**RECOGNIZE**
Some of the patients most suited for GLIADEL® Wafer (carmustine implant) could be yours.

**PRE-SURGERY**

- Does your patient have a newly-diagnosed high-grade glioma or recurrent GBM?
  - YES
- Is the tumor unifocal?\(^1,2\)
  - YES
- Patient Characteristics\(^3\)
  - Aged 18-80
  - KPS score \(\geq 60\)
  - YES
- Is surgery possible?
  - YES
- Informed Consent
  - Does your patient agree GLIADEL Wafer is an option?
  - YES

**DURING SURGERY**

- Is maximal safe resection possible?\(^4\)
  - YES
- Has communication between the surgical cavity and the ventricular system been avoided, or can a communication larger than wafer diameter be closed?
  - YES
- Is a water-tight dural closure possible?
  - YES

**POTENTIAL GLIADEL WAFER CANDIDATE**

**INDICATIONS**
GLIADEL Wafer is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation. GLIADEL Wafer is also indicated in patients with recurrent glioblastoma multiforme as an adjunct to surgery.

**IMPORTANT SAFETY INFORMATION**
The following Warnings and Precautions have been associated with the use of GLIADEL Wafer: seizures, intracranial hypertension, impaired neurosurgical wound healing, meningitis, and wafer migration. GLIADEL Wafer can cause fetal harm when administered to a pregnant woman.

Please see additional Important Safety Information on reverse, as well as the enclosed full Prescribing Information.
INDICATIONS

GLIADEL® Wafer (carmustine implant) is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation.

GLIADEL Wafer is also indicated in patients with recurrent glioblastoma multiforme as an adjunct to surgery.

IMPORTANT SAFETY INFORMATION

GLIADEL Wafer (carmustine implant) can cause fetal harm when administered to a pregnant woman. It is recommended that patients receiving GLIADEL Wafer discontinue nursing. Female patients of reproductive potential should receive counseling on pregnancy planning and prevention. Advise male patients of the potential risk of infertility, and to seek counseling on fertility and family planning options prior to implantation of GLIADEL Wafer.

WARNINGS AND PRECAUTIONS

Seizures: Fifty-four percent (54%) of patients treated with GLIADEL Wafers in the recurrent disease trial experienced new or worsened seizures within the first five post-operative days. The median time to onset of the first new or worsened post-operative seizure was 4 days. Optimize anti-seizure therapy prior to surgery. Monitor patients for seizures postoperatively.

Intracranial Hypertension: Brain edema occurred in 23% of patients treated with GLIADEL Wafers in the initial surgery trial. Additionally, one GLIADEL-treated patient experienced intracerebral mass effect unresponsive to corticosteroids which led to brain herniation. Monitor patients closely for intracranial hypertension related to brain edema, inflammation, or necrosis of the brain tissue surrounding the resection. In refractory cases, consider re-operation and removal of GLIADEL Wafers or Wafer remnants.

Impaired Neurosurgical Wound Healing: Impaired neurosurgical wound healing including wound dehiscence, delayed wound healing, and subdural, subgaleal, or wound effusions occur with GLIADEL Wafer treatment. In the initial disease trial, 16% of GLIADEL Wafer-treated patients experienced impaired intracranial wound healing and 5% had cerebrospinal fluid leaks. In the recurrent disease trial, 14% of GLIADEL Wafer-treated patients experienced wound healing abnormalities. Monitor patients post-operatively for impaired neurosurgical wound healing.

Meningitis: Meningitis occurred in 4% of patients receiving GLIADEL Wafers in the recurrent disease trial. Two cases of meningitis were bacterial; one patient required removal of the Wafers four days after implantation; the other developed meningitis following reoperation for recurrent tumor. One case was diagnosed as chemical meningitis and resolved following steroid treatment. In one case the cause was unspecified, but meningitis resolved following antibiotic treatment. Monitor postoperatively for signs of meningitis and central nervous system infection.

Wafer Migration: GLIADEL Wafer migration can occur. To reduce the risk of obstructive hydrocephalus due to wafer migration into the ventricular system, close any communication larger than the diameter of a Wafer between the surgical resection cavity and the ventricular system prior to Wafer implantation. Monitor patients for signs of obstructive hydrocephalus.

