SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Vismodegib
Basal Cell Carcinoma

PROTOCOL REF: MPHAMMEVIS
(Version No. 2.0)

Approved for use in:

- Gorlin syndrome with non-locally advanced, non-metastatic multiple basal cell carcinomas (BCC) (>=6) clinically evident at the point of decision to treat BCCs of which 3 are at least 5mm OR
- Non-locally advanced, non-metastatic multiple BCC (>=6) clinically evident at the point of decision to treat BCCs of which 3 are at least 5mm AND are appropriate for surgery i.e. surgically eligible tumours.
- ECOG Performance Status 0,1 or 2.
- Blueteq registration required-please consult for full eligibility criteria.

Dosage:

Drug	Dose	Route	Frequency
Vismodegib	150mg*	Oral	Daily*

*Continuous daily administration or an intermittent unlicensed schedule may be used:

- A 72 week period of: vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks OR
- A 72 week period of: vismodegib 24 weeks; off treatment 8 weeks; vismodegib 8 weeks; off treatment 8 weeks; vismodegib 8 weeks; off treatment 8 weeks; vismodegib 8 weeks.
- The licensed continuous dose will be set in Meditech.

Erivedge® (vismodegib) Pregnancy Prevention Programme (PPP) form need to be completed by pharmacist at each dispensing event.

Prescriptions are limited to 28 days supply only, and for women of child bearing potential (WCBP) will only be issued within 7 days of a negative pregnancy test

Administration (+/- Counselling Points):

The capsules must be swallowed whole with water (with or without food)
Vismodegib is contraindicated in women of childbearing potential who do not comply with the Pregnancy Prevention Programme.

Counselling for women of child bearing potential:
• Vismodegib exposes a teratogenic risk to the unborn child
• She must not take vismodegib if she is pregnant or plans to become pregnant
• She must have a negative pregnancy test, conducted by a health care provider within 7 days before starting vismodegib treatment
• She must have a negative pregnancy test monthly during treatment, even if she has become amenorrhoeic
• She must not become pregnant while taking vismodegib and for 24 months after her final dose
• She must use two methods of recommended contraception including one highly effective method and a barrier method during vismodegib therapy and for 24 months after the final dose.
• She must use 2 methods of recommended contraception while she is taking vismodegib, unless she commits to not having sexual intercourse
• She must tell her healthcare provider if any of the following occur during treatment and for 24 months after her final dose: 1. If she becomes pregnant or think for any reason that she may be pregnant 2. If she misses her expected menstrual period 3. If she stops using contraception unless she commits to not having sexual intercourse 4. If she needs to change contraception during treatment,
• She must not breast-feed while taking vismodegib and for 24 months after the final dose.

Counselling for male patients:
• Vismodegib is contained in semen. To avoid potential foetal exposure during pregnancy, a male patient must understand that: 1. Vismodegib exposes a teratogenic risk to the unborn child if he engages in unprotected sexual activity with a pregnant woman, 2. He must always use a condom (with spermicide, if available), even after a vasectomy, when having sex with a female partner while taking vismodegib and for 2 months after the final dose. 3. 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. 4. He should not donate semen while taking vismodegib and for 2 months after the final dose.

Pregnancy testing

In a WCBP, a medically supervised pregnancy test, conducted by a heath care provider, should be performed within 7 days prior to initiating treatment and monthly during treatment. Pregnancy tests should have a minimum sensitivity of 25 mIU/mL as per local availability. Patients who present with amenorrhea during treatment with vismodegib should continue monthly pregnancy testing while on treatment.

Blood donation: Patients should not donate blood while taking vismodegib and for 24 months after the final dose.

Additional precautions: Patients should be instructed never to give their capsules to another person, and to return any unused capsules back to the cancer centre for safe disposal.

Emetogenic risk (if applicable):

Minimal emetogenic risk

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required
Loperamide 2mg when required after each loose stool

Extravasation risk (if applicable):

Not applicable

Dosing in renal and hepatic impairment:

Renal	Mild and moderate renal impairment is not expected to impact the elimination of vismodegib and no dose adjustment is needed. Very limited data is available in patients with severe renal impairment. Patients with severe renal impairment should be carefully monitored for adverse reactions.

