

# Health technology assessment of $^{177}\text{Lu}$ -PSMA-617 treatment for metastatic castration resistant prostate cancer

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Protocol for health technology assessment

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# Summary

Prostate cancer is the most common cancer type among Norwegian men. In 10-20% of these patients, the cancer will advance to metastatic, castration resistant prostate cancer (mCRPC). As mCRPC is incurable, the treatment options are limited to palliative therapy, using radiation and chemotherapy to manage symptoms and prolong life. Radioligand therapy (RLT) is increasingly being used for treating various malignancies. RLT of mCRPC uses the radionuclide lutetium-177 coupled with a binding ligand for prostate-specific membrane antigen (PSMA). The Norwegian Institute of Public Health has been commissioned to assess the efficacy and safety of <sup>177</sup>Lu-PSMA-617 treatment of prostate cancer, in addition to organisational scenarios and health economic consequences with this treatment, in a full health technology assessment (HTA).

We will perform a systematic search for literature in relevant databases. References will be screened for title, abstract and full-text, and included in accordance with predetermined selection criteria. We will extract and analyse data from the included studies, and the results will be compiled and presented in a report written in English. The methodological quality of the included studies will be assessed, as will the certainty of the evidence, i.e., our confidence in the results. We will also perform a health economic evaluation and a five-year budget impact. If we receive a documentation package from Novartis, we will implement this in our work, while still maintaining to perform a full HTA.

**Title:**

Health technology assessment of <sup>177</sup>Lu-PSMA-617 treatment for metastatic castration resistant prostate cancer

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Protocol for  
Health technology assessment

**Commissioner:**

The Regional Health Authorities Forum  
(Bestillerforum Nye Metoder)

**Start date:**

15.06.2022

**End date:**

15.06.2023  
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Gunn Eva Næss (information specialist)  
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**External team members:**

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**Peer reviewers:**

Kjetil Gundro Brurberg, NIPH

**Approved by:**

Kåre Birger Hagen, *director*, NIPH

# Sammendrag

Prostatakraft er den mest vanlige formen for kreft blant norske menn. I 10-20% av tilfellene vil kreften utvikle seg til metastatisk kastrasjonsresistent prostatakraft (mCRPC). Ettersom mCRPC er uhelbredelig, er behandlingsmulighetene begrenset til palliasjon: stråling og kjemoterapi benyttes for symptomlindring og livsforlengende behandling. Radioligandterapi (RLT) er i økende grad brukt i behandling av ulike krefttyper. RLT-behandling av mCRPC bruker radionukliden lutetium-177 koblet med en ligand for prostataspesifikt, membranantigen (PSMA). Folkehelseinstituttet har fått i oppdrag å utrede effekt og sikkerhet ved bruk av <sup>177</sup>Lu-PSMA-617 til behandling av prostatakraft, samt organisatoriske og helseøkonomiske konsekvenser av behandlingen i en fullstendig metodevurdering.

Vi skal gjennomføre et systematisk litteratursøk i relevante databaser. Referanser vil screenes basert på tittel, sammendrag og fulltekst, og vil inkluderes i henhold til forhåndsbestemte seleksjonskriterier. Vi planlegger å ekstrahere og analysere data fra de inkluderte studiene, og resultatene vil sammenfattes og presenteres i en rapport skrevet på engelsk. Vi vil vurdere metodologisk kvalitet i de inkluderte studiene, og i tillegg til tiltro til resultatene. Vi kommer også til å gjennomføre en helseøkonomisk evaluering og en femårig budsjettinnvirkning. Dersom vi mottar en dokumentasjonspakke fra Novartis, vil dette bli implementert inn i vårt arbeid, samtidig som vi tilstreber å gjennomføre en fullstendig metodevurdering.