ADVERSE REACTIONS

The most common adverse reactions in Newly-Diagnosed High Grade Malignant Glioma patients (incidence >10% and between arm difference ≥4%) are cerebral edema, asthenia, nausea, vomiting, constipation, wound healing abnormalities and depression.

The most common adverse reactions in Recurrent Glioblastoma Multiforme patients (incidence >10% and between arm difference ≥4%) are urinary tract infection, wound healing abnormalities and fever.


Please see enclosed insert or visit www.gliadel.com for full Prescribing Information.
GLIADEL® WAFER (carmustine implant) for intracranial use
Full prescribing information for GLIADEL WAFER.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GLIADEL WAFER safely and effectively. See full prescribing information for GLIADEL WAFER.

GLIADEL® WAFER (carmustine implant) for intracranial use
Initial U.S. Approval: 1996

--- INDICATIONS AND USAGE ---
GLIADEL Wafer is an alkylating drug indicated for the treatment of:
- newly-diagnosed high-grade-malignant glioma as an adjunct to surgery and radiation (1)
- recurrent glioblastoma multiforme as an adjunct to surgery (1)

--- DOSAGE AND ADMINISTRATION ---

Recommended dose: Eight 7.7 mg wafers (61.6 mg total dose) implanted intracranially (2.1, 2.2)
Follow preparation and handling recommendations (2.3).

--- DOSAGE FORMS AND STRENGTHS ---
Each GLIADEL Wafer contains 7.7 mg of carmustine (3).

--- CONTRAINDICATIONS ---
None (4)

--- WARNINGS AND PRECAUTIONS ---
- Seizures: Monitor patients for seizures following implantation (5.1).
- Intracranial hypertension: Monitor patients for signs of increased intracranial pressure (5.2).
- Impaired neurosurgical wound healing: Monitor patients for complications of craniotomy (5.3).
- Meningitis: Monitor patients for signs of bacterial or chemical meningitis (5.4).
- Wafer migration: Monitor patients for signs of obstructive hydrocephalus (5.5).
- Embryo-fetal toxicity: Can cause fetal harm (5.6).

--- ADVERSE REACTIONS ---
- Newly-Diagnosed High-Ggrade Malignant Glioma: Most common adverse reactions (incidence >10% and between arm difference >4%) are cerebral edema, asthenia, nausea, vomiting, constipation, wound healing abnormalities and depression (6.1).
- Recurrent Glioblastoma Multiforme: Most common adverse reactions (incidence >10% and between arm difference >4%) are urinary tract infection, wound healing abnormalities and fever (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Arbor Pharmaceuticals, LLC at 1-866-516-4950 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

--- USE IN SPECIFIC POPULATIONS ---
Pediatric use: Safety and effectiveness not established (6.4)

See 17 for PATIENT COUNSELING INFORMATION

--- FULL PRESCRIBING INFORMATION: CONTENTS* ---

1. INDICATIONS AND USAGE
2. DOSAGE AND ADMINISTRATION
2.1 Recommended Dose
2.2 Insertion Instructions
2.3 Preparation and Safe Handling
3. DOSAGE FORMS AND STRENGTHS
4. CONTRAINDICATIONS
5. WARNINGS AND PRECAUTIONS
5.1 Seizures
5.2 Intracranial Hypertension
5.3 Impaired Neurosurgical Wound Healing
5.4 Meningitis
5.5 Wafer Migration
5.6 Embryo-fetal Toxicity
6. ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Post Approval Experience
7. PATIENT COUNSELING INFORMATION
8. USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Nursing Mothers
8.7 Carcinogenesis, Mutagenesis, Impairment of Fertility
8.8 Nonclinical Toxicology
9. CLINICAL PHARMACOLOGY
9.1 Mechanism of Action
9.2 Pharmacodynamics
9.3 Pharmacokinetics
9.4 Animal Data
9.5 Clinical Toxicology
9.6 Craniotomy
9.7 Carcinogenesis, Mutagenesis, Impairment of Fertility
9.8 Nonclinical Toxicology
10. REFERENCE
11. DESCRIPTION
12. CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Animal Data
12.5 Clinical Toxicology
12.6 Craniotomy
13. NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Toxicity Studies
13.3 Animal Data
14. CLINICAL STUDIES
14.1 Newly-Diagnosed High-Grade Malignant Glioma
14.2 Recurrent Glioblastoma Multiforme
15. REFERENCES
16. HOW SUPPLIED/STORAGE AND HANDLING
17. PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

--- Instructions for Opening Pouch Containing GLIADEL Wafer ---
Read all steps of the instructions prior to opening the pouch.

