BARTS HEALTH NHS TRUST & LOCAL GPs
Shared Care Guidelines

DOCUMENT TO BE FILED IN NOTES AND SCANNED INTO ELECTRONIC RECORDS

Topical 5-FLUOROURACIL (5-FU) cream: Tradename Efudix
Skin Keratoses, Bowen's Disease and BCCs

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AS AND FILED IN NOTES

Patient Name : ***Date of Birth:***
NHS No:

Name of Referring Consultant: ***Contact number:***

INTRODUCTION – Indication and Licensing

Topical fluorouracil (5-FU) is used to treat precancerous actinic (solar) keratoses and Bowen's disease (squamous carcinoma in situ) and superficial basal cell carcinomas of the skin. Fluorouracil cream destroys cancer cells and cells which may become cancerous, whilst having little effect on normal cells. It has been used topically in primary care for its licensed uses for many years and some unlicensed uses respond well also e.g. warts. GPs who do not have a special interest in dermatology are often able to diagnose the conditions for which topical 5-FU are indicated (see below table). It is not expected that GPs will diagnose keratocanthoma as this is often difficult to distinguish from other malignancies which should be referred within 2 weeks e.g. Squamous Cell Carcinoma

The normal pattern of response to topical 5-FU includes: early and severe inflammatory phases (typically characterised by erythema, which may become intense), a necrotic phase (characterised by skin erosion and crusting) and finally healing (when re-epithelialisation occurs). These local skin reactions usually occur in the second week of fluorouracil treatment and are generally well tolerated. However they may sometimes become more severe and cause pain, blistering and ulceration.

Any severe skin discomfort during treatment with topical 5-fluorouracil may be alleviated by the use of an appropriate topical steroid e.g. hydrocortisone 1% ointment/cream.

Disposal of unused topical 5-Fluorouracil: a cytostatic preparation.

Any unused product or waste material should be disposed of in accordance with local requirements. Topical 5-fluorouracil is not considered a cytotoxic product: it is a topical cytostatic preparation which exerts a beneficial therapeutic effect on neoplastic and pre-neoplastic and pre-neoplastic skin lesions.

PATIENT PATHWAY-

I**t is appropriate for the diagnosis and management of actinic keratoses to be undertaken for the most part in primary care, as recommended by NICE (2006).** The initial advice may include sun avoidance and self-monitoring for new lesions or changes in existing lesions. Where there is clinical or patient concern, cryosurgery or a topical therapy is usually used.

The table below details the indications for which topical fluorouracil can be used and monitored by GPs.

Table One

Clinical Speciality / Indication	*Prescribing Initiated by*	*Prescribing Continued by*	*Monitored by*	*Duration of treatment*
Actinic keratoses	GP	GP	GP	3-4 weeks
Bowen's Disease	GPSIs or Consultant	GPSIs or Consultant	GPSIs or Consultant	3-4 weeks
Superficial BCC	GPSIs or Consultant	GPSIs or Consultant	GPSIs or Consultant	3-4 weeks

A 4-week treatment cycle should be followed by a 4 week period off treatment and the patient should be reviewed by the GP before starting another 4 week treatment cycle if they have not previously used 5-fluorouracil.

When to refer to a Consultant Dermatologist:
Patients should be referred to a Consultant dermatologist if there is diagnostic uncertainty; concern about malignant risk; failure to respond to therapy; concerns about management (e.g. where lesions are multiple or confluent, thick and painful or at sites of poor healing such as the lower leg); or if the patient is at high risk (e.g. organ transplant recipients, multiple large lesions or previous SCC)..

ADMINISTRATION

- Apply once or twice daily to affected area of skin
- Avoid eyes or mucous membranes
- Avoid excessive sunlight
- Do not use occlusive dressing
- Do not use on broken skin
- The total area of skin being treated at any one time should not exceed 500 cm^2 (approximately 23 x 23 cm).
- Larger areas should be treated a section at a time.
- Do not use if pregnant or breastfeeding
- Do not give to patients with dihydropyrimidine dehydrogenase (DPD) deficiency
- Do not give to patients who have taken brivudine, sorivudine or similar nucleoside medications in the last four weeks.

- A patient information leaflet will be downloaded from www.patient.co.uk or www.medicines.org.uk
- A patient information leaflet for keratoses can be downloaded from www.bad.org.uk

KEY ADVERSE EFFECTS & ACTIONS

Table Two:

Adverse effects	***Symptoms/signs*** *(specify what would prompt action)*	***Actions (****what action should the GP take if identified in primary care)*
Allergy	Rarely reported. Hypersensitivity beyond the area of treatment.	Stop treatment and refer back to Consultant.
Hypersensitivity	Severe discomfort associated with inflammatory reactions	Prescribe topical corticosteroid and if no improvement after one week refer back to Consultant. Reduce frequency of administration and if no improvement after one week refer back to Consultant.
Severe dermatological reactions	Exfoliation, skin burning, erythema, blisters.	Refer back to Consultant.
Dermatological reactions on untreated areas of skin	Rash, pruritus, erythema	Refer back to Consultant
Generally unwell	Pyrexia or malaise; chills or mucosal inflammation.	GP to do full blood count
Haematological disorders associated with **systemic toxicity**	**Unlikely with topical use – especially if not used on broken skin**. Pancytopenia, neutropenia, thrombocytopenia are not usually associated with topical use	Refer back to Consultant
Gastrointestinal associated with **systemic toxicity**	**Unlikely with topical use – especially if not used on broken skin**. Diarrhoea, vomiting.	Refer back to Consultant.

