s)). A specialist medicinal product that has no proven value or equal value, or for which the available scientific evidence is not sufficient to draw conclusions on its value, does not comply with the established medical science and medical practice. This medicinal product is therefore not insurable care.
Scientific advice	The marketing authorisation holder can apply for scientific advice from the National Health Care Institute at any time. This may include anything that is unclear about the approach of the (preliminary) dossier. Scientific advice is usually given early in the assessment process. The scientific advice may be provided orally or in writing.

Scientific Advisory Council – Committee on Medicinal Products (WAR- CG)	The National Health Care Institute's integrated assessment committee, which provides scientific advice on medicinal products in the context of package management and the established medical science and medical practice. The WAR-CG also provides scientific advice on budget impact analysis, cost-effectiveness analysis and burden of disease calculation. The WAR-CG consists of external members with a medical, methodological or health economic background. The advisory committee avoids any conflicts of interest.
Preliminary consultation	Marketing authorisation holders may apply for a preliminary consultation after submitting a preliminary dossier to the National Health Care Institute. The aim of a preliminary consultation is to align the dossier to the dossier requirements and other concerns of the National Health Care Institute at an early stage.

3 Colophon

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Ministry of Health, Welfare and Sport
Dutch Federation of Cancer Patient Organisations
Netherlands Federation of University Medical Centres
Dutch Association of Hospitals
Dutch Association of Hospital Pharmacists
Dutch Healthcare Authority
Netherlands Patient Federation
Association Innovative Medicines
Association of Collaborating Parent & Patient Organisations
Association of Dutch Healthcare Insurers

The National Health Care Institute received a written response from all the consulted parties (individually or jointly), four of which were sent by letter. These letters and the response of the National Health Care Institute have been published as an annex on the website.

This report has been produced with contributions and the cooperation of the Sector Health Care and the Compliance and Legal Affairs Team of the National Health Care Institute.