

Vismodegib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
Treatment of adult patients with symptomatic metastatic basal cell carcinoma (MBCC)	C44	00236a	CDS 1/11/17
Treatment of adult patients with local advanced basal cell carcinoma inappropriate for surgery or radiotherapy.	C44	00236b	CDS 1/11/17

**If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not been 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.

Vismodegib is administered once daily until disease progression or unacceptable toxicity develops. Benefit of continued treatment should be regularly assessed, with the optimal duration of therapy varying for each individual patient.

Drug	Dose	Route	Cycle
Vismodegib	150mg daily	PO with or without food at the same time each day. Capsule must be swallowed whole with 200ml water	Continuous therapy
If a dose is missed, patients should be instructed not to take the missed dose but to resume with the next scheduled dose.			
Vismodegib is available as 150mg capsules Capsules should NOT be crushed or opened.			

ELIGIBILITY:

- Indications as above
- ECOG status 0-2
- Age 18 years or older

EXCLUSIONS:

- Pregnancy or breast feeding.
- Women of childbearing potential who do not comply with the Erivedge® Pregnancy Prevention Programme. (Please see adverse events/ regimen specific complications for further details and for precautions to be taken by males)
- Hypersensitivity to vismodegib or any of the excipients.

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile.
- Assessment and registration as per Erivedge® Pregnancy Prevention Program for both male and female patients.

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Regular tests:

- FBC, renal and liver profile every 4 weeks.
- Pregnancy test requirements based on the Erivedge® Pregnancy Prevention Programme.

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.
- No recommended dose reductions for vismodegib.
- Treatment interruptions of up to 4 weeks were allowed based on individual tolerability in clinical trials.

Renal and Hepatic Impairment:

Table 1: Dose modification of vismodegib in renal and hepatic impairment

Renal Impairment		Hepatic dysfunction
	Dose Recommendation	No dose adjustment is required in patients with mild, moderate or severe hepatic impairment based on National Cancer Institute Organ Dysfunction Working Group (NCI-ODWG)- criteria for hepatic impairment mild: TB ≤ ULN; AST > ULN or ULN < TB < 3 x ULN, AST any moderate: 1.5 x ULN < TB < 3 x ULN, AST any severe: 3 x ULN < TB < 10 x ULN, AST any
Mild	No dose adjustment is needed.	
Moderate		
Severe	Limited data, monitor patients for adverse reactions	

TB total bilirubin; AST aspartate aminotransferase; ULN upper limit of normal

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (Refer to local policy).

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions *The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.*

- **Cutaneous squamous cell carcinoma (cuSCC):** Patients with advanced BCC have an increased risk of developing cuSCC. All patients should be monitored routinely while taking vismodegib and cuSCC should be treated according to the standard of care.
- **Embryo-foetal death or severe birth defects:** Vismodegib must never be used by women who are pregnant or by women who could become pregnant unless all the conditions of the Erivedge®

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Pregnancy Prevention Programme are met. These conditions must be fulfilled for all male and female patients.

For men: Vismodegib is present in semen.

To avoid potential foetal exposure during pregnancy, a male patient must understand that:

- Vismodegib exposes a teratogenic risk to the unborn child if he engages in unprotected sexual activity with a pregnant woman,
- He must always use the recommended contraception
- He will tell his healthcare provider if his female partner becomes pregnant while he is taking vismodegib or during the 2 months after his final dose.
- **Blood donation:** Patients should not donate blood while taking vismodegib and for 24 months after the final dose.
- **Effects on post-natal development:** Premature fusion of the epiphyses has been reported in patients exposed to vismodegib. Due to the long drug elimination half-life, fusion may occur or progress after drug discontinuation. In animal species, vismodegib has been shown to cause severe irreversible changes in growing teeth (degeneration/necrosis of odontoblasts, formation of fluid-filled cysts in the dental pulp, ossification of the root canal, and haemorrhage) and closure of the epiphyseal growth plate. These findings indicate a potential risk for short stature and tooth deformities to infants and children. Vismodegib should not be used in those aged <18years.

DRUG INTERACTIONS:

- When vismodegib is administered with CYP inducers (rifampicin, carbamazepine, phenytoin, St. John's wort), exposure to vismodegib may be decreased
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Vismodegib - L01XX43

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

HCP guide: https://www.hpra.ie/img/uploaded/swedocuments/Erivedge_HCP%20Brochure_03.17-2187058-19052017123204-636307939334687500.pdf

Patient Brochure: https://www.hpra.ie/img/uploaded/swedocuments/Erivedge_Patient%20Brochure_03.17-2187058-19052017123355-636307940566250000.pdf

REFERENCES:

1. Sekulic A, Migden MR, Oro AE, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. N Engl J Med 2012;366:2171-9.
2. Erivedge ®Summary of Product Characteristics Accessed September 2017. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002602/WC500146817.pdf

Version	Date	Amendment	Approved By
1	12/10/2017		Dr Emer O'Hanrahan

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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/>

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