DANAZOL

INDICATION (unlicensed)

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

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. Record performance status (WHO/ECOG).
8. 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.
9. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN / CYCLE FREQUENCY

Staring Dose

DANAZOL 200mg oral DAILY (available as 100mg capsules)

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 12 months to exclude hepatic malignancy
- Prostate screening (PSA testing) every 6-12 months for male patients

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


REVIEW

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
</tr>
</thead>
</table>