Thames Valley
Strategic Clinical Network

DANAZOL

INDICATION (unlicensed)

Aplastic anaemia, Myeloproliferative neoplasms or Myelodysplastic syndromes, to improve haemoglobin and platelet counts

Danazol has been discontinued in the UK. Unlicensed imports may be available – discuss with pharmacy. Follow local formulary processes for unlicensed medicines.

TREATMENT INTENT

Disease Modification

PRE-ASSESSMENT

1. Investigations to include FBC, blood film and manual differential, coagulation screen, urea, creatinine, electrolytes, liver function tests, calcium, lipid profile, glucose, amylase, urate, consider erythropoietin level if anaemic.
2. Ensure diagnosis is confirmed prior to commencing treatment by WHO or BSH criteria
3. Pregnancy Test - for all women of childbearing age unless they are postmenopausal, have been sterilised or undergone a hysterectomy.
4. Females of child-bearing age should be advised to employ non-hormonal contraception throughout the course of treatment.
5. Exclude prostate cancer in male patient (PSA testing)
6. ECG and consider echo in selected patients at risk of cardiac disease
7. Baseline liver ultrasound
8. Record performance status (WHO/ECOG).
9. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
10. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN / CYCLE FREQUENCY

Starting Dose

DANAZOL **200mg** oral **DAILY**

Titrate dose monthly to a maximum of 600mg (patient <80kg) or 800mg (patient ≥80kg) daily. Doses above 200mg should be given as divided doses. Patients should be treated for a minimum period of 6 months. Responding patients should be maintained for a further 6 months on 400mg daily before titrating down to the minimum required dose to maintain a response.

DOSE MODIFICATIONS

Use with caution in renal and hepatic impairment. Titrate according to response.

CONTRAINDICATIONS

- Pregnancy or Breastfeeding
- Severely impaired hepatic, renal or cardiac function
- Porphyria: danazol can induce aminolevulinic acid synthetase activity and hence porphyrin metabolism
- Active thrombosis or thromboembolic disease and a history of such events
- Androgen dependent tumour
- Abnormal genital bleeding that has not been fully investigated.

INVESTIGATIONS

- FBC, LFTs and U&Es monthly
- Thyroid function test at baseline then every 3 months
- Liver ultrasound at baseline then every 6-12 months to exclude hepatic malignancy if continuing on treatment for more than 6 months
- Prostate screening (PsA testing) every 6-12 months for male patients

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CONCURRENT MEDICATION

Not required

EMETIC RISK

Minimal

DRUG INTERACTIONS

(Consult with pharmacist and refer to SPC for full details)

Danazol may affect the plasma level of carbamazepine, phenytoin, ciclosporin and tacrolimus. There is a higher risk of myopathy and rhabdomyolysis with simvastatin, atorvastatin and lovastatin.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

(Consult with pharmacist and refer to SPC for full details)

Care should be observed when using danazol in patients with hepatic or renal disease, hypertension or other cardiovascular disease and in any state which may be exacerbated by fluid retention as well as in diabetes mellitus, polycythaemia, epilepsy, lipoprotein disorder, in those with a history of thrombosis, and in those who have shown marked or persistent androgenic reaction to

previous gonadal steroid therapy. Adjustment in concomitant therapy may be called for particularly in patients with hypertension, diabetes mellitus or epilepsy when introducing or discontinuing danazol as well as during danazol treatment.

Caution is advised in patients with migraine.

Danazol may aggravate epilepsy and expose the condition in those predisposed.

Other commonly reported adverse effects:
Reversible erythrocytosis or polycythaemia, acne, weight gain, increased appetite, seborrhoea, hirsutism, hair loss, voice change, fluid retention, menstrual disturbances, mood change, headache, vertigo, hypertension, rash.

TREATMENT RELATED MORTALITY

Very low

REFERENCES

1. Mylan Generics. Danazol capsules. Summary of Product Characteristics Updated 03/05/2018. Accessed on 9/11/2022 via http://www.mhra.gov.uk
2. Sanofi. Danazol capsules. Summary of Product Characteristics Updated 14/08/2019. Accessed on 9/11/2022 via http://www.mhra.gov.uk
3. Reilly et al (2012) Guideline for the diagnosis and management of myelofibrosis. BJH 158(4):453-471
4. Barosi et al (2013) Revised response criteria for polycythemia vera and essential thrombocythemia: an ELN and IWG-MRT consensus project. Blood 121(23):4778-4781.
5. Tefferi et al (2013) Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood 122(8):1395-1398

REVIEW

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	New document. Annual protocol meeting	Oct 2019	1.0	Oct 2021
Yen Lim Haematology Pharmacist. NSSG Myeloid Group	Updated availability. Annual protocol meeting	Nov 2022	2.0	Nov 2024