Chemotherapy Protocol

Cutaneous T-cell Lymphoma

BEXAROTENE

Regimen

- Cutaneous T-cell Lymphoma - Bexarotene

Indication

- Bexarotene is indicated for the treatment of skin manifestations of advanced stage cutaneous T-cell lymphoma (CTCL) in adult patients refractory to at least one systemic treatment.

Toxicity

Drug	Adverse Effect
Bexarotene	Leucopenia, hypothyroidism, hyperlipaemia, hypercholesterolaemia, exfoliative dermatitis, pruritus, rash, pain, headache, asthaenia

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

Monitoring

Drugs

- FBC, LFTs and U&Es at baseline. FBC and LFTs weekly for the first month and then monthly thereafter.
- Thyroid function tests including total T_4 and TSH at baseline and then monthly thereafter.
- Fasting blood triglycerides and cholesterol at baseline, then weekly until stabilised. This usually takes 2-4 weeks and then at intervals no less than monthly thereafter.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L)

Prior to prescribing cycle 1 the following criteria must be met.

Criteria	**Eligible Level**
Neutrophils	Equal to or more than $1x10^9$/L
Platelets	Equal to or more than $100x10^9$/L

Subsequent cycles;

Neutrophils	**Bexarotene**
greater than $0.8x10^9$/L	100% dose
0.5–$0.8x10^9$/L	200mg/m^2 daily
less than $0.5x10^9$/L	Delay

Hepatic Impairment

Bilirubin and/or AST & ALT	**Bexarotene**
Any, greater than 3xupper limit of normal range	Delay

Renal Impairment

No formal studies conducted in this patient group. Renal excretion is not a major elimination pathway therefore dose reductions are unlikely unless renal impairment severe.

Other

Hyperlipidaemia

Fasting triglycerides (mmol/L)	**Bexarotene**
Less than 3.5	100%
3.51 – 4.4	200mg/m^2 daily (reduced dose)
Greater than 4.5	Delay until controlled

Maintain triglyceride levels below 3.4mmol/L

The 300 mg/m^2/day dose level may be adjusted to 200mg/m^2/day then to 100mg/m^2/day or temporarily suspended, if necessitated by toxicity. When toxicity is controlled, doses may be carefully readjusted upward. With appropriate clinical monitoring, individual patients may benefit from doses above 300mg/m^2/day. Doses greater than 650 mg/m^2/day have not been evaluated in patients with CTCL. Treatment should be continued as long as the patient is deriving benefit

Regimen

28 day cycle until disease progression or intolerance (twelve cycles will be set in ARIA)

Drug	Dose	Days	Route
Bexarotene	300mg/m^2/day	Days 1-28 inclusive	Oral

Dose Information

- Bexarotene is available as 75mg soft capsules.
- Licensed doses are based on surface area. Doses will be dose banded according to the table below;

Body Surface Area (m^2)	Dose Range (mg)	Total Daily Dose (mg/day)	Number of 75mg bexarotene capsules
0.88 - 1.12	264 – 338.9999	300	4
1.13 - 1.37	339 – 413.9999	375	5
1.38 - 1.62	414 – 488.9999	450	6
1.63 - 1.87	489 – 563.9999	525	7
1.88 - 2.12	564 – 638.9999	600	8
2.13 - 2.37	639 – 713.9999	675	9
2.38 - 2.62	714 – 786.9999	750	10

Administration Information

- Bexarotene should be taken once a day with a meal. The capsules should be swallowed whole and not chewed.

Additional Information

- Bexarotene interacts with many other agents. Always check for drug interactions. In particular bexarotene can potentially induce metabolic enzymes and thereby theoretically reduce the efficacy of oestroprogestive contraceptives. Thus, if treatment with bexarotene is intended in a woman of childbearing potential, a reliable, non-hormonal form of contraception is also required, because bexarotene is teratogenic.
- Bexarotene causes photosensitivity. Minimise exposure to sunlight and artificial UV light during treatment.
- Bexarotene is related to vitamin A. Limit intake to less than or equal to 15,000IU/day
- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001)must be followed in relation to bexarotene.
- It must be made clear to all staff, including those in the community, that bexarotene should only be prescribed under the supervision of a consultant oncologist or haematologist.

Coding

- Procurement - X71.5
- Delivery – X73.1

References

1. Eisai Ltd. Targretin Capsules Summary of Product Characteristics. Electronic Medicines Compendium. Online at http://www.medicines.org.uk/emc/medicine/26618 , accessed 18 January 2017
2. BBCA. Protocol Summary for Treatment of Cutaneous T-cell Lymphoma with Bexarotene, ULYMFBEX. Revised May 2009
3. South East London Cancer Network. Bexarotene Oral for Cutaneous T-cell Lymphoma. Sept 2008
4. UCL. Dosage Adjustment for Cytotoxic in Renal Impairment. Jan 2009
5. Duvic, M et al (2001). 'Phase 2 and 3 Clinical Trial of Oral Bexarotene (Targretin Capsules) for the Treatment of Refractory or Persistent Early-Stage Cutaneous T-Cell Lymphoma'. Arch Dermatol. 2001;137:581-593

REGIMEN SUMMARY

Bexarotene

Day One

1. Bexarotene 300mg/m^2 once a day oral
   Administration Instructions
   Bexarotene capsules should be taken as a single oral daily dose with a meal.

   The capsules should swallowed whole and not chewed.

   Oral chemotherapy

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	January 2018	None	Kathy Blight Pharmacist Dr Deborah Wright Pharmacist	Dr Rob Lown Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.