Instructions for opening the pouch containing GLIADEL Wafer can be viewed at the following website: http://gliadel.com/hcp/pouch-opening-instructions. Illustrations are also pictured below.

Figure 1: To remove the sterile inner pouch from the outer pouch, locate the folded corner and slowly pull in an outward motion.

Figure 2: Do NOT pull in a downward motion rolling knuckles over the pouch. This may exert pressure on the wafer and cause it to break.

Figure 3: The inner pouch is a multi-layered, silver colored, foil laminate. Remove the inner pouch by grabbing hold of the cramped edge of the inner pouch using a sterile instrument and pulling upward.
3 DOSAGE FORMS AND STRENGTHS
GLIADEL Wafer is an off-white to pale yellow round wafer. Each GLIADEL Wafer contains 7.7 mg of carmustine.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Seizures
Fifty-four percent (54%) of patients treated with GLIADEL Wafer for recurrent glioma in Study 2 experienced new or worsened seizures within the first five post-operative days (see Adverse Reactions [6.1]). The median time to onset of the first new or worsened post-operative seizure was 4 days. Optimize anti-seizure therapy prior to surgery. Monitor patients for seizures postoperatively.

5.2 Intracranial Hypertension
Brain edema occurred in 23% of patients with newly diagnosed glioma treated with GLIADEL Wafer in Study 1. Additionally, one GLIADEL-treated patient experienced intracranial mass effect unresponsive to corticosteroids which led to brain herniation (see Adverse Reactions [6.1]). Monitor patients closely for intracranial hypertension related to brain edema, inflammation, or necrosis of the brain tissue surrounding the resection. In refractory cases, consider re-operation and removal of GLIADEL Wafer or Wafer remnants.

5.3 Impaired Neurosurgical Wound Healing
Impaired neurosurgical wound healing including wound dehiscence, delayed wound healing, and subdural, subgaleal, or wound effusions occur with GLIADEL Wafer treatment. In Study 1, 16% of GLIADEL Wafer-treated patients with newly diagnosed glioma experienced impaired intracranial wound healing and 5% had cerebrospinal fluid leaks. In Study 2, 14% of GLIADEL Wafer-treated patients with recurrent glioma experienced wound healing abnormalities (see Adverse Reactions [6.1]). Monitor patients post-operatively for impaired neurosurgical wound healing.

5.4 Meningitis
Meningitis occurred in 4% of patients with recurrent glioma receiving GLIADEL Wafer in Study 2. Two cases of meningitis were bacterial; one patient required re-operation and removal of the Wafers four days after implantation. The other developed meningitis following re-resection for recurrent tumor. One case was diagnosed as chemical meningitis and resolved following steroid treatment. In one case the cause was unspecified, but meningitis resolved following antibiotic treatment. Monitor postoperatively for signs of meningitis and central nervous system infection.

5.5 Wafer Migration
GLIADEL Wafer migration can occur. To reduce the risk of obstructive hydrocephalus due to wafer migration into the ventricular system, close any communication larger than the diameter of a Wafer between the surgical resection cavity and the ventricular system prior to Wafer implantation. Monitor patients for signs of obstructive hydrocephalus.

5.6 Embryo-Fetal Toxicity
GLIADEL Wafer can cause fetal harm when administered to a pregnant woman. Carmustine, the active component of GLIADEL Wafer, is embryotoxic and teratogenic in rats at exposures less than the exposure at the recommended human dose on a mg/m² basis. Adverse females of reproductive potential to avoid pregnancy after implantation of GLIADEL Wafers. If the patient becomes pregnant after GLIADEL Wafer implantation, warn the patient about the potential hazard to the fetus (see Use in Specific Populations [8.1 and 8.6]).

