Nivolumab - Advanced or Metastatic Renal Cell Carcinoma and Prior mTOR Inhibitor

(This form must be completed before the first dose is dispensed.)

1. Patient Profile

* Surname: * Given Name:

* OHIN: * Chart Number:

* Postal Code:

* Height (cm): * Weight (kg): * BSA (m^2): * Gender: ○ Male ○ Female ○ Other

* Date of Birth:
Day Month Year

* Site:

* Attending Physician (MRP- Most Responsible Physician):

Requested Prior Approval ☐ Yes * Patient on Clinical Trial ○ Yes ○ No Other (specify):

Specify Arm: ○ Standard of care arm ○ Experimental arm ○ Blinded / Unknown

Prior Approval Request

* Select the appropriate prior approval scenario:

○ 1-Unknown primary (submit pathology report and clinic note)
○ 2-Clinical document review (identify the patient history that needs to be reviewed against eligibility criteria in Additional Comments below)
○ 3-Regimen modification - schedule (complete questions a and b)
○ 4-Regimen modification - drug substitutions (complete questions a and c)
○ 5-Withholding a drug in combination therapy from start of treatment (complete questions d, e and f)
○ 6-Maintenance therapy delay (submit clinic note)
○ 7-Prior systemic therapy clinical trials (complete question g)
○ 8-Modification due to supply interruption/drug shortage
○ 9-Supplemental doses requested
○ Other (specify)

All relevant supporting documentation must be submitted at the time of prior approval. Documentation may include a pathology report, clinic note, and/or CT scans.

a. Co-morbidities / toxicity / justification:

b. Intended regimen schedule:

c. Intended regimen:

d. Drug(s) to be held:

e. Rationale for holding drug(s):

f. Intention to introduce drug at a later date? ☐ Yes

g. Prior clinical trial identifier (e.g., NCT ID, trial name) and treatment description (e.g., arm, drug/regimen):

h. Anticipated date of first treatment:
Day Month Year

i. Additional comments:

2. Eligibility Criteria

Nivolumab is used as a treatment for patients with advanced or metastatic renal cell carcinoma with disease progression after at least one prior anti-angiogenic systemic treatment and who have good performance status. ☐ Yes

3. Baseline Information

a. ECOG performance status at the time of enrolment ○ 0 ○ 1 ○ 2

b. Tumour histologic type ○ Clear cell ○ Non-clear cell

c. Memorial Sloan Kettering Cancer Center (MSKCC) prognostic score ○ Favorable ○ Intermediate ○ Poor

d. Previous nephrectomy ○ Yes ○ No

e. The patient has stable brain metastases
○ Yes
○ Not applicable, the patient does not have brain metastases

f. Prior systemic treatments received for advanced or metastatic renal cell carcinoma*:

** The patient is eligible for nivolumab if everolimus or temsirolimus was started **prior to the public listing of nivolumab**.*

☐ Pazopanib (first line)
☐ Pazopanib (first line) and everolimus (second line)
☐ Sunitinib (first line)
☐ Sunitinib (first line) and everolimus (second line)
☐ Temsirolimus (first line)
☐ Other

Specify

g. Nivolumab is being given as the ____ line of treatment. ○ 2nd ○ 3rd ○ 4th line or greater

4. Funded Dose

Nivolumab 3 mg/kg IV, up to a maximum dose of 240 mg, every 2 weeks as an intravenous infusion, or nivolumab 6 mg/kg IV, up to a maximum dose of 480 mg, every 4 weeks as an intravenous infusion.

5. Notes

1. Nivolumab is funded as a second line treatment for patients that have received one prior tyrosine kinase inhibitor (e.g., first line sunitinib or pazopanib), OR as a third line treatment for patients that have received two prior tyrosine kinase inhibitors (e.g., first line sunitinib or pazopanib, second line axitinib).
2. Patients previously treated with an mTOR inhibitor (e.g., everolimus or temsirolimus), will not be eligible for coverage for nivolumab. However, patients previously treated with an mTOR inhibitor, ***prior to the public listing of nivolumab***, will be eligible to receive coverage for nivolumab upon disease progression.
3. Patients who have a disease-free interval of 6 months or greater after completion of adjuvant therapy may be eligible for one line of immune checkpoint inhibitor-based therapy for advanced or metastatic renal cell carcinoma provided all other eligibility criteria are met.
4. The patient is no longer eligible for nivolumab once there is confirmed disease progression.
5. Nivolumab funding is for single agent use only.
6. Patients who progress on prior immune checkpoint inhibitor-based treatment will not be eligible for single agent nivolumab in subsequent lines of therapy.

