LONDON CANCER ALLIANCE West and South

Skin Pathway Group – Vismodegib in Basal Cell Carcinoma (Single agent use only)

Indication:

NCDF criteria

Locally advanced or metastatic basal cell carcinoma

- Curative resection not possible as assessed by a specialist in dermatological surgery, head and neck surgeon or plastic surgeon
- Previous radiotherapy, unless contraindicated or inappropriate
- PS 0-2

Patients able to tolerate and comply with oral dosage forms

Regimen details: Vismodegib 150mg once daily Orally continuous therapy

Administration: Vismodegib capsules should be swallowed whole with water, with or without food.
Do not crush or open the capsules.

Frequency: Continuous therapy
Prescribed every 28 days - continue treatment until disease progression or unacceptable toxicity occurs

Pre-medication: Not routinely required

Anti- emetics: Low emetogenicity
Follow Local Anti-emetic Policy

Supportive medication: Diarrhoea can be managed with loperamide

Extravasation: Not applicable

Regular investigations: FBC Monthly

Version: 1.0 Supersedes: all other versions	Approved by LCA Skin Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Ravi Shaunak	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Sanna Eestila	Date prepared: January 2015 Review Date: January 2017

U&Es	Monthly
LFTs	Monthly
Pregnancy test	Monthly (for women of childbearing potential). See comments for further information

Due to potential drug interactions, update medication list at each clinic visit.

Toxicities: Muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, vomiting, loss of appetite, diarrhoea, constipation, infertility, amenorrhea in women of childbearing potential, teratogenicity raised hepatic enzymes, hyponatremia, ageusia, dyspepsia, abdominal pain, pruritis, rash, arthralgia, myalgia

DOSE MODIFICATIONS

Haematological Toxicity No dose modifications are required for haematological toxicity

Non-haematological Toxicities

Renal impairment There is insufficient data in patients with severe renal impairment. Population pharmacokinetic analysis suggests that vismodegib is not affected by mild to moderate renal impairment. No specific dose recommendations are available.

Hepatic impairment There is insufficient data in patients with moderate to severe hepatic impairment. Limited data indicate that vismodegib is not relevantly increased in patient with mild hepatic impairment. No specific dose recommendations are available.

Dose modifications for other toxicities

Treatment interruptions of up to 4 weeks were allowed based on individual tolerability in clinical trials.

Location of regimen delivery: To be supplied to the patient for oral self-administration

Comments: Teratogenicity and Contraception

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The patient must be provided with the Erivedge® Pregnancy Prevention Programme Brochure and the Erivedge® Verification of Counselling Form must be completed and signed prior to starting treatment with vismodegib and the pharmacist dispensing checklist must be completed at each dispensing event.

- Women of childbearing potential must comply with the Erivedge® Pregnancy Prevention Programme. Initial prescription and dispensing should occur within 7 days of a negative pregnancy test. A pregnancy test must be conducted monthly prior to each cycle thereafter. Women of childbearing potential must not become pregnant during treatment and for 24 months after the final dose. Two methods of recommended contraception must be used (one highly effective method and a barrier method).

- Male patients must use the recommended protection – condom (with spermicide, if available) even after a vasectomy, whilst on treatment and for 2 months after the final dose.

- Sperm donation - Male patients should not donate whilst taking vismodegib and for 2 months after the final dose.

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

Excipients
Vismodegib capsules contain lactose monohydrate. Patients with galactose intolerance, primary hypolactasia or glucose-galactose malabsorption should not take vismodegib.

Drug interactions:

Drug / Class	Impact

Strong CYP inducers (e.g. rifampicin, carbamazepine, phenytoin)	Reduced plasma concentrations of vismodegib
Proton pump inhibitors, H2-antagonists, or antacids	Alter solubility and reduce bioavailabilty of vismodegib – no formal studies have been conducted and the effect on efficacy is unknown
P-gp inhibitors (clarithromycin, erythromycin, azithromycin, verapamil, cyclosporine), CYP2C9 (amiodarone, fluconazole, miconazole), or CYP3A4 (clarithromycin, itraconazole, ketoconazole, lopinavir/ritonavir, posaconazole, saquinavir, telaprevir, telithromycin, voriconazole)	Increased systemic exposure and incidence of adverse events may be increased
CYP inducers (rifampicin, carbamazepine, phenytoin, St John's wort (*hypericum perforatum*))	Decreased exposure to vismodegib
Contraceptive steroids	Vismodegib may induce enzymes which metabolise contraceptive steroids – reduced contraceptive efficacy – women of childbearing potential must be advised to use 2 methods of recommended contraception

References: www.medicines.org.uk accessed Feb 2015
Sekulic A, Migden M, Oro A et al. Efficacy and Safety of Vismodegib in Advanced Basal-Cell Carcinoma. N Engl J Med 2012;366:2171-9

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