NOW APPROVED
for 1L HER2+ advanced GEA

ZIIHERA®
(zanidatamab-hrii)
50 mg/ml Injection for IV

The FIRST and ONLY dual HER2-targeted bispecific antibody + tislelizumab + CT regimen FDA-approved for adult patients with HER2+ advanced GEA, irrespective of PD-L1 status[1]

ZIIHERA (zanidatamab-hrii) 50 mg/mL is indicated:

- In combination with fluoropyrimidine- and platinum-containing chemotherapy and tislelizumab-jsgr, as first-line treatment for adult patients with HER2-positive (IHC 3+ or IHC 2+/ISH+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-authorized test.
- In combination with fluoropyrimidine- and platinum-containing chemotherapy, as first-line treatment for adult patients with HER2-positive (IHC 3+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-authorized test.

PRODUCT INFORMATION

How supplied[1]

Sterile, preservative free, white lyophilized powder

Description and coding

Description[1]	NDC (10-digit)[1,a]	NDC (11-digit)[a]	J Code[2]
1 single-dose vial	68727-950-01	68727-0950-01	J9276
Carton containing 2 single-dose vials	68727-950-02	68727-0950-02	J9276

Specialty distributors

BioCareSD®, Cencora, Cardinal Health™, McKesson

GPOs

ION Solutions, Onmark®, Unity Group, VitalSource™

CLICK FOR ORDERING INFORMATION

[a]Payers may require a 10-digit or 11-digit NDC. Both are provided for convenience.

See next page for dosing information and to request a clinical presentation.

1L=first-line; CT=chemotherapy; FDA=Food and Drug Administration; GEA=gastroesophageal adenocarcinoma; GPO=Group Purchasing Organization; HER2=human epidermal growth factor receptor 2; HER2+=human epidermal growth factor receptor 2-positive; IHC=immunohistochemistry; ISH=*in situ* hybridization; IV=intravenous; NDC=National Drug Code; PD-L1=programmed death-ligand 1.

IMPORTANT SAFETY INFORMATION

WARNING: DIARRHEA and EMBRYO-FETAL TOXICITY

- **ZIIHERA, in combination with fluoropyrimidine- and platinum-containing chemotherapy, with or without tislelizumab-jsgr, can cause severe diarrhea, including life threatening and fatal cases. Use antidiarrheal prophylaxis during the first cycle when ZIIHERA is given in combination with these drugs. Manage with antidiarrheals and supportive measures as clinically indicated. Interrupt, reduce the dose or discontinue ZIIHERA based on severity.**
- **Embryo-Fetal Toxicity: Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.**

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED WARNINGS and Medication Guide.

DOSING[1]

Recommended dose

ZIIHERA is administered as an IV infusion until disease progression or unacceptable toxicity

- **For patients weighing <70 kg:** 1,800 mg Q3W or 1,200 mg Q2W
- **For patients weighing ≥70 kg:** 2,400 mg Q3W or 1,600 mg Q2W
- For the recommended dosage of CT or tislelizumab to be administered in combination with ZIIHERA, refer to the respective Prescribing Information
- **NOTE:** When ZIIHERA is administered in combination with fluorouracil-containing regimens, administer fluorouracil as an IV infusion. Do NOT administer fluorouracil as an IV bolus due to the potential increase in diarrhea

If CT is discontinued for reasons other than disease progression, treatment with ZIIHERA and/or tislelizumab can continue until disease progression.

30-60 minutes prior to each administration of ZIIHERA, premedicate patients with acetaminophen, an antihistamine, and a corticosteroid. Administer loperamide 4 mg BID beginning on Day 1 and continue for at least 7 days during the first cycle of treatment.

If a planned dose of ZIIHERA is delayed or missed, administer the dose as soon as possible if 7 days or fewer have passed since the scheduled time.

If more than 7 days have passed since the planned dose, withhold ZIIHERA and resume on day 1 of the next cycle.