**Tittel:**

Metodevurdering av <sup>177</sup>Lu-PSMA-617 behandling ved metastatisk kastrasjonsresistent prostatakraft

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Protokoll for fullstendig metodevurdering

**Oppdragsgiver:**

Bestillerforum for nye metoder

**Start dato:**

15.06.2022

**Sluttdato:**

15.06.2023

**Lag:**

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**Fagfeller:**

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**Godkjent av:**

Kåre Birger Hagen, *fagdirektør*, FHI

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# Commission

On 18<sup>th</sup> June 2018, Oslo University Hospital submitted a proposal for a new national health technology assessment (HTA) regarding the use of <sup>177</sup>Lu-PSMA for treating prostate cancer. The Regional Health Authorities (RHA) Ordering forum assessed the proposal on 27<sup>th</sup> August 2018 and commissioned The Norwegian Institute of Public Health (NIPH) to contact the (then) Finnish producer of <sup>177</sup>Lutetium-PSMA: MAP Medical Technologies Oy, with a request for submitting documentation, in order to conduct a single technology assessment. At the RHA Ordering forum 22<sup>nd</sup> October 2018, NIPH informed that the Finnish producer could/would not submit a health economic assessment of <sup>177</sup>Lu-PSMA. Due to the lack of documentation, a single technology assessment was not feasible, and the RHA Ordering forum instead commissioned NIPH to conduct a full HTA to assess effect, safety, cost-effectiveness and organisational implications of <sup>177</sup>Lu-PSMA in treatment of prostate cancer. The work started in 2019, but due to lack of randomized controlled trials presenting any survival data, the project was put on hold until such data were published. When a randomized controlled trial with survival data was published in June 2021, it was decided that the commission should be kept on hold until a marketing application for the pharmaceutical was available. In February 2022, NIPH was informed by Novartis that they had submitted a marketing application for <sup>177</sup>Lu-PSMA-617. NIPH subsequently started work on the commission.

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# Background

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## Description of the problem or issue

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### Prostate cancer

Prostate cancer is the most common type of cancer to affect Norwegian men (1). Every year, around 5000 new cases are diagnosed and per December 2021, there were close to 60 000 men living with a prostate cancer diagnosis in Norway (1). Prostate cancer is also among the most frequent causes of cancer-related death among Norwegian men, with around 1000 deaths each year (1).

### Metastatic castration resistant prostate cancer

In 10-20% of patients, the prostate cancer will progress to what is known as *metastatic castration resistant prostate cancer* (mCRPC) (2;3). Normally, prostate cancer cells are dependent on testosterone to grow and develop (4). This feature is targeted through endocrine therapy by reducing the levels of testosterone in the body, either by blocking the production (through orchiectomy or gonadotropin-releasing hormone-agonists), or by blocking the receptors (using antiandrogens) (4). However, castration resistant cancer will continue to grow regardless of low testosterone levels (4). At this stage of the disease, with the cancer being castration resistant and having metastasized beyond the prostate gland (e.g., to lymph nodes and bone), a curative outcome is currently no longer possible (5;6). For this patient group, the only available treatment options are palliative therapy i.e., to provide good quality of life for as long as possible (symptom relief, life prolonging) (5;6).

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## Description of the intervention

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### Targeted radioligand therapy

Targeted radioligand therapy (RLT) is used as a treatment strategy in various malignancies, such as neuroendocrine cancer, leukaemia and lymphoma (7-9). The treatment principle is similar to that of external radiation therapy or brachytherapy: to use ionizing radiation to kill cancer cells through cytotoxic DNA-damage (10). However, RLT specifically targets cancer cells by linking the radionuclide with a ligand, e.g., a monoclonal antibody (targeted radioimmunotherapy), peptide or small molecule that has high binding affinity to a specific target on malignant cells (9;11;12). This allows for specifically directing the radiation to cancer cells, with minimal harmful effect on surrounding tissue.

## **<sup>177</sup>Lu-PSMA**

RLT-treatment of prostate cancer involves the radionuclide lutetium-177, coupled with a ligand for prostate specific membrane antigen (PSMA). Lutetium-177 makes a good therapy agent for prostate cancer due to its physical properties: it is a medium energy  $\beta$ -emitter (maximum 490 MeV), with a tissue range of around 2 mm (7;13). This allows the  $\beta$ -radiation to penetrate and affect the tumour cells, with minimal effect on surrounding tissue. Furthermore, as lutetium-177 is a reactor-made isotope the relatively long half-life ( $t_{1/2}$ ) of 6.7 days permits transportation from production facility to the clinic (13). In addition to being used for therapeutic purposes, lutetium-177 also emits low-energy  $\gamma$ -radiation that can be used in imaging for diagnostic purposes and dosimetry (7;14).

