Hydroxycarbamide in Sickle Cell Disease

DISCLAIMER: This guideline is for information purposes only and is not intended to inform any individual clinical decisions. STSTN and its members do not accept any responsibility for outcome of clinical decisions made as a result of reading these guidelines. All guidelines have been peer-reviewed and agreed to be published by the relevant lead consultants in the network.

Indications:

Adults and children with Sickle Cell Disease who have:

i) >3 admissions with painful crises in the previous 12 months, or
ii) >1 admission with painful crisis in the previous 12 months, and are symptomatic in the community, or
iii) >1 life threatening complications of the disease, such as acute chest syndrome, or
iv) other indications (such as secondary stroke prevention, pulmonary hypertension) must be discussed with the consultant in charge of the patient.

Exclusions:

i) Pregnancy or not practicing active contraception (if sexually active)
ii) Active hepatitis

Requirements

i) Discuss the possible risks of infertility with male patients and offer sperm count and banking.

Regimen details:

Commence at 15mg/kg to nearest 500mg

If there is a good clinical response continue on this dose (Minimal effective dose)
If clinical response is sub-optimal, increase by 2.5mg/kg every 8 weeks until toxicity seen.

Toxicity:

Neutrophils	< 1.5 x 10^9/l
Platelets	< 80 x 10^9/l
Retics	< 10 x 10^9/l
Haemoglobin	<3g/dl from baseline

If any of the above problems with FBC encountered, stop hydroxycarbamide, until full blood count has recovered
Restart at 2.5mg/kg (or 1 capsule – 500mg) lower. This is the maximum tolerated dose (MTD)

Caution:

i) If there is a significant rise in Hb (>11g/dl in HbSS) stop the hydroxycarbamide and consider venesection
ii) If there is a downwards trend in FBC parameters, increase frequency of monitoring
ii) Use with caution in renal impairment: start at a lower dose and increment more cautiously
iii) If Creatinine Clearance < 60ml/min, commence at 50% dose (7.5mg/kg)

Administration:

Orally
Available as 500mg strength tablets – other strengths 250mg being explored by pharmacy

Frequency:

Continuous

Extravasation:

N/A

Anti- emetics:

Nausea and vomiting are rare side effects

Regular investigations:

Day 1
- Fbc and reticulocytes
- HbF%
- U+Es and LFTs
- Urate
- LDH
- Alpha genotype if not known (optional)

Day 14 (and every 14th day until dose stable)

Fbc
Hb F%
U+Es
LFTs
Reticulocytes

Once stable every 8-12 weeks

Fbc
Hb F%
U+Es
LFTs
Reticulocytes, LDH

Toxicities: Common: Bone marrow suppression and cytopenias.
Hyperpigmentation of nails and skin
Nausea and vomiting
Diarrhoea
Skin rash

Uncommon: Alopecia
Teratogenicity
Leg ulcers
Decreased sperm count and function
Low risk of second malignancy

Dose Modifications

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Hydroxycarbamide
≥ 1.5 x 10^9/L	&	≥ 80 x 10^9/L	100% dose
< 1.5 x 10^9/L	or	< 80x 10^9/L	Stop treatment and recheck FBC until N>1.5 and Plt >80. Restart treatment at 2.5mg/kg or 500mg daily lower.

Renal Impairment Use with caution. If Creatinine Clearance < 60ml/min, commence at 50% dose (7.5mg/kg)

Hepatic Impairment Use with caution

Drug interactions: NA

Supportive Care: NA

References:
Charache S, Terrin ML, Moore RD et al. Effect of hydroxycarbamide on the frequency of painful crises in sickle cell anaemia. Multicentre Study of Hydroxyurea. N Engl J Med 1995: 332: 1317-1322

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