Zorginstituut Nederland

> Reply address P.O. Box 320, 1110 AH Diemen

To the Minister of Medical Care and Sport
P.O. Box 20350
2500 EJ DEN HAAG

***Zorginstituut Nederland*.**
Oncology

Eekholt 4
1112 XH Diemen
P.O. Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
info@zinl.nl

T +31 (0)20 797 85 55

Contact
R. Dupree
T +31 (0)6 22 444 351

2018022922

Date 23 August 2018
Re Implementation of the appropriate care of expensive drugs in cases of castration-refractory prostate cancer

Our reference
2018022922

Dear Mr Bruins,

In December 2016, as part of the *Zinnige Zorg* programme, *Zorginstituut Nederland* published the Room for Improvement Report 'Appropriate use of expensive drugs in cases of castration-refractory prostate cancer'. The implementation phase of this topic subsequently took place and was recently completed. This letter is to inform you about the changes made by parties during the implementation phase in relation to outcomes regarding improvement possibilities in the Room for Improvement Report. We appreciate the parties' efforts and we are pleased that initiatives in the field have led to changes that are evident in daily practice and which are in line with the Room for Improvement Report.

Castration-refractory prostate carcinoma (CRPC), the final stage of prostate cancer, is regarded as incurable. The use of drugs in cases of CRPC has evolved greatly in the past few years: more drugs have become available and drugs can be deployed in more phases of the disease, as a result of which patients can survive for longer and have a better quality of life. Together with the parties in the field, the *Zorginstituut* has carried out research into the use of expensive drugs in practice. That research resulted in the Room for Improvement Report. The outcomes of the research paint a picture of the first introduction of these drugs and illustrate the challenges facing the implementation of appropriate use. Improvement possibilities focussed on establishing the right indication, proper harmonisation between care professionals and care in the final life-phase.

The *Zorginstituut* concludes that all relevant parties have urgently dealt with these challenges and that many initiatives have been given a structural place in daily practice. These initiatives are in line with the improvement possibilities on establishing the right indication and harmonisation between care professionals. The initiatives are referred to concretely in the appendix with this letter. The parties' constructive attitude contributed immensely to completing this implementation phase. Initiatives on appropriate use, as discussed in this implementation phase, are ensuring a positive influence on the cost-effectiveness of care in practice (by preventing inappropriate use).

Together with the parties, we have agreed that the improvement possibility regarding the use of expensive drugs in the final life-phase will be included in the

implementation phase of the larger *Zinnige Zorg* project, 'Care in the final life-phase of people with lung cancer and intestinal cancer'. This was decided because of the strong substantive link between these two topics. As a result, this topic can be implemented integrally in an overarching project that has already started.

As the implementation phase of the Room for Improvement Report on the use of expensive drugs in cases of CRPC has ended, the monitoring phase has now started. The *Zorginstituut* has agreed with the parties involved that they will jointly monitor the status of progress and the sustainability of the results achieved. The *Zorginstituut* will remain in dialogue with the parties in the field during the monitoring phase, whereby the *Zorginstituut* will remain available for further implementation research or advice, if required by the parties. We will inform you about the outcomes of the monitoring phase in the second half of 2019.

The appendix provides an explanation of these conclusions.

Yours sincerely,

Sjaak Wijma
Member of the Executive Board

Appendix: explanation of the conclusions from the implementation phase

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Reason

The use of expensive drugs in cases of castration-refractory prostate cancer (CRPC) was one of the topics that we systematically screened in the in-depth phase of the *Zinnige Zorg* programme. This topic was chosen based on signals received from parties in the field which indicated that possible improvements could be achieved in care using expensive drugs for this indication field.[1,2] In accordance with the working method of the *Zinnige Zorg* programme (included at the end of this appendix), the implementation phase starts after the in-depth phase.

During the in-depth phase, in close collaboration with the parties in the field, the *Zorginstituut* commissioned research in 2016 based on information on daily practice. This resulted in the Room for Improvement Report.[3] This formulated three concrete improvement measures for the more appropriate use of expensive drugs in cases of CRPC. This related to:

1. Appropriate diagnosis
2. Good harmonisation between care professionals
3. Reduced use of active treatments in the final life-phase

Implementation phase

The implementation phase is primarily the responsibility of the parties in health care: patients, care professionals, institutions, health insurers and the government. It takes place based on agreements made in the in-depth phase. In the implementation phase the *Zorginstituut* can play a supportive and facilitating role, for instance, by organising meetings, providing data and feedback, and by carrying out additional research. The *Zorginstituut* reports progress to the Minister of VWS. On 24 April 2018 the *Zorginstituut* organised an implementation meeting that was attended by representatives of the patients' association, health care insurers and professional groups. At this meeting, initiatives of parties in the field were discussed that are in line with the three improvement possibilities.