6. FAQs

1. **My patient is currently receiving nivolumab through private means. Can my patient be transitioned over to receive funding through the New Drug Funding Program (NDFP)?**

   Provided the funding rules were met at the time of treatment initiation and the patient's disease has not progressed, your patient may be eligible for continued coverage of nivolumab through the New Drug Funding Program.

2. **My patient has previously been treated with everolimus. Is my patient eligible to receive nivolumab?**

   Patients previously treated with an mTOR inhibitor (e.g., temsirolimus or everolimus), will not be eligible for coverage for nivolumab. However, patients previously treated with an mTOR inhibitor, prior to the public listing of nivolumab, will be eligible for coverage for nivolumab upon disease progression.

3. **Is axitinib or everolimus funded after nivolumab?**

   For patients treated with nivolumab, public funding will not be provided for subsequent drug therapies (e.g,. axitinib, everolimus).

   The recommendation not to fund subsequent treatment with everolimus following nivolumab in metastatic renal cell cancer was made based on consideration of factors including information about clinical impact, budget impact, unmet medical need, and availability of existing therapies, among other factors. The lack of direct evidence of clinical benefit and the high cost of these existing treatments were considered in the recommendations.

   Please refer to the document: "Cancer Drug Funding in Ontario" for further information on the drug funding decision-making process.

4. **Contrary to other provinces in Canada, the Ministry's funding criteria for axitinib requires that the patient either is "unable to tolerate an ongoing use of an effective dose of everolimus" or "have a contraindication to everolimus." Why are there jurisdictional differences in the axitinib criteria?**

   Ontario's axitinib criteria is aligned with pCODR's axitinib recommendation. pCODR's Provincial Advisory Group is preparing a request for pCODR to clarify the clinical criteria for axitinib. Ontario's axitinib criteria will be revisited pending the outcome of pCODR's clarification.

5. **My patient is currently receiving nivolumab on an every 2 week schedule. Can my patient be transitioned over to the every 4 week schedule?**

   The decision to switch should be based on a discussion between the clinician and patient. Switches between schedules (from every 2 weeks to every 4 weeks or vice versa) will be eligible for continued funding provided the patient's disease has not progressed.

6. **What is the rationale for having a maximum dose for the every 2 week schedule?**

   Exposure-response relationships for efficacy and clinical safety have shown that the benefit-risk profile is comparable between weight-based dosing and the 240 mg flat dose. Weight-based dosing, up to a maximum dose, will be applied across all nivolumab policies and is in alignment with other Canadian jurisdictions who have implemented nivolumab.

7. **My patient is currently on the every 2 week schedule at a dose greater than 240 mg. Will this dose continue to be eligible for funding?**

   On a time-limited basis (until November 2, 2018), CCO will allow funding for doses greater than 240 mg for patients who initiated treatment with the 3 mg/kg every 2 week schedule prior to September 7, 2018. This time-limited funding allows clinicians an opportunity to inform patients of the revised dosing schedule, and to update their computerized prescriber order entry (CPOE) systems accordingly. Starting November 3, 2018, reimbursement will be capped at 240 mg for the every 2 week schedule. Patients who switch to the 6 mg/kg every 4 week schedule are required to adhere to the maximum dose of 480 mg as of the effective funding date.

8. **My patient is currently on a 'treatment break' and requires resumption of their nivolumab therapy. If their original dose exceeded 240 mg, are clinicians required to adopt the maximum dose cap?**

   Upon resumption of therapy, patients on a 'treatment break' will be required to adhere to the funded dose for any dose(s) given after November 2, 2018 (e.g., 3 mg/kg, up to 240 mg, every 2 weeks or 6 mg/kg, up to 480 mg, every 4 weeks).

7. Supporting Documents

None required for this policy.

In the event of an audit, the following should be available to document eligibility:

- CT scans every 3 to 6 months, along with clinic notes indicating no disease progression.
- In instances where there is pseudoprogression,
  - a clinic note **documenting** the assessment and decision to continue, AND
  - a confirmatory scan conducted preferably at 6 to 8 weeks but no later than 12 weeks after the initial disease progression to confirm the absence of true progression.

Signature of Attending Physician (MRP-Most Responsible Physician): .....

Day ..... Month ..... Year .....

Form 1009