Formulary Review: **Halaven™** **Reviewed: March 2011**
Generic Name: **Eribulin mesylate**
Manufacturer: **Eisai Inc.**

Executive Summary

Introduction

Eribulin mesylate is a microtubule inhibitor indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens containing an anthracycline and a taxane.

Pharmacology

Eribulin inhibits the growth phase of microtubules without affecting the shortening phase and sequesters tubulin in nonproductive aggregates. Erbulin exerts its effects via a tubulin-based antimitotic mechanism leading to G_2/M cell-cycle block, disruption of mitotic spindles, and ultimately, apoptotic cell death after prolonged mitotic blockage.

Pharmacokinetics

Table 1. Pharmacokinetic profile

Distribution, $V_{d\,(ss)}$	43-114L/m2
Metabolism	CYP450-3A4
Elimination half-life	40 hrs

Clinical Efficacy

In an open-label, randomized, multicenter trial, 762 patients with metastatic breast cancer who had received at least two chemotherapeutic regimens for the treatment of metastatic disease and experienced disease progression within 6 months of their last chemotherapeutic regimen were randomized (2:1) to receive Eribulin 1.4mg/m2 (n=508) or a single agent therapy selected prior to randomization (control arm, n=254). A statistically significant improvement in overall survival was observed in the patients randomized to the Eribulin arm compared to the control arm. (13.1 vs. 10.6 months, p=0.041)

Adverse Drug Reactions

The most common adverse reactions (≥ 25%) reported in patients receiving Eribulin were neutropenia, anemia, asthenia/fatigue, alopecia, peripheral neuropathy, nausea, and constipation. The most serious adverse reactions reported in patients receiving Eribulin were febrile neutropenia (4%) and neutropenia (2%). The most common adverse reaction resulting in discontinuation of Eribulin was peripheral neuropathy (5%).

Drug Interactions

No drug interactions are known or expected.

Dosage & Administration

The recommended dose is 1.4mg/m2 administered IV over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle. The dose is reduced to 1.1mg/m2 in patients with mild hepatic impairment (Child-Pugh A) or moderate renal impairment (creatinine clearance of 30-50mL/min), and 0.7mg/m2 with moderate hepatic impairment (Child-Pugh B)

Recommended dose reductions	
Event description	Recommended dose
Permanently reduce the dose to 1.1mg/m2 for any of the following	
ANC <500/mm3 for > 7 days	1.1mg/m2
ANC<1,000/mm3 with fever or infection	
Platelets < 25,000/mm3	
Platelets <50,000/mm3 requiring transfusion	
Non-hematologic Grade 3 or 4 toxicities	
Omission or delay of Day 8 dose in previous cycle for toxicity	
Occurrence of any event requiring permanent dose reduction while receiving 1.1mg/m2	0.7mg/m2
Occurrence of any event requiring permanent dose reduction while receiving 0.7mg/m2	Discontinue eribulin

Summary	Eribulin is a microtubule inhibitor that has been shown to improve survival in patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens containing an anthracycline and a taxane.
Formulary Status	**Formulary; restricted to outpatient use only**