PSMA is a type II glycoprotein that sits in the plasma membrane of prostate epithelium, with a large extracellular part that ligands can bind to (15). PSMA is an ideal binding target in RLT-treatment as expression levels are low in normal prostate tissue, but high in almost all prostate cancers (16). Tumour aggressiveness, androgen-independence and metastatic disease seem to be related to the level of PSMA expression, as higher levels are seen in more serious forms of prostate cancer than in less aggressive forms (16;17). PSMA is however, not exclusively expressed in prostate cells, as low levels are found in the kidney, small intestine and salivary glands (14;18-20). As <sup>177</sup>Lu-PSMA will bind specifically to all sites that express PSMA, some radiation will inevitably be delivered to non-malignant tissues that express PSMA (14). An additional factor that makes PSMA a good binding target is its ability to internalize molecules bound to the cell surface, into intracellular endosomes (21). For RLT-treatment, this allows the radionuclide lutetium-177 to be concentrated inside the cell, and thus cause the cells to be radiated from within (21).

There are several different types of PSMA-ligands, although the most studied are PSMA-I&T and PMSA-617 (22). These two ligand types differ in molecular structure (i.e., type of chelator) and have been shown to have somewhat different biodistribution in preclinical trials, although differences in effect have not (yet) been shown in clinical studies (22;23).

In March 2022 the RLT drug <sup>177</sup>Lu-PSMA-617 (Pluvicto) was approved for treatment of men with mCRPC in USA (24). Novartis has also submitted marketing authorisation to the European Medicines Agency (EMA), and it is assumed that Pluvicto will be approved in Europe and subsequently Norway, towards the end of 2022 (25).

### **Use of <sup>177</sup>Lu-PSMA in Norway**

<sup>177</sup>Lu-PSMA has not yet (as of November 2022) received marketing authorisation in Norway and is therefore generally not offered as a treatment for mCRPC. However, the Norwegian Health Authorities have funded <sup>177</sup>Lu-PSMA treatment of about 11 Norwegian patients abroad, either in Finland or in Germany. Furthermore, two patients have received treatment with <sup>177</sup>Lu-PSMA I&T in Norway: one at the University Hospital of North Norway, Tromsø, and one at Haukeland University Hospital, Bergen, either funded by the regional health authorities or locally by hospital department. Additionally, some patients have received treatment with <sup>177</sup>Lu-PSMA abroad in Finland or Germany, at their own expense.

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## Why is it important to do this systematic review?

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As of 1<sup>st</sup> January 2018, all new drugs marketed in Norway must be assessed by a HTA (26;27), and the funding will be determined through the HTA and well-defined priority criteria (27). <sup>177</sup>Lu-PSMA is a new drug that provide treatment to mCRPC patients that have few if any further treatment options. As such, it is important to assess the efficacy and safety, as well as to perform a health economic evaluation and describe organisational implications of treatment with <sup>177</sup>Lu-PSMA for this patient group.

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## Aims

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The aim of this HTA is to:

- 1) Systematically identify, assess and summarize available research regarding efficacy and safety of <sup>177</sup>Lu-PSMA-617 in the treatment of prostate cancer
- 2) Conduct a health economic evaluation for current organisational scenarios
- 3) Assess organisational challenges, consequences, and radiation safety linked to establishing <sup>177</sup>Lu-PSMA-617 as a treatment option in Norway

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# Methods

Our commission was to perform a full HTA, with assessments on effect and safety, health economy, and organisational aspects. However, we have been in dialogue with Novartis, who have agreed to submit documentation on treatment with their product Pluvicto (<sup>177</sup>Lu-PSMA-617). If Novartis is able to send us a documentation package within the time frames of this HTA, we will include the studies and results presented in our report, and further use any data or model regarding health economic analyses in our own work. Regardless of us receiving a documentation package or not, we will still write a full HTA in accordance with the handbook “Slik oppsummerer vi forskning”, by the Norwegian Institute of Public Health (28).

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## Inclusion criteria

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Our framework for searching for and selecting relevant literature for our HTA is outlined in the PICO.

