

Temsirolimus Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
First-line treatment of adult patients with advanced renal cell carcinoma (RCC) who have at least three of six prognostic risk factors	C64	00326a	Hospital

**If the reimbursement status is not defined¹, the indication has yet to be assessed through the formal HSE reimbursement process.*

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Temsirolimus is administered once every 7 days by IV infusion until disease progression or unacceptable toxicity occurs (4 weeks = 1 cycle).

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1,8,15 and 22	Temsirolimus	25mg	IV	250ml 0.9% NaCl over 30min	Every 28 days
In line filter with non-PVC tubing should be used with temsirolimus infusion					

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to temsirolimus, its metabolites (including sirolimus), polysorbate 80 or any of the excipients
- Caution is advised for patients with pre-existing significant lung compromise due to the risk for pneumonitis
- Pregnancy
- Lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Total cholesterol and triglycerides
- Fasting serum glucose
- Chest X-ray

Regular tests:

NCCP Regimen: Temsirolimus Monotherapy	Published: 03/06/2016 Review: 30/05/2020	Version number: 2
Tumour Group: Genitourinary NCCP Regimen Code: 00326	ISMO Contributor: Prof Maccon Keane	Page 1 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens

- FBC weekly
- Renal and liver profile every 4 weeks
- Total cholesterol and triglycerides as clinically indicated
- Monitoring of fasting serum glucose as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Management of severe and/or intolerable suspected adverse reactions may require dose reduction and/or temporary interruption of temsirolimus therapy.
- If a suspected reaction is not manageable with dose delays, then temsirolimus may be reduced by 5 mg/week decrements.
 - Dose level -1 : 20mg
 - Dose level -2 : 15mg

Haematological:

Table 1: Dose modification of temsirolimus for haematological toxicity

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
≥1	and	≥ 75	No dose adjustment required
<1	or	< 75	Hold until ANC ≥1 x 10 ⁹ /L and/or platelets recover to ≥75x10 ⁹ /l. Reduce dose by 5mg.

Renal and Hepatic Impairment:

Table 2: Dose modification of temsirolimus in renal and hepatic impairment

Renal Impairment	Hepatic Impairment				
No dose adjustment recommended in patients with renal impairment. Use with caution in patients with severe renal impairment	Child Pugh Class	Platelets (x10 ⁹ /L)	Total Bilirubin	Dose	
	Mild to moderate	A or B	≥100	≤3 x ULN	No recommended dose adjustment
	Severe	C	≥100	> 3 x ULN	10mg IV once weekly infused over 30min

NCCP Regimen: Temsirolimus Monotherapy	Published: 03/06/2016 Review: 30/05/2020	Version number: 2
Tumour Group: Genitourinary NCCP Regimen Code: 00326	ISMO Contributor: Prof Maccon Keane	Page 2 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens

Management of adverse events:

Table 3: Dose Modification of temsirolimus for Adverse Events

Adverse reactions	Recommended dose modification
Grade 0-2	100% Grade 2 adverse events that are persistent and intolerable can result in dose delays or dose reductions to the next lower dose level
Grade 3-4	Hold therapy until recovery to Grade 0-2. If recovery within 3 weeks, reduce dose by one dose level for subsequent treatment.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low (Refer to local policy).

PREMEDICATIONS:

Patients should be given intravenous diphenhydramine 25 mg to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of temsirolimus

OTHER SUPPORTIVE CARE:

No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Hypersensitivity:** Hypersensitivity/infusion reactions (including some life-threatening and rare fatal reactions), including and not limited to flushing, chest pain, dyspnoea, hypotension, apnoea, loss of consciousness, hypersensitivity and anaphylaxis, have been associated with the administration of temsirolimus.
- These reactions can occur very early in the first infusion, but may also occur with subsequent infusions. Patients should be monitored early during the infusion and appropriate supportive care should be available. Temsirolimus infusion should be interrupted in all patients with severe infusion reactions and appropriate medical therapy administered. A benefit-risk assessment should be done prior to the continuation of temsirolimus therapy in patients with severe or life-threatening reactions.
 - If a patient develops a hypersensitivity reaction during the temsirolimus infusion, despite the premedication, the infusion must be stopped and the patient observed for at least 30 to 60 minutes (depending on the severity of the reaction).
 - At the discretion of the prescribing consultant, treatment may be resumed after the administration of an H1-receptor antagonist (diphenhydramine or similar antihistamine) and a H2-receptor antagonist (intravenous famotidine 20 mg or intravenous ranitidine 50 mg) approximately 30 minutes before restarting the temsirolimus infusion.
 - Administration of corticosteroids may be considered; however, the efficacy of corticosteroid treatment in this setting has not been established.

