Indication	Vismodegib for the treatment of: Gorlin syndrome with non-locally advanced, non-metastatic multiple (>/=6) BCCs clinically evident lesions at the point of decision to treat of which 3 are at least 5mm and Non-locally advanced, non-metastatic multiple BCC (>/=6) clinically evident lesions at the point of decision to treat of which 3 are at least 5mm AND are appropriate for surgery. NB: Patients must be appropriate for surgery i.e. surgically eligible tumours. NB: Trust policy regarding the use of unlicensed treatments must be followed as this is an unlicensed dosing schedule and indication for vismodegib.
Treatment Intent	Palliative
Frequency and number of cycles	Vismodegib Intermittent schedule 150mg daily for 12 weeks, followed by 8 weeks off treatment. Continue until disease progression or unacceptable toxicity or patient choice to stop treatment.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • Monitor FBC, LFT's and U&E's prior to each cycle. If neuts <1.0 and/or PLT <100 d/w consultant. • WCBP must have a negative pregnancy test, conducted by a health care provider <u>within 7 days before starting treatment</u> and have a negative pregnancy test monthly during treatment, even if the patient becomes amenorrhoeic. • **Hepatic impairment:** no dose adjustment required. • **Renal impairment:** no dose adjustment required in mild and moderate renal impairment. Limited data in severe impairment, patients should be monitored closely for adverse reactions. • **Management of adverse reactions and dose adjustments:** o Dose adjustments are not recommended. o Severe cutaneous adverse reactions (SCARs) including cases of Stevens-Johnson syndrome/Toxic epidermal necrolysis (SJS/TEN), Drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP), have been reported during treatment with vismodegib, if the patient develops any of these reactions' treatment with vismodegib must be discontinued and not restarted at any time. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** o Avoid concomitant treatment with potent CYP inducers (e.g rifampicin, phenytoin, St. Johns' Wort, carbamazepine). o Vismodegib has the potential to act as an inhibitor of breast cancer resistance protein (BCRP) and may give rise to increased exposure of medicinal products transported by this protein, such as rosuvastatin, topotecan, and sulfasalazine. Concomitant administration should be performed with caution and a dose adjustment may be necessary. • **Missed dose:** If a dose is missed the patient should not take an additional dose and take at the dose at the next scheduled time.

	• **Pregnancy/contraception:**
	  ○ Vismodegib must not be used during pregnancy and female and male patients will be counselled as described below.
	  ○ Counselling for **female** patients:
	  ○ I confirm the patient has been counselled about the adverse use of vismodegib in pregnancy AND, if a woman of child-bearing potential, has been advised that she should use two forms of contraception (including one highly effective method and one barrier) during vismodegib therapy and for 24 months after the final dose, AND has had a negative medically supervised pregnancy test within the past seven days.
	  ○ Counselling for **male** patients:
	  ○ I confirm that the patient has been counselled about the adverse use of vismodegib in relation to pregnancy and has been advised that he should always use a condom (with spermicide if available), during vismodegib therapy and for 2 months after the final dose. Male patients should not donate semen while taking vismodegib and for 2 months after the final dose.
	• **Patients must comply with the "Erivedge Pregnancy Prevention Programme" materials**.
	• **Blood donation:** Patients should not donate blood while taking Erivedge and for 24 months after the final dose
	• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.

References	Blueteq form accessed online 18.10.21 SPC accessed online 21.10.21 KMCC proforma SKI-005 v1

NB For funding information, refer to CDF and NICE Drugs Funding List

Intermittent schedule of vismodegib given for 12 weeks, followed by 8 weeks off treatment.

TTO	Drug	Dose	Route	Directions
Day 1	**VISMODEGIB**	**150mg**	PO	OD for 12 weeks followed by an 8-week break. Swallow whole with water with or without food. Do not open capsules. Available as 150mg capsule
	Metoclopramide	10mg	PO	Up to TDS PRN Do not take for more than 5 days continuously.
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if required.