PICOS	Inclusion	Exclusion
<b>Population</b>	Men diagnosed with metastatic castration resistant prostate cancer	Local prostate cancer, no metastases, castration sensitive cancer
<b>Intervention</b>	Radionuclide: Lutetium-177, PSMA-ligand: 617	Other radionuclides Other PSMA ligands
<b>Comparator</b>	All possible comparators: <ul style="list-style-type: none"><li>• Standard care treatment: (chemotherapy, radiation, antiandrogens)</li><li>• Best supportive care</li><li>• Placebo</li><li>• No treatment</li></ul>	Other types of PRRT
<b>Outcome</b>	Efficacy: <ul style="list-style-type: none"><li>• Overall survival</li><li>• Progression-free survival</li><li>• PSA-level</li><li>• Time to first skeletal event</li><li>• Quality of life</li></ul> Safety: <ul style="list-style-type: none"><li>• Severe adverse events grade 3 and 4</li></ul>	Other outcomes

	<ul style="list-style-type: none"> <li>• Serious adverse events</li> </ul>	
<b>Study design</b>	Randomised controlled trials	Non-randomised studies Systematic reviews Conference abstracts

Papers written in other languages than English, or any of the Scandinavian languages will be excluded. A list of publications excluded based on language alone will be listed separately.

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## Literature search

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### Databases

A research librarian will perform the literature search using peer-reviewed search strategies. The search will be conducted in August 2022. The relevant databases to be search are as follows:

- Ovid MEDLINE
- Embase (Ovid)
- Cochrane Central Register of Controlled Trials (Wiley)
- Epistemonikos
- Scopus

We will search for ongoing, completed and terminated clinical trials in the following databases:

- ClinicalTrials.gov
- WHO ICTRP
- EU Clinical Trials Register

In addition, we will specifically search various manufacturers' web pages for relevant publications regarding <sup>177</sup>Lu-PSMA-treatment. We will also perform reference searches, where we specifically search for relevant studies as referenced in included studies, as well as in systematic reviews.

### Search strategy

In order to find as many relevant studies as possible, we plan to base the search strategy only on the population and the intervention of the research question: i.e., mCRPC and <sup>177</sup>Lu-PSMA-617, respectively. The research librarian will combine various free text terms for the population (prostate cancer) and intervention (<sup>177</sup>Lu-PSMA), as well as index terms, e.g., medical subject headings (MeSH), for the population (prostate cancer), separated by Boolean operators (AND/OR).

### Filters

As <sup>177</sup>Lu-PSMA for treating prostate cancer is quite new, we assume there will be few randomized controlled trials available for our HTA. Because of this, we will not filter our search in terms of language or study design, to avoid missing relevant studies.

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## Study selection

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We will select studies found in the literature search in a two-step selection strategy:

- 1) Screening: two researchers will independently screen titles and abstracts (where available) using Rayyan QCRI software (29), to include or exclude articles based on their relevance to our research question. When in doubt, full-text version will be retrieved.
- 2) Full-text assessment: two researchers will read the full-text articles to assess which will be included in our HTA.

Both steps will adhere to the eligibility criteria listed above. Disagreements in either of the two steps will be resolved through discussion, or by consultation with a third researcher. Since this is a new treatment, we assume the search will generate few references for us to screen, and very few relevant studies to include. As such, we choose not to use machine learning in our screening process.

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## Data collection

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Relevant data will be extracted from the full-text articles to a self-made Excel-sheet, by one researcher. The extracted data will be verified by a second researcher. Any potential disagreements will be resolved through discussion, or by consultation with a third researcher. If necessary (e.g., if data are unintelligible, etc.), we will contact the authors for them to provide us with sufficient information to use in our HTA.

We will extract information regarding the following:

About	Information to be extracted
<b>The study</b>	Authors, publication year, study design, country, clinical identification number, eligibility criteria, follow-up time
<b>The participants</b>	Numbers of participants in each group, age, diagnosis, ethnicity, previous cancer treatment, PSA-level, ECOG (Eastern Cooperative Oncology Group) performance status, site of metastases
<b>The intervention and comparator</b>	PSMA-ligand, type of comparator used, dose, treatment cycles, treatment duration
<b>The outcome</b>	All outcome-data relevant for our HTA (see Eligibility criteria)

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## Assessment of risk of bias

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Two researchers will assess the quality of the included studies by using the Cochrane Risk of Bias Tool RoB1 for randomised controlled trials (30). Any potential differences will be resolved through discussion between the researchers, or by consultation with a third researcher.