Outcomes

<u>Appropriate diagnosis</u>
An appropriate diagnosis is necessary to be sure that patients receive the drugs that will benefit them most at that moment. Patient characteristics and disease characteristics must be involved when making a diagnosis, i.e. choosing treatment. Furthermore, patients' preferences have a major influence on weighing up possible alternatives, or possibly choosing not to carry out burdensome

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[1] *Zorginstituut Nederland* (2015): Systematic analysis of Neoplasms. Via: https://www.zorginstituutnederland.nl/publicaties/rapport/2015/04/16/zinnige-zorg-sreeningsrapport---systematische-analyse-nieuwvormingen-icd-10-c00-d48

[2] *Zorginstituut Nederland* (2015): Report on the initial meeting on Appropriate use of expensive drugs in cases of mCRPC. Via https://www.zorginstituutnederland.nl/publicaties/verslag/2015/09/17/verslag-startbijeenkomst-zinnig-gebruik-van-dure-geneesmiddelen-bij-patienten-met-mcrpc

[3] *Zorginstituut Nederland* (2016): The Room for Improvement Report on the Appropriate use of expensive drugs in cases of castration-refractory prostate cancer. Via: https://www.zorginstituutnederland.nl/publicaties/rapport/2016/11/21/verbetersignalement-zinnig-gebruik-van-geneesmiddelen-bij-patienten-met-castratie-refractair-prostaatcarcinoom

treatment. The guidelines describe patient characteristics and disease characteristics in relation to the treatment options.

In the Room for Improvement Report, we saw how – due to the increasing complexity of a rapidly changing treatment landscape – a broader range of characteristics are being used to make treatment choices than those mentioned in the guidelines. This is linked to the lack of scientific evidence on the best sequence of treatments with drugs. Moreover, research is not feasible in view of the complexity. For this reason no single treatment algorithm can be defined that applies to all patients. The focus is on realising 'matched care': the treatment that is eligible based on the diagnosis, whereby choosing between the various possible alternatives – or ending treatment – takes place based on shared decision-making. An integral aspect of matched care is that the options include choosing not to undergo burdensome systemic treatment, but instead choosing for the best supportive care.

In the meantime various initiatives have been developed in the field to ensure that choosing treatment takes place as systematically as possible, as part of a multidisciplinary consultation (MDO), while also taking into account the indication and the patient's preferences. Decision aids are available for various oncology indications, both for carers and for patients. A decision aid for doctors that is receiving a lot of attention is the Oncoguide (IKNL).[4] This uses patient characteristics and disease characteristics in a 'decision tree', based on the guidelines, to choose appropriate treatment in consultation with the patient. Choosing appropriate treatment is thus encouraged because the relevant patient characteristics and disease characteristics are systematically involved. The Oncoguide for prostate cancer is currently being developed. Moreover, the Oncoguide can provide the MDO with structure.

The Netherlands Association for Medical Oncology (NVMO) has started a pilot study to be able to issue 'viewpoints' on breast cancer and colonic cancer. These can be regarded as a prelude to the guidelines and as a supplement to the assessment of the NVMO's 'Committee for the assessment of oncology drugs' (cieBOM). In instances in which the cieBOM assesses value, per drug, against the current treatment, the viewpoints should provide an integrated, up-to-date picture of treatment possibilities and advice in instances in which the guidelines are no longer current and until such time that they have been updated.[5] If this pilot study is positive, prostate cancer is another field of indication suited to the initiative.

Moreover, also available for patients with prostate cancer are decision aids, one of which is for the castration-refractory setting. Its value is currently being examined. These help patients, in consultation with their care providers, to have their preferences taken optimally into account in the treatment decision. The added value of the geriatric screening instrument (G8) is also being investigated. Publication of the first results is expected in January 2019.
By coupling the registration of patient characteristics and disease characteristics to treatment choices and outcomes at source, e.g. in the CAPRI register, care providers will be able to assess their own action.

[4] https://www.iknl.nl/oncologische-zorg/oncoguide

[5] https://www.nvmo.org/2018/07/procedure-voor-opstellen-standpunten/

Harmonisation between care providers

Harmonisation between care providers in cases of CRPC, in particular the urologist and the medical oncologist, takes place largely in a multidisciplinary consultation (MDO), where a care provider introduces a case and follow-up policy can be discussed integrally. According to the SONCOS norms, in cases involving castration-refractory disease, patients must be discussed in the MDO. The MDO has to meet at least weekly and must include an internist-oncologist, a urologist, a radiotherapist-oncologist and a pathologist.[6] In cases of prostate cancer, the urologist is generally in charge of treatment in the stages prior to CRPC, while systemic therapy is prescribed by a medical oncologist. Concern was expressed during the screening phase about whether there was sufficient harmonisation and whether urologists did structurally refer patients to a medical oncologist. The Room for Improvement Report also found signs that, based on patient characteristics and disease characteristics, some patients were eligible for systemic therapy who had not been seen by a medical oncologist. However, the MDO's role could not be examined, nor the influence of patients' preferences.

