Systemic Anti Cancer Treatment Protocol

Vismodegib

PROTOCOL REF: MPHAMMEVIS
(Version No: 1.0)

Approved for use in:

Locally advanced or symptomatic metastatic basal cell carcinoma.
Funding available via the cancer drugs fund

Dosage:

Drug	Dosage	Route	Frequency
Vismodegib	150mg	Oral	Daily

Continuous until disease progression or unacceptable toxicity

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:

Not applicable

Administration:

The capsules must be swallowed whole with water (with or without food)

Drug Interactions
Proton pump inhibitors, H2 receptor antagonists (e.g. ranitidine) and antacids may reduce the bioavailability of vismodegib and should be avoided if possible.

P-gp inhibitors (such as clarithromycin, erythromycin, verapamil, ciclosporin)
CYP2C9 inhibitors (such as amiodarone, fluconazole, miconazole)
CYP3A4 inhibitors (such as clarithromcyin, itraconazole, ketoconazole, voriconazole, ritonavir) increase systemic exposure and incidence of adverse events of vismodegib

Whereas CYP inducers (such as rifampicin, St Johns wort, carbamazepine, phenytoin) may decrease the effectiveness of vismodegib

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

Patient counselling points

Vismodegib is contraindicated in women of child bearing 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.

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 Hyponatremia
Gastrointestinal disorders	Nausea and vomiting Diarrhoea / constipation Dyspepsia Abdominal pain
Skin and subcutaneous tissue disorders	Alopecia, including eye lashes and eyebrows 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

Investigations:

- FBC prior to each cycle
- U&Es & LFTs prior to each cycle, Discuss with the consultant oncologist if these have increased to above the upper limit of normal whilst on treatment.
- For WCBP: Pregnancy test, Repeat every 4 weeks whilst on 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:

Renal and hepatic impairment
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:

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 24/06/2014.