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## Data synthesis

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The data synthesis will depend on the data provided in the included articles. If possible, we will synthesize the data in a meta-analysis (31). If a meta-analysis cannot be performed (e.g., if we have too heterogeneous studies, too few studies, etc.) we will present the data in a narrative synthesis. Regardless, all outcomes will be presented in summary-of-findings tables. For analysis of dichotomous outcomes (e.g., “time-to-event” such as death), we can use effect measures such as relative risk, odds ratio or hazard ratio. Uncertainty will be presented as 95% confidence interval (CI). Continuous data outcomes can be presented as absolute or relative mean difference between groups. If the studies are using different scales to measure the same outcome, we will use standardised or weighted mean difference, with 95% CI. Where possible, each primary outcome will be subjected to subgroup (e.g., age group, etc.) or sensitivity analysis, with respect to risk of bias and disease activity. Heterogeneity will be tested for using I<sup>2</sup>-test (31), and possible reasons for heterogeneity will be explored in sensitivity analysis.

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## Assessment of confidence in the findings

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We will assess the certainty of evidence for each selected outcome using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system (32). In brief, the GRADE system evaluates the certainty of evidence through assessment of several criteria, either downgrading (data from RCTs) or upgrading (data from observational studies) the certainty of evidence (32). For this HTA, based on RCTs, downgrading may be applied due to a) study limitations (risk of bias), b) inconsistency of results, c) indirectness of evidence, d) imprecision, and e) publication bias.

The certainty of evidence is classified as follows:

Quality level (GRADE)	Definition	Symbols
<b>High</b>	We are very confident that the true effect lies close to that of the estimate of the effect	⊕⊕⊕⊕
<b>Moderate</b>	We are moderately confident in the effect estimate: The true effect is <u>likely</u> to be close to the estimate of the effect, but there is a possibility that it is substantially different	⊕⊕⊕
<b>Low</b>	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect	⊕⊕
<b>Very low</b>	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect	⊕

Two researchers will independently GRADE effect estimates for each outcome extracted. Any potential disagreements will be resolved through discussion, or by consultation with a third researcher.

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## Health economic assessment

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To assess the cost-effectiveness of  $^{177}\text{Lu}$ -PSMA-617, we will estimate and describe costs and effectiveness related to  $^{177}\text{Lu}$ -PSMA-617 and comparator(s) in the Norwegian context. Efficacy estimates will be taken from the results of the systematic literature review, and we will make final decisions about the appropriate methods for the health economic evaluation when the efficacy results are available. In addition, we will receive documentation on efficacy and economic evaluation from Novartis, the supplier of  $^{177}\text{Lu}$ -PSMA-617. If the available documentation on efficacy and safety proves sufficient, we will perform a cost-utility analysis (CUA) (a cost-per-quality-adjusted-life-year (QALY) analysis) using a probabilistic Markov decision analytic model. If we do not find documentation of sufficient quality, other types of analyses can be more appropriate. Structure, assumptions, and input in the health economic analysis will be based on the available evidence on efficacy, safety, feedback from clinical experts, Norwegian cost databases, registers, and literature. We will also critically assess the received documentation from the supplier and use that input into our analysis wherever appropriate. Further, we will perform a five-year budget impact analysis of a potential introduction of  $^{177}\text{Lu}$ -PSMA-617 as a treatment option for patients with prostate cancer in Norway. In these analyses, we will use an *extended* health care perspective, which is relevant for prioritization of interventions within a fixed health care budget. This is in line with the guidance from the Priority-setting White Paper (33).

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## Other assessments/analyses

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### Organisational aspects

We will assess organisational challenges and consequences linked to a potential establishment of  $^{177}\text{Lu}$ -PSMA as a treatment option in Norway. The assessment will be based on feedback from clinical experts, Novartis and the Norwegian Radiation and Nuclear Safety Authority, related to current organization and capacity, e.g.:

- Will implementation of  $^{177}\text{Lu}$ -PSMA cause a need for specific training of personnel?
- Will implementation of  $^{177}\text{Lu}$ -PSMA cause a need for changes related to work hours, staffing, work environment, safety, etc?
- Will implementation of  $^{177}\text{Lu}$ -PSMA cause new structural needs at the hospital; are the premises suitable for using  $^{177}\text{Lu}$ -PSMA, e.g., patient rooms, hospital pharmacies, storage rooms, etc.?
- How will other departments or service functions at the hospital potentially be affected by implementation of the  $^{177}\text{Lu}$ -PSMA, e.g., hospital pharmacies, patient transportation, etc.?
- How will implementation of  $^{177}\text{Lu}$ -PSMA potentially cause changes of patient flow between hospitals and health regions?
- How will implementation of  $^{177}\text{Lu}$ -PSMA potentially affect the cooperation with the primary health care?
- Additional diagnostics and follow-up implications
- Adverse effects to be handled

