

USER'S GUIDE

Drug monographs are arranged alphabetically by generic name. Monographs prepared **after** 1994 follow a slightly **different format** to incorporate a number of new features, including fully referenced citations in lieu of bibliography. All monographs will eventually be updated using this new format. Each monograph contains the following sections:

DRUG NAME:

- Generic name as listed in the Compendium of Pharmaceutical Specialties

SYNONYM(S):

Alternate generic names used in Canada and the US, abbreviations, even though their use for writing prescriptions is discouraged in favour of the full name of the drug.

COMMON TRADE NAMES:

Trade names used in Canada and the US, with the date of first notice of compliance and patent expiration in Canada if available.

CLASSIFICATION:

General pharmacologic classification, including whether it is considered a cytotoxic agent or not.

MECHANISM OF ACTION:

Brief description on the mechanism of action to provide the rationale for the choice of drug and to help predict its effect, toxicity and side effects.

PHARMACOKINETICS:

Brief description on the pharmacokinetic data to help predict the effect, toxicity and side effects of the drug, including any known variability affected by patient factors (e.g., gender, age, ethnicity). Numeric data are presented as mean \pm standard deviation unless otherwise specified.

USES:

These are the malignant conditions that may be treated with this drug. Inclusion of an indication in this section however does not imply it is a BCCA approved indication. **Primary uses** include indications approved by the Health Canada Therapeutic Products Programme and common unlabelled indications.

SPECIAL PRECAUTIONS:

These include considerations for identifying patients who should not receive the drug, or should receive it with cautions or dose adjustment. Readers are also alerted to the risks of chemotherapy on carcinogenicity, mutagenicity, fertility, pregnancy and breastfeeding. Note that these are special considerations and we have not stated the obvious. For example, none of these drugs should be used in patients known to be hypersensitive to them. Similarly, patients being treated with immunosuppressive agents should not receive live virus vaccinations. Immunosuppressive agents should probably not be administered during active viral infection (e.g., chicken pox, herpes zoster) because of the risk of developing more severe disease.

SIDE EFFECTS:

These include adverse events that may present during the drug treatment but that does not necessarily have a causal relationship with the drug,^{1,2} and adverse reactions that may be suspected to be related to the drug.^{1,2} Side effects are in a table format, with more details on selective side effects described after the table. The side effects are generally categorised according to the US National Cancer Institute guidelines,¹ with the exception of *febrile neutropenia* which is included in the *blood/bone marrow* category for ease of cross-reference between course of neutropenia and infection. Other features of the table include:

- *Extravasation hazard* is classified as vesicant, irritant, or none (see Extravasation Policy in the Appendix for definitions).
- *Emetogenic potential* is classified according to the percentage of patients who will vomit without antiemetics: high (> 90%); high moderate (60-90%); low moderate (10-60%); non-emetogenic (< 10%).
- Frequency for overall (all grades) and severe (grade 3 or 4) side effects are reported when known.
- Onset of side effects is coded as immediate (hours to 7 days); early (1 to 4 weeks); delayed (1 to 3 months); or late (more than 3 months). Note that this is usually an estimate by the writers of the Cancer Drug Manual as it is rarely fully described in the literature. **Assignment of an onset has been discontinued in monographs developed or revised after July 2006.**
- Dose-limiting side effects, previously underlined, are in **bold and italics** in monographs prepared after 1994. These include side effects requiring modification to keep toxicity within acceptable limits.

Inclusion of side effects is based on the following:

- Unintended effects related to the pharmacology (side effects) or noxious and unintended responses to the drug (adverse drug reactions).²
- Case reports showing at least possible causal association² and collaborated with other investigations (e.g., pharmacokinetic evidence).³
- Report frequency of > 1%³ in the product monograph or pivotal trials. If data came from placebo-controlled trials, side effects are included if the reported frequency was > 5% higher than the placebo group.
- Rare side effects that are potentially life-threatening, more commonly reported in related drugs, or of special interest to patients (e.g., alopecia).

INTERACTIONS:

Common drug-drug and drug-herb interactions are listed, with the outcome of the interaction, mechanism, and management strategy. Interactions due to obvious, simple additive or antagonistic effects based on known pharmacologic activity of the interacting agents are not usually included.⁴ Data from *in vitro* studies of cytochrome P-450 enzymes are also included as their clinical utility is increasingly recognised by the regulatory authorities.^{5,6} Readers are encouraged to speculate about potential interactions, especially for new agents. No interaction may have yet been reported with a specific drug, but if it shares a metabolic pathway with the cytotoxic drug in question or is affected with important clinical consequences by agents which are highly plasma protein bound, then extreme caution and vigilance should prevail if the drugs are used in combination.

SOLUTION PREPARATION AND COMPATIBILITY:

This provides pharmaceutical information on parenteral agents, including inactive ingredients of potential clinical significance,⁷⁻⁹ reconstitution, dilution, storage, expiration dates, and physicochemical compatibility¹⁰ for infusion solution and drugs commonly administered concurrently with cancer drugs. However, this manual should not replace current specialty references dealing specifically with injectable drugs.

SUPPLY AND STORAGE:

This provides pharmaceutical information on oral agents, including inactive ingredients of potential clinical significance⁷⁻⁹ and storage.

PARENTERAL ADMINISTRATION:

This includes commonly used routes and rates of administration, as well as routes that are relatively or absolutely contraindicated. The recommended routes and rates of administration at the BCCA are in **bold and italics**. Routes not in common use are preceded with the term "investigational".

DOSAGE GUIDELINES:

This provides the common dosing regimens used without support by colony stimulating factors and other cytokines. Note that this information is mainly to help find out which dosing regimens may be used with this drug. Inclusion of a dosing regimen in this section however does not imply its efficacy or safety for a particular indication. Readers should always refer to the protocol by which a patient is being treated. The usual dosing regimens used at the BCCA in **bold and italics**.

Dosing regimens information is generally based on the recommendations of the US National Institutes of Health and National Cancer Institute¹¹:

- cycle length (except chronic daily dosing, e.g., tamoxifen)
- dosage expressed per body surface area or weight
- amount of drug per dose and range
- frequency of administration and/or days on which the drug is given
- total dose per cycle and range
- any other information pertinent to the safe administration of the drug
- Additional information such as maximum lifetime dose, dose modifications for toxicity or disease states (e.g., renal failure, hepatic failure), and children's doses.

FOR THE PATIENT:

This describes briefly to the patient how the drug works and is given. Side effects are generally included if they occur in more than 10% of the patients. These are listed in a table format, with a brief description on their clinical manifestations and suggested management strategy. In addition, information on how to identify symptoms which should be reported to the doctor a timely manner is included after the table. The risk of secondary cancers with some cytotoxic drugs is not generally included. This subject is left between the patient and physician as the treatment plan is discussed and decisions made.

REFERENCES:

This has replaced the Bibliography in previous editions

APPENDICES:

These include ancillary information on selective support medications, antiemetic drugs, administration guidelines, safe handling of cytotoxics and wastes, extravasation, hypersensitivity reactions, etc.

REFERENCES

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5. CYP3A. In: Levy RH, Thummel KE, Trager WF, Hansten PD, Eichelbaum M, editors. Metabolic drug interactions. Philadelphia, PA: Lippincott Williams and Wilkins; 2000. p. 115-34.
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