6 ADVERSE REACTIONS
The following serious adverse reactions are discussed elsewhere in the label:

- Seizures (see Warnings and Precautions [5.1])
- Intracranial Hypertension (see Warnings and Precautions [5.2])
- Impaired Neurosurgical Wound Healing (see Warnings and Precautions [5.3])
- Meningitis (see Warnings and Precautions [5.4])

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Newly Diagnosed High Grade Malignant Glioma

The safety of GLIADEL Wafers was evaluated in a multicenter, randomized (1:1), double-blind, placebo controlled trial of 240 adult patients with newly-diagnosed high-grade malignant glioma who received up to eight GLIADEL Wafers or matched placebo implanted against the resection surfaces after maximal tumor resection (Study 1).

The population in Study 1 was 67% male, 97% white, the median age was 53 years (range: 21-72). Eighty-seven percent had a Karnofsky performance status ≥ 70 and 71% had a Karnofsky performance status of ≥ 80. Seventy-eight percent had a histologic subtype of glioblastoma multiforme as determined by central pathology review. Thirty-eight percent of patients received 8 wafers and 78% received ≥ 6 wafers. Starting three weeks after surgery, 80% of patients received standard limited field radiation therapy (RT) described as 55-60 Gy delivered in 28 to 36 fractions over six weeks; an additional 11% received no radiotherapy and the remainder received non-standard radiotherapy or a combination of standard and non-standard radiotherapy. At the time of progression, 24% received systemic chemotherapy.

Deaths occurred within 30 days of wafer implantation in 5 (4%) patients receiving GLIADEL Wafers compared to 2 (2%) of patients receiving placebo. Deaths on the GLIADEL arm resulted from cerebral herniation (n=3), pulmonary embolism (n=1) and acute coronary event (n=1). Deaths on the placebo arm resulted from sepsis (n=1) and malignant disease (n=1).

The incidence of common adverse reactions in GLIADEL Wafer-treated patients is listed in Table 1. The incidence of local adverse reactions is shown in Table 2.

| Table 1. Per-Patient Incidence of Adverse Reactions Occurring in GLIADEL Wafer-Treated Patients with Newly-Diagnosed High Grade Malignant Glioma (Study 1) (Between Arm Difference of ≥ 4 %) |

<table>
<thead>
<tr>
<th>BODY SYSTEM</th>
<th>GLIADEL Wafer</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=120</td>
<td>N=120</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>GASTRO-INTESTINAL DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Constipation</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arborescence</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Chest pain</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>INJURY, POISONING AND PRECEDURAL COMPLICATIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound healing abnormalities*</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>PSYCHIATRIC DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>16</td>
<td>10</td>
</tr>
</tbody>
</table>

*Included: (1) Fluid, CDS, or subdural fluid collection; (2) CSF leak; (3) Wound dehiscence, breakdown, or poor healing; and (4) Subgaleal or wound effusions (including yellow discharge at the incision)

| Table 2. Incidence of Local Adverse Reactions, Study 1* |

<table>
<thead>
<tr>
<th>Local Adverse Reactions</th>
<th>GLIADEL Wafer</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=120</td>
<td>N=120</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Intracranial hypertension</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral hematoma</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Brain abscess</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Brain cyst</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>23</td>
<td>19</td>
</tr>
</tbody>
</table>

*Not seen at baseline or worsened if present at baseline.
The incidence of seizures is shown in Table 4. The incidence of hydrocephalus, cerebral edema and intracranial hypertension is shown in Table 5.

### Table 4. Incidence of Seizures, Study 2

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>GLIADEL Wafer N=110</th>
<th>Placebo N=112</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with seizures</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>New or worsening seizures</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>Time to new or worsening seizures (days)*</td>
<td>Mean (SD)</td>
<td>26.09 (0.75)</td>
</tr>
<tr>
<td>Median</td>
<td>3.5</td>
<td>61.0</td>
</tr>
</tbody>
</table>

*Days from implantation to onset of first new or worsening seizure.

