



## Therapeutic Class Review<sup>SM</sup>

### Antineoplastics – liposomal cytarabine (DepoCyt<sup>®</sup>)

February 2009

#### New Product for Review:

cytarabine (Tarabine<sup>®</sup>) [various]  
liposomal cytarabine (DepoCyt<sup>®</sup>) [Enzon]

#### Dossier Provided by Manufacturer: N/A

#### Dossier Evaluation: N/A

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

#### Executive Summary

- Neoplastic meningitis occurs when cancers from other parts of the body metastasize to the brain.
  - Prognosis is poor with a life expectancy of a few months.
  - Treatment is generally palliative with the goal of delaying onset of neurological deficits and allowing patients to die from progression of systemic disease.
- Intrathecally administered cytarabine (Ara-C), liposomal cytarabine (DepoCyt), and methotrexate have all been used for palliative treatment of neoplastic meningitis. Intrathecal administration requires either a lumbar puncture or insertion of an intraventricular device.
- Liposomal cytarabine (DepoCyt) is a long-acting, preservative-free liposomal formulation of cytarabine for intrathecal use. This formulation results in sustained concentrations of cytarabine in the brain tissue, and may therefore be administered less frequently than cytarabine (Ara-C).
- Although the available evidence for liposomal cytarabine (DepoCyt<sup>®</sup>) is limited and flawed, it appears likely that this product has similar efficacy to cytarabine (Ara-C<sup>®</sup>).
- Because liposomal cytarabine (DepoCyt) results in sustained concentrations of cytarabine in brain tissue, it is associated with a higher incidence of adverse effects, such as chemical arachnoiditis.
- Cytarabine in either form is used as a second- or third-line treatment for metastatic brain tumors.

## Summary of Products

	<b>DepoCyt</b>	<b>Ara-C</b>
Route of administration	intrathecal	intrathecal/intravenous/subcutaneous
Frequency of intrathecal (IT) administration	every 2 weeks	2 to 3 times per week
Adverse Events	Chemical arachnoiditis (nausea, vomiting, headache and fever)	Bone marrow suppression, anorexia, hepatic dysfunction, nausea, vomiting, fever, rash, diarrhea, thrombophlebitis, oral and anal inflammation or ulceration, bleeding (all sites).
Approved for pediatric use?	Not studied in pediatrics	Studied and approved for use in pediatrics

Note: Intrathecal methotrexate is also a possible treatment alternative and is administered 2 to 3 times per week.

## Evidence

Available evidence is limited and unreliable. The trials are small, and studied multiple disease states. The trial is of open-label design and is not powered for superiority.

## Decision

Liposomal cytarabine (DepoCyt) is non-preferred/non-formulary because:

- It carries risk of significant side effects (specifically, chemical arachnoiditis).
- There are other treatment options that may have similar efficacy and fewer safety risks.
- Other treatment options may provide a better cost value for members.

## Products

<b>Drug Products</b>	<b>FDA approval<sup>a</sup></b>	<b>Patent expiration<sup>b</sup></b>	<b>FDA approved indications</b>	<b>Usual Dose/Route</b>
Liposomal cytarabine (DepoCyt <sup>®</sup> )	11/1995	5/2013	intrathecal treatment of lymphomatous meningitis	Intrathecal
Cytarabine (generics)	8/1989	expired	<ul style="list-style-type: none"> <li>• Meningeal leukemia (intrathecal administration)</li> <li>• Acute non-lymphocytic leukemia of adults and children.</li> <li>• Acute lymphocytic leukemia and the blast phase of chronic myelocytic leukemia.</li> </ul>	Intravenous/intrathecal

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> Based on patents listed in the Orange Book as of 12/09/2008.

## **References**

1. Depocyt<sup>®</sup> (cytarabine liposome injection) Prescribing Information. April 2007. Enzon Pharmaceuticals, Inc. Bridgewater, NJ
2. Cytarabine Injection Prescribing Information. November 2007. Hospira, Inc. Lake Forest, IL
3. Rueda Domínguez A, Olmos Hidalgo D, Viciano Garrido R, Torres Sánchez E. Liposomal cytarabine (DepoCyt) for the treatment of neoplastic meningitis. *Clin Transl Oncol*. 2005 Jul;7(6):232-8.
4. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Nervous System Cancers v.1.2008v.1.2008. Available at: <http://www.nccn.org>. Accessed on 11/17/08.
5. Drugs@FDA [page on the internet]. Label, approval history and review for DepoCyt. Available at [http://www.fda.gov/cder/foi/nda/99/21-041\\_DepoCyt.htm](http://www.fda.gov/cder/foi/nda/99/21-041_DepoCyt.htm). Accessed 11/10/2008.
6. Benesch M, Urban C. Liposomal cytarabine for leukemic and lymphomatous meningitis: recent developments. *Expert Opin Pharmacother*. 2008 Feb;9(2):301-9.