The MDO was still being developed during the screening phase, while collecting data for use in the Room for Improvement Report(2010-2012). At the implementation meeting all parties agreed that the MDO has been properly implemented everywhere. Other initiatives are in place for MDOs on a supra-regional level, whereby discussions take place about possible treatments in the MDO while chemotherapy can actually be administered in the hospital that is closest to the patient. However, according to the attendees, the MDO has not yet finished developing. It is important that patients are introduced into the MDO by a doctor who is directly involved, and in certain cases it must be possible to reintroduce patients into the MDO in the pre-terminal phase. The MDO is therefore still being developed, within hospitals or on a (supra-)regional level.

Final life-phase

We saw in the Room for Improvement Report how care consumption, e.g. hospital admissions and supportive treatment for CRPC patients, was high in the last three months of patients' lives. Care consumption was even higher among patients who started a new active treatment in the final life-phase, but in the Room for Improvement Report we were unable to demonstrate whether this higher consumption was due to the initiation of systemic treatment.

In practice, however, it is difficult to predict just when the final three months of life have started. It is particularly in the final life-phase that patients' preferences are really important, and a timely discussion must take place with the patient, though without causing him/her unnecessary distress. Central to this is encouraging a patient to realise that treatment will come to an end, and to think about how he wants to spend his final life-phase. This is referred to as 'advance care planning' (ACP). Although prostate cancer can be very protracted, and many (follow-up) treatments are possible in principle, no key moment can be specified as the moment for having these discussions with the patient.

Within the *Zinnige Zorg* Programme, the *Zorginstituut* has published a Room for

[6] Oncological Collaboration Foundation (2018). Norm report, version 6. Via: https://www.soncos.org/kwaliteit/normeringsrapport/

Improvement Report about care in the final life-phase with other forms of cancer.[7] The implementation phase for that topic will also soon be starting. Due to the similarities of the findings on CRPC, this improvement possibility will be included in the implementation phase of care in the final life-phase for other forms of cancer.

Financial impact

In the Room for Improvement Report, the costs of using expensive drugs in cases of castration-refractory prostate cancer in 2015 were estimated at €56 million, about three-quarters of which was spent on abiraterone and enzalutamide. By now the treatments are also being used for earlier stages of prostate cancer, which means the costs will increase even further in the next few years. As yet it is difficult to predict with any degree of certainty how the treatment landscape will look in the next few years. All in all, these rapid new developments make it difficult to properly map out the financial impact of the implementation activities. There are signs that the use of some drugs may not be cost-effective, despite being used appropriately. Therefore paying attention to the costs of using expensive drugs for prostate cancer remains relevant. Initiatives on appropriate use, as discussed for instance in this implementation phase, ensure that care in daily practice is not being used even less cost-effectively (by preventing inappropriate use).

Monitoring phase

During the monitoring phase of a *Zinnige Zorg* project, the *Zorginstituut* monitors, together with the parties involved, whether the intended goals are achieved by means of the results mentioned in this implementation report.

A number of points for continued attention came up during the implementation phase. At the end of 2019 the *Zorginstituut* will approach the parties involved (again). This will pay attention to progress surrounding how the MDO takes shape and continued guideline development (e.g., realising NVMO standpoints and the Oncoguide on prostate cancer). The improvement regarding the final life-phase of CRPC was not discussed in this evaluation because it will be included in the overarching project, 'Care in the final life-phase of people with lung cancer and intestinal cancer'.

Should monitoring reveal signs of the need for further harmonisation, then the *Zorginstituut* will provide the required support.

Working method of the *Zinnige Zorg* Programme

The *Zorginstituut* designed a systematic working method for the *Zinnige Zorg* Programme that analyses the way in which the insured package of care is deployed. The key is to identify and combat ineffective and/or unnecessary care, thus improving quality of care for patients, increasing health gains and avoiding unnecessary costs. We do this based on a circle of improvement as in figure 1.

