



Therapeutic Class ReviewSM

Antineoplastics – vorinostat (ZolinzaTM)

October 2008

New Product for Review:

vorinostat (Zolinza[®]) [Merck & Co]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: 2

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

Executive Summary

Background on CTCL

- Cutaneous T-cell lymphoma (CTCL):
 - Is a rare form of non-Hodgkin lymphoma, with about 1,500 cases diagnosed each year in the U.S.
 - Is twice as likely to occur in men.
 - Has a median age of diagnosis of 55 years of age.
 - Generally has a good prognosis if diagnosed early.
 - Is often limited to the skin, but may also involve lymph nodes and other organs
- There are several different types of CTCL. Mycosis fungoides (MF) is the most common form of CTCL, accounting for approximately 50% of newly diagnosed cases.
- Important predictors of survival include the extent to which the lymphoma has affected the skin, the type of skin involvement (patch vs. plaque vs. tumor), whether the tumor has spread to other areas of the body, and patient age.
- Treatment options for CTCL depend on the staging of the disease at diagnosis, and may include:
 - Topical nitrogen mustard.
 - Photochemotherapy.
 - Electron beam radiation.
 - Chemotherapy.
 - Other targeted therapies.
- There are no known treatments for advanced CTCL that produce reliable durable remissions or curative results, with the possible exception of allogeneic bone marrow transplantation.^[19]

Vorinostat (Zolinza)

- Vorinostat (Zolinza) is an oral chemotherapy agent approved under the Orphan Drug Act for patients with advanced forms of CTCL who have failed multiple other systemic treatment options.
- Response to vorinostat (Zolinza) was determined by measuring the surface area of the skin that was affected by the disease. Tumor response at sites other than the skin has not been demonstrated.
- It is not known whether treatment with vorinostat (Zolinza) improves overall survival.
- There is a high likelihood of off-label use with vorinostat (Zolinza) as evidenced by recruitment of subjects for approximately 36 clinical trials in over 10 different types of cancer.
- FDA approval of vorinostat (Zolinza) was based on:
 - Need for additional treatment options in populations with advanced CTCL.
 - An acceptable safety profile for this population.

Evidence

- There is no reliable evidence (open-label trials with no randomization and no comparators) supporting the efficacy of vorinostat (Zolinza) in the treatment of CTCL. Better quality studies are not likely because an adequate population of eligible patients does not exist.
- There is no evidence comparing the efficacy of vorinostat (Zolinza) with other treatment options.

Decision

Vorinostat (Zolinza) is non-preferred/non-formulary because:

- It provides unknown benefit in the treatment of CTCL.
- There are other preferred/formulary options available.
- There is no information available regarding improved safety and effectiveness over other options.

Products

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route for CTCL treatment	Potential Off-label Uses ^b
bexarotene gel 1% (Targretin [®]) ^[11] [60 gm tube]	06/2000	10/2016	Topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies, or who have not tolerated other therapies.	Cover lesions with a generous coat one to four times per day as tolerated. Continue for as long as patient derives benefit.	Psoriasis, Kaposi's sarcoma
bexarotene tablet (Targretin [®]) ^[2] [75 mg capsules]	12/1999	7/2015	Treatment of cutaneous manifestations of CTCL in patients who are refractory to at least one prior systemic therapy.	300 mg/m ² orally once per day with food. [maximum: 400 mg/m ² /day].	Psoriasis, Kaposi's sarcoma, breast cancer, non-small cell lung cancer (nsclc), advanced renal cell carcinoma
chlorambucil (Leukeran [®]) ^[3] [2 mg tablets]	03/1957	Patents expired (generic available)	For the treatment of: <ul style="list-style-type: none"> Chronic lymphatic (lymphocytic) leukemia. Malignant lymphomas including lymphosarcoma. Giant follicular lymphoma. Hodgkin's disease. 	0.15 to 0.2 mg/kg/day for 2 to 4 weeks (for 6 to 8 cycles).	CTCL, rheumatoid arthritis, ovarian cancer, dermatomyositis, Hairy cell leukemia, Hodgkin's disease, nephrotic syndrome, sarcoidosis, Sjögrens syndrome
denileukin diftitox (Ontak [®]) ^[4] [150 mcg/ml; 2 ml vials]	02/1999	No information available	For the treatment of persistent or recurrent CTCL whose malignant cells express the CD25 component of the IL-2 receptor.	9 or 18 mcg/kg/day intravenously for 5 days every 21 days.	Chronic lymphoid leukemia, psoriasis, rheumatoid arthritis, non-Hodgkin's lymphoma
doxorubicin, liposomal (Doxil [®]) ^[5] [2 mg/ml; 10 ml and 25 ml vials]	11/1995	Patents expired (no generics)	For the treatment of: <ul style="list-style-type: none"> Ovarian Cancer AIDS-related Kaposi's sarcoma. Multiple myeloma 	20 to 40 mg/m ² intravenously every four weeks.	CTCL, breast cancer, angiosarcoma, colorectal cancer, head and neck cancer, multiple myeloma, NSCLC
etoposide capsules (VePesid [®]) ^[6] [50 mg capsules]	12/1986	Patents expired (generic available)	First-line treatment for small cell lung cancer in combination with other approved chemotherapeutic agents.	50 mg/m ² orally daily for 21 days, repeated every 28 to 35 days.	CTCL, testicular cancer, many other cancers including cancer of the cervix, prostate, liver, uterus, thymus, bone, etc.
gemcitabine (Gemzar [®]) ^[7] [200 mg and 1 gm vials]	05/1996	10/2008	For the treatment of: <ul style="list-style-type: none"> Ovarian cancer Breast cancer Non-small cell lung cancer Pancreatic cancer 	1,200 mg/m ² intravenously on days 1, 8, and 15 every four weeks.	CTCL, malignant mesothelioma, testicular cancer; malignant neoplasms of the adrenal cortex, soft tissue, bladder, and urinary tract
methotrexate (generics) ^[8] [2.5 mg tablets]	12/1953	Patent expired (generic available)	For treatment of: <ul style="list-style-type: none"> Neoplastic diseases Psoriasis Rheumatoid arthritis 	15 to 25 mg/m ² orally per week.	CTCL, esophageal cancer, retinoblastoma, sarcoma of bone, polymyalgia rheumatica
vorinostat (Zolinza [®]) ^[9] [100 mg capsules]	10/2006	10/2013	Treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) when there is progressive, persistent, or recurrent disease on or follow-ing two systemic therapies.	400 mg (4 capsules) once daily with food.	Malignant gliomas, myelodysplastic syndromes, leukemias, kidney cancer, prostate cancer, metastatic colorectal cancer

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b As listed under recruiting clinical trials on clinicaltrials.gov.

^c Based on patents listed in the Orange Book as of April 2008.

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