Hepatic	No dose adjustment is required in patients with mild, moderate or severe hepatic impairment

Interactions:

Concomitant treatment with strong CYP inducing drugs (such as rifampicin, St John's wort, carbamazepine or phenytoin) should be avoided, as a risk for decreased plasma concentrations and decreased efficacy of vismodegib cannot be excluded.

Contraceptive steroids: Results of a drug-drug interaction study conducted in cancer patients demonstrated that the systemic exposure of ethinyl estradiol and norethindrone is not altered when co-administered with vismodegib. However, the interaction study was of only 7 days duration and it cannot be excluded that vismodegib upon longer treatment is an inducer of enzymes which metabolize contraceptive steroids. Induction could lead to decreases in systemic exposure of the contraceptive steroids and thereby reduced contraceptive efficacy.

In vitro studies indicate that vismodegib has the potential to act as an inhibitor of breast cancer resistance protein (BCRP). In vivo interaction data is not available. It may not be excluded that vismodegib may give rise to increased exposure of medicinal products transported by this protein, such as rosuvastatin, topotecan, and sulfasalazin. Concomitant administration should be performed with caution and a dose adjustment may be necessary.

In vitro, vismodegib is an inhibitor of OATP1B1. It cannot be excluded that vismodegib may increase the exposure to substrates of OATP1B1, e.g. bosentan, ezetimibe, glibenclamide, repaglinide, valsartan and statins. In particular, caution should be exercised if vismodegib is administered in combination with any statin.

For more detailed interactions please refer to the SPC.

Main toxicities:

Vismodegib may cause embryo-foetal death or severe birth defects when administered to a pregnant woman, and must not be used during pregnancy. There is a Pregnancy Prevention Programme that must be adhered to.

Vismodegib	
Hepatotoxicity	Increased hepatic enzymes
Metabolism and nutrition disorders	Decreased appetite Dehydration
Gastrointestinal disorders	Nausea and vomiting Diarrhoea / constipation Dyspepsia Abdominal pain
Skin and subcutaneous tissue disorders	Alopecia Pruritus Rash Abnormal hair growth
Musculoskeletal disorders	Muscle spasms Arthralgia Pain in extremity Back pain Musculoskeletal chest pain Myalgia Flank pain Musculoskeletal pain
Other	Amenorrhea Weight decrease Fatigue Pain Asthenia

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

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment	X			X	Every 3 months and as clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
FBC	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	Every cycle
Pregnancy testing for WCBP		X	X	X	Every cycle, test should be performed within 7 days prior to treatment

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

WCC ≥ 3.0 x 10^9/L	ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Haematological toxicity is uncommon.
If neutrophils < 1.0 x 10^9/L and/or platelets < 100x 10^9/L, discuss with the consultant before continuing treatment

Non- Haematological toxicity:

There are no specific dose recommendations for patients with renal or hepatic impairment, and these patients should therefore be monitored closely for adverse reactions.

References:

1. https://www.medicines.org.uk/emc. Erivedge 150 mg hard capsules, vismodegib. Summary of Product Characteristics, Roche Registration Limited, United Kingdom, 12/07/2013. Available from www.medicines.org.uk/emc/medicine. Last Updated 04/03/2021.
2. BNF available via: https://bnf.nice.org.uk/
3. Clinical Commissioning Policy: Vismodegib for adults with either Gorlin syndrome or non-Gorlin syndrome related multiple basal cell carcinomas. (Adults) Publication date: July 2021 Version number: 1.0
4. Dreno, B., Kunstfeld, R., Hauschild, A., Fosko, S., Zloty, D., Labeille, B., Grob, J-J. et al. (2017) Two intermittent vismodegib dosing regimens in patients with multiple basal-cell carcinomas (MIKIE): a randomised regimen-controlled, double-blind, phase 2 trial. The Lancet Oncology 18:404-12.

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
10th of June 2016	1.0	Helen Flint Consultant Pharmacist	New protocol
14th of April 2023	2.0	Hugh O'Neill Skin SRG Pharmacist	Updated to new template Updated indication