**ADVERSE REACTIONS**

**INFORMATION DOCTORS ABOUT UNEXPECTED REACTIONS AFTER USE**

Docetaxel is a chemotherapy agent and is a cytotoxic and so is effectively a biologically active drug. As such, all chemotherapy, adverse effects are common and many side-effects have been documented. Breast cancer treatment is a cell cycle specific agent, it is cytotoxic to all dividing cells in the body including tumor cells as well as hair follicles, bone marrow and the gut.

Pharmacological adverse effects include Neutropenia, Anaemia, Febrile neutropenia, Neutropenic sepsis, Maculopapular rash, and other skin disorders.

**WARNINGS & PRECAUTIONS**

TAXEWELL® is a cytotoxic drug and should be used in the treatment of advanced breast cancer, non-small cell lung cancer, ovarian cancer, prostate cancer, and other cancers. Docetaxel should be administered under the supervision of a qualified health professional and is not recommended for use in patients with severe liver, renal, or cardiac impairment. Pre-treatment with corticosteroids has been shown to decrease asthenia.

High incidence of treatment-related mortality associated with docetaxel therapy has been reported. In patients with advanced breast cancer, mortality rates of up to 8% have been reported in patients receiving docetaxel. Pre-treatment with corticosteroids has been shown to decrease asthenia.

TAXEWELL® should be administered under the supervision of a qualified health professional and is not recommended for use in patients with severe liver, renal, or cardiac impairment. Pre-treatment with corticosteroids has been shown to decrease asthenia.

**OVERDOSAGE**

There is no known antidote for TAXEWELL® (Docetaxel Injection Concentrate). In overdose, in case of overdose, the patient should be kept in a specialized cancer hospital and supportive measures and treatment administered as necessary. Anticipated complications of overdosage may include severe asthenia and neutropenia, which may be severe and in some instances, fatal. Severe asthenia and neutropenia may be seen in patients receiving docetaxel.

Pre-treatment with corticosteroids has been shown to decrease asthenia. There is no known antidote for TAXEWELL® (Docetaxel Injection Concentrate). In overdose, in case of overdose, the patient should be kept in a specialized cancer hospital and supportive measures and treatment administered as necessary. Anticipated complications of overdosage may include severe asthenia and neutropenia, which may be severe and in some instances, fatal. Severe asthenia and neutropenia may be seen in patients receiving docetaxel.
Each vial of TAXEWELL® 30 (Docetaxel Injection Concentrate IP 30 mg docetaxel trihydrate IP eqv. to Anhy. Docetaxel) contains:

- Alcohol IP (95 % v/v) 13 % w/v
- Polysorbate 80 IP 2.0 ml
- Water for Injection® IP 9.0 ml

Each vial of TAXEWELL® 60 (Docetaxel Injection Concentrate IP 60 mg docetaxel trihydrate IP eqv. to Anhy. Docetaxel) contains:

- Alcohol IP (95 % v/v) 13 % w/v
- Polysorbate 80 IP 2.0 ml
- Water for Injection® IP 9.0 ml

Each vial of TAXEWELL® 120 (Docetaxel Injection Concentrate IP 120 mg docetaxel trihydrate IP eqv. to Anhy. Docetaxel) contains:

- Alcohol IP (95 % v/v) 13 % w/v
- Polysorbate 80 IP 2.0 ml
- Water for Injection® IP 9.0 ml

Each vial of TAXEWELL® 180 (Docetaxel Injection Concentrate IP 180 mg docetaxel trihydrate IP eqv. to Anhy. Docetaxel) contains:

- Alcohol IP (95 % v/v) 13 % w/v
- Polysorbate 80 IP 2.0 ml
- Water for Injection® IP 9.0 ml

Each vial of TAXEWELL® 240 (Docetaxel Injection Concentrate IP 240 mg docetaxel trihydrate IP eqv. to Anhy. Docetaxel) contains:

- Alcohol IP (95 % v/v) 13 % w/v
- Polysorbate 80 IP 2.0 ml
- Water for Injection® IP 9.0 ml

Clinical Pharmacology & Mechanism of Action

The antitumor activity of TAXEWELL® (docetaxel) is derived from its ability to disrupt the normal process of microtubule assembly and disassembly that is essential for mitotic and interphase cellular functions. Microtubules are cytoskeletal structures that form the basis of the cellular skeleton and are essential to the growth, reproduction and spread of tumor cells. Normally, as part of the mitotic process, microtubules are metabolized to form a spindle. Assembly of microtubules from tubulin requires the presence of guanosine triphosphate (GTP). Docetaxel induces in a dose-dependent manner tubulin polymerization, promoting polymerization and preventing depolymerization of microtubules in the absence of GTP thus forming the structure of microtubules, which form bands that disintegrate.

Accumulation within tumor cells

Tubulin polymerization leading to cell death

Braun Pharmacokinetics & Pharmacodynamics

Docetaxel competitively binds to the microtubule lattice destructive good tissue distribution and is extensively metabolized in the liver. After intravenous administration, docetaxel is distributed throughout the body, is concentrated in organs and tissue where extremely low levels are found. It is also detected in the feces, tumor tissue and milk. Its concentration is very rapidly, although a lower rate from tumor tissue than from normal tissue. It is excreted mainly in the feces after undergoing conjugation with glucuronic acid and sulfate esterification. Docetaxel is almost completely eliminated in the urine of all species studied. Lastly, in man, the metabolic profile of docetaxel is comparable to that of the rat. TAXEWELL® is a cytotoxic anticancer drug and as with other potentially toxic medicines, the degree of severity of the side effects may be reduced by appropriate handling, application and/or storage in accordance with the recommendations stated.