# EVEROLIMUS

**INDICATION (ICD10) C25, C34, C50C64 or M-8013/3, M-8246/3 or M-8574/3 morphology**

1. Everolimus with exemestane for treating ER +ve, HER2 –ve metastatic, advanced breast cancer with no symptomatic visceral disease after endocrine therapy, having received no more than 1 line of chemotherapy for advanced disease, nor exemestane for metastic disease. (TA421)
2. Everolimus for advanced renal cell carcinoma after previous treatment, which has progressed during or after treatment with vascular endothelial growth factor targeted therapy. (TA449)
3. The treatment of unresectable or metastatic well differentiated neuroendocrine tumours of pancreatic origin with disease progression in the past 12 months, without previous treatment with a mTOR inhibitor. PS 0 or 1. (TA449)
4. The treatment of unresectable or metastatic well differentiated neuroendocrine tumours of gastrointestinal or lung origin with disease progression without active symptoms t suggest functional tumour, without previous treatment with a mTOR inhibitor. PS 0 or 1. (TA449**)**

**REGIMEN**
EVEROLIMUS 10mg orally daily

**CYCLE FREQUENCY AND NUMBER OF CYCLES**
Daily for 28 days continuously until progression or toxicity

**ADMINISTRATION**
Available as 2.5mg, 5mg and 10mg tablets
Swallow whole with or without food.

**ANTI-EMETICS**
Minimal risk all days

**CONCURRENT MEDICATION REQUIRED**
Breast cancer only - Exemestane 25mg orally daily must be prescribed (use support regimen)
All - Mouth care eg difflam, gelclair

**EXTRAVASATION AND TYPE OF LINE / FILTERS**
Not applicable

**INVESTIGATIONS**
Blood results required before SACT administration
FBC, U&E and LFTs minimum monthly for first 3 months then alternate months
Neutrophils x $10^9$/L ≥1.5
Platelets x $10^9$/L ≥100
Random blood sugar, lipid profile each cycle; if elevated to repeat on fasting blood minimum monthly for 1st 3 months then alternate months

**MAIN TOXICITES AND ADVERSE REACTIONS**

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| Everolimus | Increased glucose, lipids and triglycerides<br>Decreased haemoglobin, lymphocytes, neutrophils and platelets<br>Hypersensitivity reactions<br>Pneumonitis, Infections<br>Oral ulceration, mucositis |

**INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS**
**(not exhaustive list check SPC/BNF/Stockleys)**

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| Everolimus | Strong CYP3A4 inhibitors (eg clarithromycin, itraconazole, posaconazole, voriconazole) should be avoided.<br>CYP3A4 inducers (eg carbamazepine, phenytoin) should be avoided.<br>ACE inhibitors increase risk of angioedema<br>Grapefruit and grapefruit juice should be avoided |

**DOSE MODIFICATIONS**
**Haematological**

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| Thrombocytopenia grade 2 (platelets <75, ≥50x10$^9$/l) | Temporary dose interruption until recovery to grade ≤1 (platelets ≥75x10$^9$/l).<br>Re-initiate treatment at same dose. |
| Thrombocytopenia grade 3 and 4 (platelets <50x10$^9$/l | Temporary dose interruption until recovery to grade ≤1 (platelets ≥75x10$^9$/l).<br>Re-initiate treatment at 5mg daily. |
| Neutropenia grade 2 (ANC ≥1x10$^9$/l) | No dose adjustment required. |
| Neutropenia grade 3 (ANC <1, ≥0.5x10$^9$/l) | Temporary dose interruption until recovery to grade ≤2 (ANC ≥1x10$^9$/l).<br>Re-initiate treatment at same dose. |
| Neutropenia grade 4 (ANC <0.5x10$^9$/l) | Temporary dose interruption until recovery to grade ≤2 (≥1x10$^9$/l).<br>Re-initiate treatment at 5mg daily. |
| Febrile neutropenia grade 3 | Temporary dose interruption until recovery to grade ≤2 (≥1.25x10$^9$/l) and no fever.<br>Re-initiate treatment at 5mg daily. |
| Febrile neutropenia grade 4 | Discontinue treatment. |

**Non-haematogical**

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| Non-infectious pneumonitis grade 2 | Consider interruption of therapy until symptoms improve to grade ≤1. Re-initiate treatment at 5mg daily. Discontinue treatment if failure to recover within 4 weeks. |
| Non-infectious pneumonitis grade 3 | Interrupt treatment until symptoms resolve to grade ≤1. Consider re-initiating treatment at 5mg daily. If toxicity recurs at grade 3, consider discontinuation. |
| Non-infectious pneumonitis grade 4 | Discontinue treatment. |
| Stomatitis grade 2 | Temporary dose interruption until recovery to grade ≤1. Re-initiate treatment at same dose. If stomatitis recurs at grade 2, interrupt dose until recovery to grade ≤1. Re-initiate treatment at 5mg daily. |
| Stomatitis grade 3 | Temporary dose interruption until recovery to grade ≤1. Re-initiate treatment at 5mg daily. |
| Stomatitis grade 4 | Discontinue treatment. |
| Other non-haematological toxicities (excluding metabolic events) grade 2 | If toxicity is tolerable, no dose adjustment required.<br>If toxicity becomes intolerable, temporary dose interruption until recovery to grade ≤1.<br>Re-initiate treatment at same dose.<br>If toxicity recurs at grade 2, interrupt treatment until recovery to grade ≤1. Re-initiate treatment at 5mg daily. |
| Other non-haematological toxicities (excluding metabolic events) grade 3 | Temporary dose interruption until recovery to grade ≤1. Consider re-initiating treatment at 5mg daily. If toxicity recurs at grade 3, consider discontinuation. |
| Other non-haematological toxicities (excluding metabolic events) grade 4 | Discontinue treatment. |
| Metabolic events (e.g. hyperglycaemia, dyslipidaemia) grade 2 | No dose adjustment required. |
| Metabolic events (e.g. hyperglycaemia, dyslipidaemia) grade 3 | Temporary dose interruption.<br>Re-initiate treatment at 5mg daily. |
| Metabolic events (e.g. hyperglycaemia, dyslipidaemia) grade 4 | Discontinue treatment. |

**Hepatic impairment**

Child-Pugh scores are based on ascites, encephalopathy, INR, albumin, total bilirubin

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| Moderate hepatic impairment (Child-Pugh class B) | Reduce to 5mg daily. |
| Severe hepatic impairment (Child-Pugh class C) | Everolimus has not been evaluated and is not recommended for use in this patient population. |

**Renal impairment**

No dose adjustment is required

**REFERENCES**

1. SPC April 2019
2. Baselga, J et al; NEJM 2012; 366: 520–529 (breast)
3. Lancet. 2008 Aug 9;372 (9637):449-56. Epub 2008 Jul 22.
   Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. Motzer RJ, Escudier B, Oudard S, Hutson TE, Porta C, Bracarda S, Grünwald V, Thompson JA, Figlin RA, Hollaender N, Urbanowitz G, Berg WJ, Kay A, Lebwohl D, Ravaud A; RECORD-1 Study Group. (Renal)
4. Cancer. 2010 Jun 14. [Epub ahead of print]
   Phase 3 trial of everolimus for metastatic renal cell carcinoma : final results and analysis of prognostic factors. Motzer RJ, Escudier B, Oudard S, Hutson TE, Porta C, Bracarda S, Grünwald V, Thompson JA, Figlin RA, Hollaender N, Kay A, Ravaud A; for the RECORD-1 Study Group. (Renal)
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