Pediatric Use
See"INDICATIONS" Section.

DRUG INTERACTIONS
Reversible decreases in steady-state plasma digoxin concentrations and renal glycoside excretion were observed in patients receiving beta-acetyldigoxin and chemotherapy regimens containing cyclophosphamide, vincristine, and prednisone with or without cytarabine or procarbazine. Monitoring of plasma digoxin levels may be indicated in patients receiving similar combination chemotherapy regimens. The utilization of digitoxin for such patients may be considered as an alternative. An *in vitro* interaction study between gentamicin and cytarabine showed a cytarabine-related antagonism for the susceptibility of *K. pneumoniae* strains. Inhibition of fluorocytosine efficacy during therapy with cytarabine has been reported.

ADVERSE REACTIONS
Expected Reactions
Because cytarabine is a bone marrow suppressant, anemia, leukopenia, thrombocytopenia, megaloblastosis and reduced reticulocytes can be expected as a result of administration with Cytarabine.
The severity of these reactions are dose and schedule dependent. Cellular changes in the morphology of bone marrow and peripheral smears can be expected.

Infectious Complications
Infection: Viral, bacterial, fungal, parasitic, or saprophytic infections, in any location in the body may be associated with the use of Cytarabine Injection, BP alone or in combination with other immunosuppressive agents following immunosuppressant doses that affect cellular or humoral immunity.
These infections may be mild, but can be severe and at times fatal.

The Cytarabine Syndrome
It is characterized by fever, myalgia, bone pain, occasionally chest pain, maculopapular rash, conjunctivitis and malaise. It usually occurs 6 to 12 hours following drug administration. Corticosteroids have been shown to be beneficial in treating or preventing this syndrome. If the symptoms of the syndrome are deemed treatable, corticosteroids should be contemplated as well as continuation of therapy with Cytarabine.

Most Frequent Adverse Reactions
Anorexia ,oral and anal inflammation, rash, nausea or ulceration, thrombophlebitis, vomiting, hepatic dysfunction, bleeding (all sites) ,diarrhea ,fever. Nausea and vomiting are most frequent following rapid intravenous injection.

Less Frequent Adverse Reactions
Sepsis, esophageal ulceration, conjunctivitis (may occur with rash),pneumonia, esophagitis, dizziness
cellulitis at injection site chest pain, alopecia,skin ulceration, pericarditis anaphylaxis ,urinary retention, bowel necrosis ,allergic edema, renal dysfunction, abdominal pain, pruitus, neuritis, pancreatitis, shortness of breath, neural toxicity ,freckling urticaria, sore throat, jaundice etc.

DOSAGE AND ADMINISTRATION
Cytarabine Injection is not active orally. The schedule and method of administration varies with the program of therapy to be used. Cytarabine may be given by intravenous infusion or injection, subcutaneously, or intrathecally.
Thrombophlebitis has occurred at the site of drug injection or infusion in some patients, and rarely patients have noted pain and inflammation at subcutaneous injection sites. In most instances, however, the drug has been well tolerated.
Patients can tolerate higher total doses when they receive the drug by rapid intravenous injection as compared with slow infusion. This phenomenon is related to the drug's rapid inactivation and brief exposure of susceptible normal and neoplastic cells to significant levels after rapid injection. Normal and
neoplastic cells seem to respond in somewhat parallel fashion to these different modes of administration and no clear-cut clinical advantage has been demonstrated for either.
In the induction therapy of acute non-lymphocytic leukemia, the usual cytarabine dose in combination with other anti-cancer drugs is 100 mg/m^2/day by continuous IV infusion (Days 1-7) or 100 mg/m^2 IV every 12 hours (Days 1-7).

Intrathecal Use in Meningeal Leukemia
Cytarabine has been used intrathecally in acute leukemia in doses ranging from 5 mg/m^2 to 75 mg/m^2 of body surface area. The frequency of administration varied from once a day for 4 days to once every 4 days. The most frequently used dose was 30 mg/m^2 every 4 days until cerebrospinal fluid findings were normal, followed by one additional treatment. The dosage schedule is usually governed by the type and severity of central nervous system manifestations and the response to previous therapy.
Cytarabine Injection given intrathecally may cause systemic toxicity and careful monitoring of the hemopoietic system is indicated. Modification of other anti-leukemia therapy may be necessary. Major toxicity is rare. The most frequently reported reactions after intrathecal administration were nausea, vomiting and fever; these reactions are mild and self-limiting. Paraplegia has been reported. Necrotizing leukoencephalopathy occurred in 5 children; these patients had also been treated with intrathecal methotrexate and hydrocortisone, as well as by central nervous system radiation. Isolated neurotoxicity has been reported. Blindness occurred in two patients in remission whose treatment had consisted of combination systemic chemotherapy, prophylactic central nervous system radiation and intrathecal Cytarabine.

When Cytarabine is administered both intrathecally and intravenously within a few days, there is an increased risk of spinal cord toxicity, however, in serious life-threatening disease, concurrent use of intravenous and intrathecal Cytarabine is left to the discretion of the treating physician.

Focal leukemic involvement of the central nervous system may not respond to intrathecal Cytarabine and may better be treated with radiotherapy.

Chemical Stability in Infusion Solutions

Chemical stability studies were performed by a stability indicating HPLC assay on Cytarabine Injection in infusion solutions. These studies showed that when Cytarabine Injection was diluted with Water for Injections, 5% Dextrose Injection or Sodium Chloride Injection, 97-100% of the Cytarabine was still present after 8 days storage at room temperature. **Parenteral drugs should be inspected visually for particulate matter and discoloration, prior to administration, whenever solution and container permit.**

This chemical stability information in no way indicates that it would be acceptable practice to infuse a Cytarabine admixture well after the preparation time. Good professional practice suggests that administration of an admixture should be as soon after preparation as feasible.

Handling and Disposal
Procedures for proper handling and disposal of anticancer drugs should be considered. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

OVERDOSE
There is no antidote for overdosage of Cytarabine
Doses of 4.5 g/m^2 by intravenous infusion over 1 hour every 12 hours for 12 doses has caused an unacceptable increase in irreversible CNS toxicity and death. Single doses as high as 3 g/m^2 have been administered by rapid intravenous infusion without apparent toxicity.

STORAGE
Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Protected from light.

SHELF LIFE
24 Months

HOW SUPPLIED
Cytalon™ 100
Cytarabine Injection BP 100mg/1mL
Single dose vial, individually packed in a carton.
Cytalon™ 500
Cytarabine Injection BP 500mg/5mL
Single dose vial, individually packed in a carton.
Cytalon™ 1000
Cytarabine Injection BP 1000mg/10mL
Single dose vial, individually packed in a carton.
Cytalon™ 2000
Cytarabine Injection BP 2000mg/20mL
Single dose vial, individually packed in a carton.

Manufactured & Marketed by:
CELON LABS
CELON LABORATORIES PVT. LTD.,
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