

Recommendations and Reasons

Committee to Evaluate Drugs (CED)

Azacitidine

Product:

AZACITIDINE (Vidaza®)

Class of drugs:

anti-cancer agent; pyrimidine analogue

Indication:

myelodysplastic syndrome (MDS)

Manufacturer:

Celgene Inc.

CED Recommendation

The CED recommended that azacitidine (Vidaza®) be funded for the treatment of myelodysplastic syndrome (MDS) according to specific criteria. The CED noted that this drug has been demonstrated to improve survival in MDS patients with a higher-risk form of the disease.

Executive Officer Decision

Based on the CED's recommendation and a listing agreement with the manufacturer that helps to address concern raised by the CED, the Executive Officer decided to fund Vidaza through the New Drug Funding Program according to specific criteria.

Status

Funded through the New Drug Funding Program.

Highlights of Recommendation:

- ♦ Azacitidine is an anti-cancer drug that can be used for the treatment of myelodysplastic syndrome (MDS), including a subset of patients with acute myelogenous leukemia (AML).
- ♦ A clinical study in patients with a higher-risk form of MDS showed that azacitidine prolonged survival by 9.4 months compared with conventional care.
- ♦ Patients with MDS currently have limited effective treatment options. Azacitidine is the first drug that has been shown in a clinical trial to improve survival in this setting.
- ♦ Azacitidine costs approximately \$6,000 for each 28-day treatment cycle. If on average each patient receives 10 cycles of azacitidine, the total cost amounts to \$60,000. Given the high drug cost and the substantial number of patients anticipated to require this treatment, the financial impact of funding azacitidine is significant.
- ♦ **Overall, the CED acknowledged that azacitidine has been shown to provide survival benefits in patients with a higher-risk form of MDS, a condition with limited effective treatment alternatives. The CED was, however, concerned with the high costs associated with funding this drug.**

Background:

Myelodysplastic syndrome (MDS) is a group of disorders that affect the ability of the bone marrow to produce healthy, mature red blood cells, white blood cells, and platelets.

MDS primarily affects older patients, with approximately 80 to 90% of cases diagnosed in patients over the age of 60. It is estimated that one in three people who have MDS will progress to develop acute myelogenous leukemia (AML), a type of bone marrow cancer.

Prognosis is determined by using the International Prognostic Scoring System (IPSS), which classifies MDS patients as either lower risk (low- and intermediate-1) or higher risk (intermediate-2 or high). In patients with a higher-risk form of the disease, the bone marrow is more widely affected and the disease has a higher tendency to progress to AML.

The only proven cure for MDS is stem cell transplantation. However, only a small number of patients are eligible for this procedure. Most patients rely on supportive treatments aimed at improving symptoms and quality of life. Supportive care may include: red blood cell transfusions to help with fatigue and anemia; erythropoietin (a drug used to stimulate red blood cell production) to reduce the number of blood transfusions; and antibiotics and growth factor therapies for treating infections. For higher-risk patients, chemotherapy may also be considered but these conventional treatments have not been shown in clinical studies to improve survival.

Azacitidine is indicated for use in patients who are not eligible for stem cell transplantation with intermediate-2 or high-risk MDS, including a subset of AML patients with 20-30% blasts (immature cells).

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Detailed Discussion:

- ♦ A single open-label randomized controlled study (*Fenaux et al. The Lancet Oncology 2009*) was the focus of this review. The study enrolled 358 patients with intermediate-2 or high-risk MDS and included a subset of AML patients with 20-30% blasts. Patients were assigned to receive azacitidine or one of three different conventional care regimens (best supportive care, low-dose cytarabine, or standard chemotherapy).
- ♦ The study found that the median overall survival was 24.5 months for patients who were treated with azacitidine and 15 months in patients who received conventional care, a difference of 9.4 months.
- ♦ The median time to AML transformation was 17.8 months for patients treated with azacitidine and 11.5 months for patients on conventional care. The six months difference was not statistically significant.
- ♦ Quality of life was not assessed in the study.
- ♦ Azacitidine is estimated to cost approximately \$60,000 per patient. Funding this therapy would have significant economic impact due to the large number of patients expected to require treatment.
- ♦ **Overall, the CED recognized that azacitidine is the first treatment that has been shown in a clinical study to prolong survival in patients with higher-risk MDS, but noted with concern the high treatment cost and financial impact.**

The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as it does all other cancer drugs.

NDFP Funding:

Based on the CED's recommendation and a listing agreement with the manufacturer, the Executive Officer decided to fund azacitidine (Vidaza®) through the New Drug Funding Program (NDFP) according to specific criteria.

The NDFP eligibility criteria can be found at the Cancer Care Ontario website: <http://www.cancercare.on.ca/toolbox/drugs/ndfp/>



Ministry of
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