# SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

# Procarbazine
# CNS

PROTOCOL REF: MPHAPROCNS
(Version No. 2.2)

## Approved for use in:

- Third line treatment for recurrent glioma following treatment with temozolomide and lomustine
- ECOG Performance Status 0 – 2

## Dosage:

| Drug | Dose | Route | Frequency |
|---|---|---|---|
| Procarbazine | 50mg TWICE daily | Oral | Days 1 – 14* every 28 days until disease progression |

*May be given for 10 days initially if caution is needed due to toxicities from prior treatments (can then increase to 14 days for subsequent cycles if well tolerated).

## Supportive treatments:

- Ondansetron PO 4mg twice a day on treatment days
- Cyclizine PO 50mg three time daily when required

## Emetogenic risk:

Mildly emetogenic.

## Extravasation risk:

Not applicable

## Administration:

Procarbazine is available as a 50mg capsule and can be taken with or without food.

Please refer to “Interactions” section for information about high tyramine-containing foods which should be avoided whilst on procarbazine (a diet patient information sheet should be provided to patients at pre-assessment).

## Interactions:

**Anti-depressants, opioids and anti-emetics** - Procarbazine is a weak monoamineoxidase inhibitor (MAOI) so concurrent use may increase the risk of Serotonin Syndrome

**Anti-epileptics** – increased risk of hypersensitivity reaction when phenobarbital, phenytoin or carbamazepine are given with procarbazine

**Alcohol** - consumption of alcohol whilst taking procarbazine may cause a disulfiram-like reaction (nausea, vomiting, flushing, dizziness, and headache)

**High tyramine-containing foods** – tyramine is released as proteins age and breakdown therefore is usually found in aged, fermented, pickled or smoked foods or in food that has not been stored correctly and has started to spoil.

The reaction to eating these foods whilst on procarbazine can be relatively mild (facial flushing and rash) but can also be quite severe (sudden onset headache, neck stiffness, nausea and vomiting, sensitivity to light, sweating, chills, pounding heart). Symptoms of any reaction usually resolve within a few hours.

Food that should be completely avoided includes mature or aged cheese, concentrated yeast or meat extracts (marmite, gravy or stock cubes) and broad-bean pods. Food that may be eaten but in moderation include over-ripe fruit, beer, wine, sour cream, yoghurt, cured meats, banana and soy sauce.

For further information please refer to the SPC: **Procarbazine Capsules 50mg - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)**

## Main toxicities:

| Procarbazine | | |
|---|---|---|
| **System Organ Class** | Frequency | |
| **Infections and infestations** | Not known | Infections |
| **Blood and lymphatic system disorders** | Not known | Leucopenia<br>Thrombocytopenia<br>Neutropenia |
| **Immune system disorders** | Not known | Severe hypersensitivity reactions with angioedema, urticaria and a precipitous drop in serum complement |
| **Psychiatric disorders** | Not known | Lethargy |
| **Respiratory, thoracic and mediastinal disorders** | Not known | Pneumonitis |
| **Ear and labyrinth disorders** | Common | Deafness, vertigo, tinnitus, earache |
| **Gastrointestinal disorders** | Very common | Loss of appetite, nausea, vomiting |
| **Hepatobiliary disorders** | Not known | Hepatic complications including jaundice and abnormal liver function tests |
| **Skin and subcutaneous tissue disorders** | Not known | Allergic skin reactions |
| **Reproductive system and breast disorders** | Not known | Azoospermia, ovarian failure |

## Investigations and treatment plan:

| | Pre | Cycle 1 Day 1 | Cycle 2 | Cycle 3 | Ongoing |
|---|---|---|---|---|---|
| Informed Consent | x | | | | |
| Clinical Assessment | x | x | x | x | Every cycle |
| SACT Assessment (to include PS and toxicities) | x | x | x | x | Every cycle |
| FBC | x | x | x | x | Every cycle |
| U&E & LFTs | x | x | x | x | Every cycle |
| MRI scan | x | | | | Every 3 cycles |
| Weight recorded | x | x | x | x | Every cycle |
| Height recorded | x | | | | |

## Dose Modifications and Toxicity Management:

## Haematological toxicity:

Proceed on day 1 if-

| | |
|---|---|
| ANC ≥ 1.5 x $10^9$/L | Platelets ≥ 100 x $10^9$/L |

Delay 1 week on day 1 if-

| | |
|---|---|
| ANC < 1.5 x $10^9$/L | Platelets ≤ 99 x $10^9$/L |

Consider reducing course length to 10 days in event of haematological toxicity.

## Non-haematological toxicities

In the event of non-haematological toxicities, consider reducing course length to 10 days.

## Dosing in renal and hepatic impairment:

## Renal impairment

Procarbazine is eliminated primarily via the kidneys. Caution is advised for patients with renal dysfunction. Patients with a serum creatinine > 177µmol/l should be considered for a dose reduction.

## Hepatic toxicity

Procarbazine is metabolized by the liver therefore should be used with caution in patients with hepatic impairment. Consider a dose reduction if bilirubin > 50 µmol/L. Procarbazine is contra-indicated if bilirubin is > 85µmol/L or AST > 180 IU/L.

## References:

1. The British National Formulary (BNF). Available at https://bnf.nice.org.uk
2. Procarbazine 50mg Capsules Summary of Product Characteristics (November 2014) Available at: https://www.medicines.org.uk/emc/product/3732
3. The North London Cancer Network "Dose Adjustments for Cytotoxics in Hepatic Impairment" (January 2009)
4. The North London Cancer Network "Dose Adjustments for Cytotoxics in Renal Impairment" (January 2009)

## Circulation/Dissemination

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|---|---|
| Date added into Q-Pulse | 7th September 2023 |
| Date document posted on the Intranet | N/A |

## Version History

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| As of 6th April 2023 | V2.2 | **Hugh O'Neill** | Updated into new protocol format<br>Updated supportive treatments |
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