Significant systemic drug toxicity is unlikely percutaneously when topical 5-fluorouracil is used correctly. It has been prescribed and monitored by GPs in primary care for many years. There is not a requirement for GPs to measure DPD levels prior to initiation of topical 5-fluorouracil treatment.

The likelihood of systemic toxicity is increased if the product is used excessively, especially on skin areas in which the barrier function is impaired (e.g. cuts) and/or in individuals with deficiency in dihydropyrimidine dehydrogenase (DPD); DPD is a key enzyme involved in metabolising and eliminating fluorouracil.

Determination of DPD activity may be considered where systemic drug toxicity is confirmed or suspected. The determination of this would be done by the Consultant after referral back by GP on suspicion of systemic toxicity. There have been reports of increased toxicity in patients who have reduced activity/deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD).

This only lists the key important ADRs-For comprehensive information on cautions, contra-indications and interactions, please refer to the current British National Formulary and Summary of Product Characteristics.

DRUG INTERACTIONS

An interval of at least four weeks should elapse between treatment with brivudine, sorivudine or analogues and subsequent administration of 5-fluoruracil.

Co-administration of 5-fluorouracil with antiviral nucleoside drugs (e.g. brivudine and analogues) may lead to a substantial increase in plasma levels of fluorouracil and associated toxicity and is contraindicated. Brivudine and analogues are potent inhibitors of DPD, a fluorouracil metabolising enzyme. DPD is a key enzyme involved in metabolising and eliminating fluorouracil.

No other known interactions.

PREGNANCY AND BREAST FEEDING

It is recommended that the patient should not become pregnant whilst on topical 5-Fluorouracil. Both men and women patients will be counselled about contraception and what to do if pregnancy occurs. The counselling should be documented in the patient notes.

For comprehensive information please refer to the current British National Formulary and Summary of Product Characteristics.

SHARED CARE

Shared care guideline: *is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use.*

If seen initially by the Consultant-role of the consultant/hospital team

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
3. Initiate treatment if deemed urgent and prescribe until the GP formally agrees to share care.
4. Evaluation of any reported adverse effects by GP or patient.
5. Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.

6. Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
7. Ensure that backup advice is available at all times.

General Practitioner

1. Diagnosis of AK, Bowen's Disease or Basal cell carcinoma. Reinforce the patient's understanding of the nature, effect and potential side effects of the drug before prescribing it as part of and contact the specialist for clarification where appropriate.
2. Provide patient with relevant patient information leaflets
3. Advise when they should return for review or if treatment is not working in the expected fashion.
4. Monitor patient's overall health and well-being.
5. Report any adverse events to the consultant, where appropriate.
6. Report any adverse events to the CSM, where appropriate.
7. Refer back to the Consultant according to table
8. Help in monitoring the progression of disease
9. Maintain a patient held monitoring booklet where used
10. Prescribe the drug treatment as described.

CCG/CSU

1. To provide feedback to trusts via Trust Medicines Committee.
2. To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
3. To support trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy
5. Take/ administer the medication as prescribed
6. Undertake any monitoring as requested by the GP and/or specialist

Costs

Drug Product	*Cost in primary care*
5-Fluorouracil cream (Efudix)	£32.90

Based on BNF edition 66 September 2013

RESOURCES AVAILABLE

Barts Health NHS Trust	
Consultant via switchboard	*0203 416 5000 extn 42122*
Registrar on-call out of hours	*Aircall via switchboard bleep 1167*

Dermatology Nurse	*0203 416 5000 extn 42123 (or paediatric 41457)*
Medicines Information Pharmacist	*0203 416 5000 ext 60120*
Prescribing Advice for Tower Hamlets CCG	020 36882543
Prescribing Advice for Newham CCG	020 36882360
Prescribing Advice for Waltham Forest CCG	020 36882655
Prescribing Advice for Redbridge CCG	0208 8223074/6

References

1. British National Formulary (BNF 65), March-Sep 2013, p.772
2. Ceilley et al. Current issues in the management of AK. J Am Acad Dermatol 2013;68:S28-38.
3. Drug and Therapeutic Bulletin, DTB Bulletin, Vol 51, No.7, July 2013 www.dtb.bmj.com
4. Meda Pharmaceuticals Ltd, Efudix cream (5-FU), Summary of Product Characteristics (SPC), Feb 2011
5. Meda Pharmaceuticals Ltd, Efudix cream (5-FU), Patient Information Leaflet (PIL), Feb 2011
6. www.bad.org British Association of Dermatology website: AK factsheets
7. www.patient.co.uk for patient factsheets

Guideline written by Sarah Garrett- Head of Medicines Information . Approved by Joint Prescribing Group on January 2014. Review date: January 2016