### **Radiation safety**

We will assess radiation safety challenges and consequences linked to a potential establishment of <sup>177</sup>Lu-PSMA as a treatment option in Norway. We will discuss aspects of radiation safety in connection with the Norwegian legislations where it is necessary. The assessment will be based on peer reviewed publications, international guidelines, and the Norwegian radiation protection legislations, and will include aspects regarding, e.g.:

- Radiation protection of hospital staff, the public, family members of patients, and the environment
- Dosimetry: Absorbed doses to patient's tumor and organs at risk
- Scanner capacity

We will also assess aspects about radiation protection that may have organizational or health economic consequences.

### **User involvement**

We will recruit at least one patient representative as part of the external project participants, for input on aspects on <sup>177</sup>Lu-PSMA based treatment of prostate cancer that are important for patients. We will collect this information through a survey that will be sent by e-mail. Similar to clinical experts and other external team members, the patient representative(s) will be given the opportunity to read and comment on the project plan and the HTA report before submission to the commissioner.

### **Ethical aspects**

We will not assess potential ethical challenges and aspects regarding the use of <sup>177</sup>Lu-PSMA for treating prostate cancer.

### **Legal aspects**

We will not assess potential legal challenges and aspects regarding the use of <sup>177</sup>Lu-PSMA for treating prostate cancer.

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## **Peer review of the protocol and report**

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**Protocol:** Kjetil Gundro Brurberg, NIPH

### **HTA report:**

- Internal reviewers: Kjetil Gundro Brurberg, NIPH
- External reviewers: *to be decided*

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## **Timeframe**

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**Start date:** 15.06.2022

**End date:** 15.06.2023

<b>Step</b>	<b>From date</b>	<b>To date</b>
<i>Project plan</i>	15.06.2022	November 2022
<i>Literature search</i>	22.06.2022	04.08.2022
<i>Screening references</i>	15.08.2022	02.09.2022
<i>Data extraction</i>	September 2022	October 2022
<i>Assessment Risk of bias</i>	October 2022	October 2022
<i>Receiving documentation package</i>	October 2022	November 2022
<i>Analysis</i>	October 2022	December 2022
<i>Health economy model development</i>	October 2022	February 2023
<i>Assessment certainty of evidence</i>	December 2022	December 2022
<i>Draft report</i>	December 2022	February 2023
<i>Review by externa participants and Novartis</i>	March 2023	April 2023
<i>Peer-review</i>	March 2023	April 2023
<i>Approval of report</i>	April 2023	May 2023
<i>Send to commissioner</i>	May 2023	June 2023
<i>Publish</i>	June 2023	June 2023

### **Measures to be taken in the event of delays/unforeseen developments**

In case of events that will affect the timeframe, e.g., unforeseen long-term absence of team members, heavier workload than expected, measures will be taken to ensure delivery of the HTA report. This may include:

- Increased staffing
- Replacement of team members

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### **Deliverables and publication**

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#### **Publication**

The end product from this project is an HTA report, to which the target audience is the RHA-forum (Beslutningsforum Nye Metoder). The HTA report will be published as a NIPH report in English at the homepages of NIPH and the RHA-forum ([www.nyemetoder.no](http://www.nyemetoder.no)). If possible, it may also be published as a scientific article to reach international readers. Abstracts may be submitted to relevant conferences.

#### **Indexing for the homepage**

**Keywords:** <sup>177</sup>Lu, lutetium-177, radiation therapy, prostate cancer, PSMA, prostate specific membrane antigen

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### **Related NIPH projects/publications/studies**

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We are not aware of any ongoing projects or publications published at NIPH that are related to this project of <sup>177</sup>Lu-PSMA-617 for treatment of prostate cancer. NIPH have published one HTA regarding the use of <sup>177</sup>Lu-PSMA for the treatment of neuroendocrine tumors (9), and several HTAs on treatment of prostate cancer.

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