NCCP Regimen: Temsirolimus Monotherapy	Published: 03/06/2016 Review: 30/05/2020	Version number: 2
Tumour Group: Genitourinary NCCP Regimen Code: 00326	ISMO Contributor: Prof Maccon Keane	Page 3 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens

- The infusion may then be resumed at a slower rate (up to 60 minutes) and should be completed within six hours from the time that temsirolimus is first added to sodium chloride 9 mg/ml (0.9%) solution for injection.
- **Hyperglycaemia:** Hyperglycaemia is a common adverse event. Dose adjustment or initiation of anti-diabetic therapy may be required. Patients should be advised to report excessive thirst or any increase in the volume or frequency of urination
- **Interstitial lung disease:** It is recommended that patients be followed closely for occurrence of clinical respiratory symptoms and patients should be advised to report promptly any new or worsening respiratory symptoms. If clinically significant respiratory symptoms develop, consider withholding temsirolimus administration until after recovery of symptoms and improvement of radiographic findings related to pneumonitis. Opportunistic infections such as PCP should be considered in the differential diagnosis. Empiric treatment with corticosteroids and/or antibiotics may be considered. For patients who require use of corticosteroids, prophylaxis of PCP should be considered based upon current standard of care.
- **Hyperlipaemia:** Use of temsirolimus has been associated with increases in serum triglycerides and cholesterol. This may require initiation or increase in the dose of lipid-lowering agents. Serum cholesterol and triglycerides should be tested before and during treatment with temsirolimus.
- **Infections:** Patients may be immunosuppressed and should be carefully observed for the occurrence of infections, including opportunistic infections
- **Wound healing complications:** The use of temsirolimus has been associated with abnormal wound healing; therefore, caution should be exercised with the use of temsirolimus in the peri-surgical period.

DRUG INTERACTIONS:

- Coadministration of temsirolimus and CYP3A4/5 inducers may decrease composite exposure of the active moieties, temsirolimus and its metabolite sirolimus. For patients with RCC, continuous administration beyond 5-7 days with agents that have CYP3A4/5 induction potential should be avoided.
- Concomitant treatment with agents that have strong CYP3A4 inhibition potential should be avoided and they may lead to increased toxicity of temsirolimus, and/or its metabolite sirolimus, due to reduced clearance.
- Coadministration with medicinal products that are P-glycoprotein substrates may lead to increased effects/toxicity of these drugs due to inhibition of P-gp by temsirolimus resulting in reduced clearance.
- Angioneurotic oedema-type reactions (including delayed reactions occurring two months following initiation of therapy) have been observed in some patients who received temsirolimus and ACE inhibitors concomitantly.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Temsirolimus – L01XE09

REFERENCES:

1. Hudes G, Carducci M, Tomczak P et al. Temsirolimus, Interferon Alfa, or Both for Advanced Renal-Cell Carcinoma. NEJM 2007;356 (22): 2271-2281

NCCP Regimen: Temsirolimus Monotherapy	Published: 03/06/2016 Review: 30/05/2020	Version number: 2
Tumour Group: Genitourinary NCCP Regimen Code: 00326	ISMO Contributor: Prof Maccon Keane	Page 4 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

2. Torisel[®] Summary of Product Characteristics Accessed May 2018. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Product_Information/human/000799/WC500039912.pdf

Version	Date	Amendment	Approved By
1	03/06/2016		Prof Maccon Keane
2	30/05/2018	Updated with new NCCP regimen template. Standardisation of treatment table	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

ⁱ ODMS – Oncology Drug Management System

CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes

Further details on the Cancer Drug Management Programme is available at;

<http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/>

NCCP Regimen: Temozolomide Monotherapy	Published: 03/06/2016 Review: 30/05/2020	Version number: 2
Tumour Group: Genitourinary NCCP Regimen Code: 00326	ISMO Contributor: Prof Maccon Keane	Page 5 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		