### Table 5. Hydrocephalus and Cerebral Edema, Study 2*

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>GLIADEL Wafer N=110</th>
<th>Placebo N=112</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocephalus</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

*Not seen at baseline or worsened if present at baseline.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

- **Risk Summary**
  - GLIADEL Wafer can cause fetal harm when administered to a pregnant woman. There have been no studies with GLIADEL Wafer; however, carmustine, the active component of GLIADEL Wafer, is embryotoxic and teratogenic in rats at exposures similar to exposures at the recommended human dose on a mg/m² basis.
  - GLIADEL Wafer can cause fetal malformations when dosed at a multiple of 1.3 times the recommended human dose. In male rats, carmustine caused testicular degeneration at intraperitoneal doses of 8 mg/kg/week for eight weeks. In human beings, the recommended dose of carmustine is about 10 mg/m²/day, given as an intravenous injection at doses lower than those delivered by GLIADEL Wafer at the recommended dose. There were increases in tumor incidence in all treated animals. Carmustine was mutagenic in vitro (Ames assay, human lymphoblastoid HGPRT assay) and clastogenic both in vivo (V79 hamster cell micronucleus assay) and in vivo (GCE assay in rodent brain tumors, mouse bone marrow micronucleus assay).

#### 8.2 Menstrual Periods

- Nausea and vomiting observed in the postmenopausal women may be related to systemic chemotherapy. Leukopenia, thrombocytopenia,jual, and anemia were more frequent in women receiving systemic chemotherapy.

#### 8.3 Nursing Mothers

- GLIADEL Wafers are biodegradable when implanted into the human brain. Wafer remnants may be observed on brain imaging scans or at re-operation. Wafer remnants were visible in 11 of 18 patients on CT scans obtained 49 days after implantation of GLIADEL Wafer. More than 70% of the copolymer degrades within three weeks. Wafer remnants have been present at re-operation and autopsy up to 232 days after GLIADEL Wafer implantation, and consistent mostly of wafer and monomeric components with minimal detectable carmustine present.

### 12 CLINICAL PHARMACOLOGY

#### 12.1 Mechanism of Action

- The clinical effects of GLIADEL Wafer include the release of cytotoxic concentrations of carmustine, a DNA and RNA alkylating agent, into the tumor resection cavity. Exposure to the aqueous environment of the resection cavity, the strychnine bonds in the copolymer are hydrolyzed, releasing carmustine, carboslophanosynprparpoyne, and sebacic acid into the surrounding brain tissue.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

- Carmustine caused testicular degeneration in animals at oral doses as high as 170 mg/kg/day. The average terminal half-life, clearance and steady-state volume of distribution were 32 minutes, 56 ml/min/kg and 3.25 L/kg, respectively. Approximately 20% of the intravenous 200 mg/m² dose of 1°C-carmustine was excreted in the urine over 96 hours and 9% was excreted as O2C. Carmustine degrades both spontaneously and metabolically.

### 14 CLINICAL STUDIES

#### 14.1 Newly-Diagnosed High-Grade Malignant Glioma

- Study 1 was a multicenter, double-blind, placebo-controlled, clinical trial in adult patients with newly-diagnosed high-grade malignant glioma. A total of 243 patients were randomized (1:1) to receive up to eight GLIADEL Wafers or matched placebo wafers following maximal tumor resection. Patients received post-operative radiation therapy (55-60 Gy delivered in 28 to 30 fractions over six weeks) starting three weeks after surgery. Patients with anaplastic oligodendroglioma also received systemic chemotherapy (6 cycles of PCI- lomustine 110 mg/m² day 1, procarbazine 60 mg/m² days 8-21, vincristine 1.4 mg/m² days 8 and 29).

- The population in Study 1 was 67% male, 97% white, the median age was 53 years (range: 21-72). Seventy percent had a Karnofsky performance status ≥ 70% and 71% had a Karnofsky performance status ≥ 40%.

- Efficacy results for patients randomized in Study 1 are summarized in Table 6 and Figure 6. Overall survival among all patients with newly diagnosed high grade glioma, the primary outcome measure, was prolonged in the GLIADEL arm. Overall survival in the subset of patients with glioblastoma multiforme, a secondary outcome measure, was not significantly prolonged.
14.2 Recurrent Glioblastoma Multiforme

Study 2 was a multicenter, double-blind, placebo-controlled, clinical trial in adult patients with recurrent malignant glioma. Patients were required to have had prior definitive external beam radiation therapy sufficient to disqualify them from additional radiation therapy. Following maximal tumor resection and confirmation of malignant glioma, a total of 222 patients were randomized (1:1) to receive a maximum of eight GLIADEL Wafers (n=110) or matched placebo wafers (n=112) positioned to cover the entire resection surface. All patients were eligible to receive chemotherapy which was withheld at least four weeks (six weeks for nitrosourea) prior to and two weeks after surgery. Patients were followed for up to 71 months.

