Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

MTTN Regimen

Mitotane (Palliative)

Disease Site	Endocrine Adrenal
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	Standard therapy for patients with unresectable symptomatic adrenocortical carcinoma (functional and non-functional)
Supplementary Public Funding	**mitotane** ODB - General Benefit (mitotane) (ODB Formulary)

back to top

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

B - Drug Regimen

mitotane	2 to 6 g	PO	Daily* as tolerated

(Outpatient prescription in multiples of 500mg tablets)

*Dose to be divided into TID or QID. Maximum tolerated dose may vary from 2-16 g / day. Dose may be increased based on clinical response and patient tolerance.

back to top

C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate – Consider prophylaxis daily

Other Supportive Care:

- Antiemetics: Adjust according to symptoms
- Supplement with replacement cortisone (glucocorticoid) and fludrocortisone (mineralocorticoid) (see mitotane drug monograph)

Also refer to CCO Antiemetic Recommendations.

back to top

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

E - Dose Modifications

Refer to protocol by which patient is being treated.

Dosage with toxicity

Mitotane has a long half life an accumulates in fat. Dose adjustments may not result in immediate improvement in drug related effects.

Toxicity / Event	Dose
Severe trauma, stress or infection	Interrupt; start steroids
Myelosuppression	No dose adjustment required
Adrenal insufficiency	Use corticosteroid supplementation
Mild to moderate GI, skin or CNS toxicity	Decrease dose* or hold, depending on severity
Mitotane levels > 20 mg/L	Hold and monitor levels; restart when levels within therapeutic range
Grade 3 related non-hematologic toxicity	Hold, consider dose reduction* * reduce to maximum dose tolerated by patient
Grade 4 related non-hematologic toxicity	Discontinue

Hepatic Impairment

No specific dose adjustments found. Exercise caution in mild to moderate hepatic impairment (unless due to metastatic disease), as mitotane is mainly metabolized by the liver. Not recommended for use in patients with severe hepatic impairment.

Renal Impairment

No specific dose adjustments found. Exercise caution in mild to moderate renal impairment. Not recommended for use in patients with severe renal impairment. Mitotane is unlikely to be dialyzable in the case of an overdose.

Dosage in the Elderly

No specific dose adjustment found. Titrate dosage and monitor patient carefully; consider starting at the low end of the dosage range.

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

back to top

F - Adverse Effects

Refer to mitotane drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Adrenocortical insufficiency • Fatigue • Anorexia • Somnolence and other CNS effects (may be severe) • Nausea and vomiting • Diarrhea • Rash • ↑ LFTs (may be severe) • Hyperlipidemia • Myelosuppression (± infection/bleeding - may be severe)	• Hematuria, hemorrhagic cystitis • Toxic retinopathy, maculopathy • Prolonged bleeding time

back to top

G - Interactions

Refer to mitotane drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to mitotane drug monograph(s) for additional details

Patients should use medical alert tag or bracelet warning of adrenal suppression.

back to top

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Observe for adrenal insufficiency
- Clinical CNS evaluation especially with long-term usage
- Regular clinical assessment of GI and skin toxicity, adrenal insufficiency, ophthalmic and CNS effects
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Neurological assessments; baseline and regular
- Serum cortisol levels; baseline and periodic
- Urine test; periodic
- CBC; baseline and regular
- Liver function tests; baseline and as clinically indicated
- If mitotane plasma level testing is available and clinically necessary, consider levels q2 weeks after starting treatment, after each dose adjustment, in hepatic/renal impairment, obese patients or recent weight loss; every 1 week monitoring if a high starting dose has been used. Monitor levels regularly (e.g. monthly) after reaching maintenance dose especially with toxicity and in obese patients. If treatment is interrupted, monitor levels q2 months.

back to top

J - Administrative Information

Outpatient prescription for home administration

back to top

K - References

Barzon L, Fallo, F, Sonino N, et al. Adrenocortical carcinoma: experience in 45 patients. Oncology 1997; 545:490-6.

Baudin E, Pellegriti G, Bonnay M, et al. Impact of monitoring plasma 1,1-dichlorodiphenildichloroethane (o,p'-DDD) levels on the treatment of patients with adrenocortical

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

carcinoma. Cancer 2001;92:1385–92.

Haak HR, Hermans J, van de Velde CJ , et al. Optimal treatment of adrenocortical carcinoma with mitotane: results in a consecutive series of 96 patients. Br J Cancer 1994;69(5):947-51.

Mitotane drug monograph, Cancer Care Ontario.

Terzolo M, Pia A, Berruti A, et al. Low-dose monitored mitotane treatment achieves the therapeutic range with manageable side effects in patients with adrenocortical cancer. J Clin Endocrinol Metab 2000;85:2234–38.

Wooten M, King D. Adrenal cortical carcinoma: epidemiology and treatment with mitotane and a review of the literature. Cancer 1993. 72:3145-55.

November 2021 Added mitotane public funding info

back to top

L - Other Notes

Mitotane causes adrenal suppression; it is important to maintain adequate replacement of both the glucocorticoid and mineralocorticoid steroids throughout mitotane treatment, and possibly after mitotane is discontinued.

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Any use of the information is subject, at all times, to CCO's Terms and Conditions.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top

Any use of the information is subject, at all times, to CCO’s Terms and Conditions.