[7] *Zorginstituut Nederland* (2017): Room for Improvement Report on care in the final life-phase of patients with incurable intestinal cancer or lung cancer. Via: https://www.zorginstituutnederland.nl/publicaties/rapport/2017/09/29/verbetersignalement-zorg-in-de-laatste-levensfase-longkanker-en-darmkanker

This circle is comprised of four sequential phases:

1. Screening phase
2. In-Depth Analysis Phase
3. Implementation phase
4. Evaluation phase

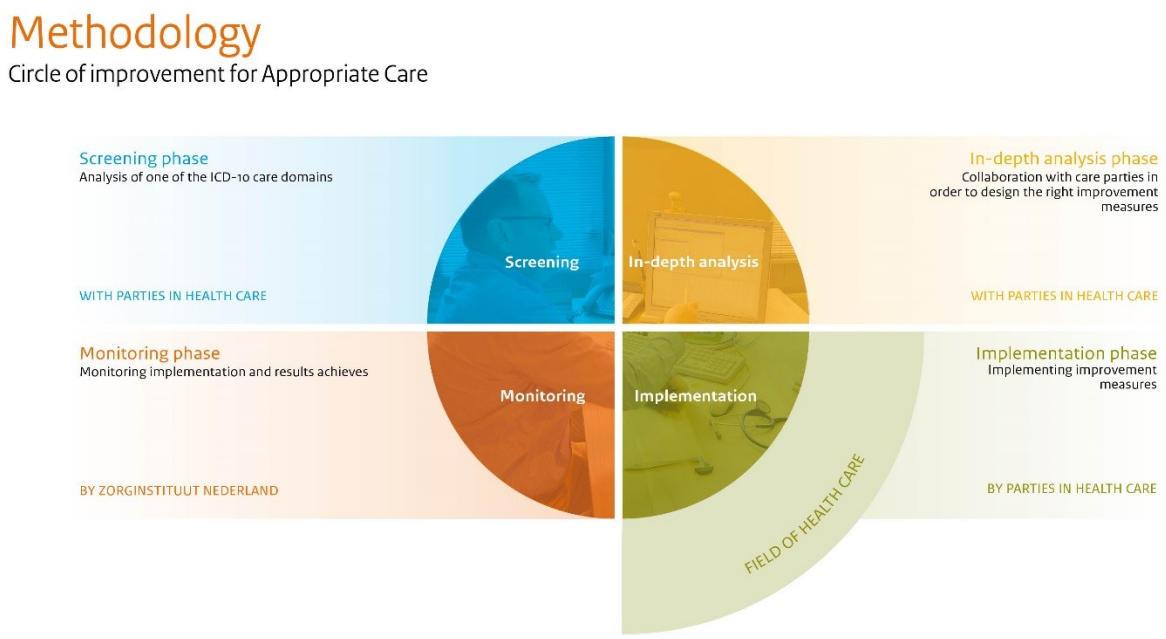

Figure 1: *Zinnige Zorg*'s circle of improvement

Screening phase
The objective of the screening phase is to select a number of topics for in-depth analysis with a potential for improving quality of care and avoiding unnecessary costs by using care more appropriately. These topics are recorded in a 'Systematic Analysis' report and sent, together with the underlying analysis, to the Minister of VWS.

Various sources are consulted to arrive at a good analysis and the right choice of in-depth topics. Sources include guidelines, scientific literature, claims data and other data, and the parties in health care. This involves not only collecting and analysing all the detailed information, but also searching for signals from daily practice in order to obtain a succinct picture of the care provided in the current situation. This is done from the perspective of the *Zorginstituut*, using the "criteria of good care".

In-Depth Analysis Phase

The screening phase is followed by the in-depth phase. The objective of this phase is to make the method for achieving potential improvements in the selected topics as concrete as possible.

Per topic, detailed analyses are carried out and the missing data can be completed via extra data analyses, practice research and/or a literature study.

In this phase too, the *Zorginstituut* works very closely with the parties involved. The final results are recorded in a so-called Room for Improvement Report. This states which improvements in care and in health are considered possible, in respect of both content and extent, and provides an estimate of the total sum of avoidable costs (budget impact). The *Zorginstituut* also sends the Room for Improvement Report to the Minister of VWS.

Implementation phase
The implementation phase is primarily a task for the parties in health care: patients, care professionals, institutions, health insurers and the government. It takes place based on agreements made in the in-depth phase. In the implementation phase the *Zorginstituut* can play a supportive and facilitating role, for instance, by organising meetings, providing data and feedback, and by carrying out additional research. Periodically, the *Zorginstituut* reports progress made to the Minister of VWS.

Evaluation phase
During the monitoring phase, the *Zorginstituut* examines, together with the parties involved, whether results have been achieved. Based on this, we decide whether new actions are necessary. During this phase, we also examine whether all necessary information is structurally available.