The population in Study 2 was 64% male, 92% white, and had a median age of 49 years (range: 19-80). Sixty-five percent had a histologic subtype of glioblastoma multiforme, 26% had anaplastic astrocytoma or another anaplastic variant, 73% had a Karnofsky performance status ≥ 70, 53% had a Karnofsky performance status of ≥ 80%, 73% had only one prior surgery, and 46% had prior treatment with nitrosourea. Eighty-one percent of patients received 8 wafers and 96% received ≥ 6 wafers.

Survival and 6-month mortality rate in the subgroup of patients with recurrent glioblastoma multiforme, were exploratory outcome measures and are summarized in Table 7 and Figures 7 and 8. No survival prolongation was observed in patients with pathologic diagnoses other than glioblastoma multiforme. Study 2.

Table 7. Main efficacy outcome measures in patients with recurrent glioblastoma multiforme, Study 2.

<table>
<thead>
<tr>
<th>GLIOBLASTOMA MULTIFORME</th>
<th>GLIADEL Wafer</th>
<th>Placebo Wafer</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-Month Survival</td>
<td>n=72</td>
<td>n=73</td>
</tr>
<tr>
<td>Number of deaths, n (%)</td>
<td>32</td>
<td>47</td>
</tr>
<tr>
<td>6-month survival rate (%)</td>
<td>56%</td>
<td>36%</td>
</tr>
<tr>
<td>Gehan’s generalized Wilcoxon Test p-value</td>
<td>0.013**</td>
<td>0.015**</td>
</tr>
<tr>
<td>Overall Survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of deaths, n (%)</td>
<td>71 (99%)</td>
<td>72 (99%)</td>
</tr>
<tr>
<td>Median overall survival (95% CI) (months)</td>
<td>6.51 (5.32, 7.49)</td>
<td>4.63 (3.78, 5.52)</td>
</tr>
<tr>
<td>Log-Rank test p-value</td>
<td>0.181**</td>
<td>0.021**</td>
</tr>
<tr>
<td>Gehan’s generalized Wilcoxon Test p-value</td>
<td>0.015**</td>
<td>0.013**</td>
</tr>
</tbody>
</table>

*p-value not adjusted for multiple comparisons

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

GLIADEL Wafer is supplied in a single dose treatment box containing eight individually pouched wafers. Each wafer contains 7.7 mg of carmustine and is packaged in two aluminum foil laminate pouches. The inner pouch is sterile and is designed to maintain product sterility and protect the product from moisture. The outer pouch is a peelable overwrap. The outside surface of the outer pouch is not sterile.

NDC for single dose treatment box: 24338-050-08
Store GLIADEL Wafer at or below -20ºC (-4ºF).
Do not keep unopened foil pouches at ambient room temperature for more than six hours at a time for up to three cycles within a 30-day period.
GLIADEL Wafer is a cytotoxic drug and special handling and disposal procedures should be considered.

17 PATIENT COUNSELING INFORMATION

Seizures: Advise patients to report any new or change in their seizure activity [see Warnings and Precautions (5.1)].

Intracranial Hypertension: Advise patients to report severe headaches, nausea, vomiting or new onset visual disturbances [see Warnings and Precautions (5.2)].

Impaired Neurosurgical Wound Healing: Advise patients to report any evidence of wound dehiscence, fever or cerebrospinal fluid leak [see Warnings and Precautions (5.3)].

Menopausal: Advise patients to report symptoms of menopausal such as fever or stiff neck [see Warnings and Precautions (5.3)].

Embryo-Fetal Toxicity: Counsel patients on pregnancy planning and prevention. Advise females of reproductive potential to use effective contraception during treatment with GLIADEL [see Warnings and Precautions (5.6)].

Nursing Infants: Advise nursing mothers to discontinue nursing after GLIADEL WAFER implantation [see Use in Specific Populations (8.3)].

Manufactured by Eisai Inc.
Woodcliff Lake, NJ 07677
Distributed by Arbor Pharmaceuticals, LLC
Atlanta, GA 30328
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QL-79-01
202978 IN-1600