**Regimen Monograph**



## A - Regimen Name

# VISM Regimen

**Vismodegib**

**Disease Site**

Skin
Basal Cell

**Intent**

Curative
Palliative

**Regimen Category**

**Evidence-Informed :**

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

**Rationale and Uses**

Treatment of histologically confirmed metastatic basal cell carcinoma or locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy

**Supplementary Public Funding**

**vismodegib**
Exceptional Access Program (vismodegib - Treatment for metastatic basal cell carcinoma (BCC) or with locally advanced BCC (including patients with basal cell nevus syndrome, i.e. Gorlin syndrome), according to specific criteria) (EAP Website)

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## B - Drug Regimen

Vismodegib may only be prescribed and dispensed by physicians and pharmacists registered with the Erivedge® Pregnancy Prevention Program (EPPP). Patients must also be registered and meet all conditions of the program. Call 1-888-748-8926 or log onto www.erivedge.ca

| | | | |
|---|---|---|---|
| **vismodegib** | 150 mg | PO | Daily |

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## C - Cycle Frequency

**CONTINUOUS TREATMENT**

Until disease progression or unacceptable toxicity. The majority of responses occurred in the first 16 weeks; the benefit of continued treatment after this period should be re-evaluated.

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Minimal – No routine prophylaxis; PRN recommended

- Also refer to CCO Antiemetic Recommendations.

**Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

**Women of child-bearing potential must have a negative pregnancy test within 7 days before starting treatment.**

### Dosage with toxicity

There are no dose reductions for vismodegib. Interruptions up to 8 weeks are allowed for intolerable side effects* or for a planned surgical procedure. New onset of cutaneous squamous cell carcinoma should be managed according to the standard of care.

*intolerable side effects: Grade 3 or 4 related toxicities that are likely to be clinically significant, life-threatening or irreversible.

The following were excluded in the phase II clinical trial:

- Hematologic or metabolic/chemistry abnormalities not considered clinically significant
- Nausea, vomiting, or diarrhea that are adequately controlled after optimization of medical management.
- Transient and manageable grade 3 infection
- Asymptomatic thromboembolism found incidentally on imaging and managed with anti-coagulation therapy)

| Toxicity | Action |
|---|---|
| Pancreatitis | Consider hold or discontinuation |
| Grade 3 or 4 treatment-related | Hold up to 8 weeks |
| Planned surgery | Hold up to 8 weeks |
| Grade 3 or 4 hepatotoxicity | Hold or discontinue |
| Severe cutaneous adverse reactions (SCARs) (such as Stevens-Johnson syndrome, toxic epidermal necrolysis, DRESS, acute generalized exanthematous pustulosis) | Discontinue |

## Hepatic Impairment

| Hepatic Impairment | Total bilirubin / AST | | AST | Vismodegib dose |
|---|---|---|---|---|
| Mild | ≤ ULN | And | >ULN | No change; exercise caution |
| | >ULN to 1.5x ULN | And | any | No change; exercise caution |
| Moderate | >1.5 to < 3x ULN | And | any | No change; exercise caution |
| Severe | 3 to <10x ULN | And | any | Not recommended for use |

## Renal Impairment

The safety and efficacy of vismodegib have not been established in patients with severe renal impairment.

| Creatinine clearance (ml/min) | Vismodegib dose |
|---|---|
| ≥ 50 | No change |
| 30 to 49 | No change |
| < 30 | No data |

## Dosage in the Elderly

No specific dose adjustment is necessary. However, monitor with caution.

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## F - Adverse Effects

Refer to vismodegib drug monograph(s) for additional details of adverse effects.

| Very common (≥ 50%) | Common (25-49%) | Less common (10-24%) | Uncommon (< 10%), but may be severe or life-threatening |
|---|---|---|---|
| • Musculoskeletal pain* (may be severe)<br>• Alopecia<br>• Dysgeusia* | • Anorexia, weight loss*<br>• Fatigue<br>• Amenorrhea<br>• Nausea, vomiting<br>• Abnormal electrolytes<br>• Diarrhea<br>• Increase LFTs (may be severe) | • Constipation<br>• Cough, dyspnea<br>• Creatinine increased (may be severe)<br>• Headache<br>• Insomnia<br>• Infection | • Arterial thromboembolism<br>• Venous thromboembolism<br>• GI obstruction, perforation, bleeding<br>• Psychiatric (e.g. paranoia)<br>• Arrhythmia<br>• Cardiotoxicity<br>• Hypertension<br>• Rhabdomyolysis<br>• Secondary malignancy (squamous cell carcinoma)<br>• Pancreatitis<br>• Stevens-Johnson syndrome<br>• Toxic epidermal necrolysis<br>• DRESS<br>• Acute generalized exanthematous pustulosis |

*may persist at least 12 months post-treatment discontinuation

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## G - Interactions

Refer to vismodegib drug monograph(s) for additional details.

- Vismodegib is a possible inhibitor of BCRP, CYP2C9 and CYP2C19. Use caution when administering vismodegib and these respective substrates with a narrow therapeutic range.

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## H - Drug Administration and Special Precautions

Refer to vismodegib drug monograph(s) for additional details.

**Administration:**

Vismodegib may only be prescribed and dispensed by physicians and pharmacists registered with the EPPP. Patients must also be registered and meet all conditions of the program. Call 1-888-748-8926 or log onto www.erivedge.ca

- Capsules must be swallowed whole with a glass of water and not crushed or opened; can be taken with or without food.
- If dose is missed, skip this dose and give the next scheduled dose. Do not double the dose to make up for the missed one.
- Store at room temperature (15 - 30°C), in original package away from moisture and heat.

**Contraindications:**

- Patients who have a hypersensitivity to this drug or any of its components
- In patients aged below 18 years
- Females patients of childbearing potential and male patients who do not comply with the EPPP requirements
- Breastfeeding female patients

**Warnings/Precautions:**

- Vismodegib is not recommended for use in patients with severe hepatic impairment. Use with caution in patients with mild to moderate hepatic impairment.
- Use with caution in patients with a history of pancreatitis and gallbladder disease.
- Patients should not donate blood or semen while taking vismodegib, during dose interruptions and for 24 months (2 months for semen) after stopping therapy.

- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Patients with history of significant cardiovascular disease or risk factors for syncope: Severe related adverse events have been reported in these patients groups. There was no effect of vismodegib on the QT interval.

**Pregnancy and Lactation:**

- This regimen is **contraindicated for use in pregnancy and in males and females of childbearing potential who do not comply with the EPPP**. Refer to the EPPP for complete details.
- Breastfeeding is **contraindicated** during treatment and dose interruptions, and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Yes

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## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- Liver function tests; baseline, before each cycle and as clinically indicated
- Renal function tests; baseline and before each cycle
- Amylase and lipase; baseline and as clinically indicated
- Controlled distribution program requirements regarding pregnancy tests for women of child-bearing potential; as per the EPPP
- Clinical toxicity assessment for musculoskeletal pain, fatigue, syncope, hypersensitivity, diarrhea, anorexia and other GI, cardiovascular effects, thromboembolism and psychiatric effects; at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Electrolytes, including magnesium; baseline and as clinically indicated

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## J - Administrative Information

Outpatient prescription for home administration

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## K - References

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.

Vismodegib drug monograph, Ontario Health (Cancer Care Ontario).

**August 2023** Updated Dose modifications and Adverse effects sections

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## M - Disclaimer

***Regimen Abstracts***

*A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

*Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.*

***Regimen Monographs***

*Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.*

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