Busulfan

Indication
Myeloproliferative neoplasms, including chronic myeloid leukaemia (CML) where hydroxycarbamide is not appropriate.

ICD-10 codes
Codes with the following prefixes; C92.0, D47.1, D47.3, D45.0, D75.81

Regimen details

Day	Drug	Dose	Route
Day 1-7 (or 14)	Busulfan	2 - 4 mg OD for 7-14 days	PO
OR Day 1	Busulfan	25 - 40 mg STAT	PO

* dose (and duration if applicable) according to magnitude of desired effect

Cycle frequency
Should not be repeated within 8 weeks of last dose.

Number of cycles
See above. Response should be assessed after 2 cycles and stopped if no effect.

Administration
Busulfan is available as 2mg tablets. Tablets should be swallowed whole with plenty of water.

Pre-medication
Nil

Emetogenicity
This regimen has low-moderate emetic potential.

Additional supportive medication
Allopurinol 300mg OD (100mg OD if creatinine clearance <20mL/min) for 4 weeks.
Antiemetics as per local policy

Extravasation
N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy**)**
FBC	14 days
U + E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	2 weekly during treatment
U + E (including creatinine)	2 weekly during treatment
LFTs	2 weekly during treatment

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
CrCl	> 30mL/min
ALT/AST	< ULN

Dose modifications

- **Haematological toxicity**

The aim of treatment is to reduce the WCC to 15 - 25 x 10^9/L and platelets < 400 x 10^9/L.

There is individual variation in the response to busulfan and in a small proportion of patients the bone marrow may be extremely sensitive.

The acute dose-limiting toxicity of busulfan is myelosuppression. The main effect of chronic overdose is bone marrow depression and cytopenias. If profound myelosuppression does occur, appropriate supportive treatment should be given during the period of haematological toxicity according to local policy.

- **Renal impairment**

Busulfan has not been studied in renal impairment. It is moderately excreted in the urine. Dose modification is not recommended, however busulfan should be used with caution.

- **Hepatic impairment**

Caution in severe hepatic impairment. If ALT/AST raised, consider a dose reduction (consultant decision)

- **Other toxicities**

Treatment should be discontinued if lung toxicity develops.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Hepatic veno-occlusive disease
Acute myeloid leukaemia
Pulmonary toxicity
Infertility
Teratogenicity
Azoospermia (may be irreversible)
Convulsions (high dose)

- **Frequently occurring side effects**

Myelosuppression
Hyperuricaemia, uric acid nephropathy
Nausea, vomiting
Diarrhoea
Alopecia
Rhinitis
Pharyngitis

- **Other side effects**

Hyperpigmentation

Significant drug interactions – for full details consult product literature/ reference texts

Itraconazole: may reduce clearance of busulfan. Monitor for signs of toxicity.
Metronidazole: co-administration is not recommended, metronidazole may reduce clearance of busulfan.
Paracetamol: may decrease glutathione levels in blood and tissues, and may therefore decrease busulfan clearance.
Phenytoin: may increase busulfan clearance.

Additional comments

Busulfan should not be given in conjunction with radiotherapy.

Busulfan is ineffective once blast transformation has occurred.

Busulfan may be teratogenic. Adequate contraceptive measures should be taken during and for 2 years after treatment if either partner is receiving busulfan.

Busulfan should be discontinued if lung toxicity develops.

If anaesthesia is required the anaesthetist should be made aware that the patient has taken busulfan.

References

- Polycythemia vera and essential thrombocythemia: 2013 update on diagnosis, risk-stratification, and management. Tefferi A. Am J Hematol. 2013 Jun; 88(6):507-16. doi: 10.1002/ajh.23417.
- Summary of Product Characteristics Busulfan (Sanofi) accessed 17 December 2014 via http://www.medicines.org.uk

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