Recommended administration time: Decrease over time to 60 minutes

Infusion Duration	
1st	120 minutes
2nd	90 minutes, if previous infusion was well-tolerated
3rd+	60 minutes, if previous infusions were well-tolerated

To request a clinical presentation, please contact your Jazz Account Manager

First Name and Last Name	*Phone Number*	*Email*

BID=twice daily; Q2W=every 2 weeks; Q3W=every 3 weeks.

IMPORTANT SAFETY INFORMATION (CONT.)

Diarrhea

ZIIHERA can cause severe diarrhea.

When ZIIHERA is used in combination with fluoropyrimidine- and platinum-containing chemotherapy with or without tislelizumab-jsgr, severe, life threatening, and fatal cases of diarrhea can occur despite loperamide prophylaxis. The risk of severe and life threatening diarrhea is higher when ZIIHERA is administered with chemotherapy and tislelizumab-jsgr, with a higher risk in patients aged ≥ 65 years compared to younger patients. Advise patients to increase oral fluids, begin antidiarrheals, and notify their healthcare provider immediately if diarrhea occurs.

Administer antidiarrheal prophylaxis with loperamide in cycle 1 for all patients receiving ZIIHERA in combination with fluoropyrimidine- and platinum-containing chemotherapy with or without tislelizumab-jsgr. Begin loperamide at the first loose stool when ZIIHERA is administered in combination with chemotherapy. Administer fluids, electrolytes, and additional antidiarrheal agents as necessary. Before modifying the dose of ZIIHERA, evaluate, modify or discontinue drug(s) contributing to diarrhea in accordance with their respective prescribing information. Withhold, reduce the dose, or permanently discontinue ZIIHERA based on severity.

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IMPORTANT SAFETY INFORMATION (CONT.)

Diarrhea (cont.)
If treating patients with ZIIHERA in combination with FOLFOX, do not administer the fluorouracil bolus.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr

Diarrhea was reported in 85% of 330 patients in clinical studies, including Grade 4 (2.1%), Grade 3 (24%), and Grade 2 (31%) events. Fatal outcomes resulting from diarrhea occurred in 1.5% of patients. Diarrhea leading to dose reduction of ZIIHERA occurred in 10% of patients, and permanent discontinuation of ZIIHERA occurred in 3.9% of patients.

In cycle 1, diarrhea at Grade 4 severity occurred in 1.5% and Grade 3 severity occurred in 15% of patients despite use of loperamide prophylaxis. The median time to onset for cycle 1 diarrhea was 6 days and median time to resolution was 18 days.

ZIIHERA in combination with chemotherapy

Diarrhea was reported in 81% of 395 patients in clinical studies, including Grade 4 (1.3%), Grade 3 (20%) and Grade 2 (33%). Diarrhea leading to dose reduction of ZIIHERA occurred in 10% of patients, and permanent discontinuation of ZIIHERA occurred in 1.8% of patients.

In cycle 1, diarrhea at Grade 4 severity occurred in 0.8% and Grade 3 severity occurred in 14% of patients despite use of loperamide prophylaxis. The median time to onset for cycle 1 diarrhea was 6 days and median time to resolution was 18 days.

Embryo-Fetal Toxicity
Based on the mechanism of action, ZIIHERA can cause fetal harm when administered to a pregnant woman. There are no human or animal data on the use of ZIIHERA in pregnancy. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death.

Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception while receiving ZIIHERA and for 4 months following the last dose of ZIIHERA

Left Ventricular Dysfunction (LVD)
ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF).

Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions.

The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is < 50%.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr

LVEF decrease (an absolute decline in LVEF of > 10%, resulting in a final value of < 50%) was observed in 9% of 330 patients in clinical studies. LVD leading to permanent discontinuation of ZIIHERA was reported in 3% of patients. Fatal outcomes due to LVD occurred in one patient (0.3%). The median time to first occurrence of LVD was 6.9 months (range: 1.2 to 29.1 months). LVD resolved in 78% of patients.

ZIIHERA in combination with chemotherapy

LVEF decrease was observed in 5% of 395 patients. LVD leading to permanent discontinuation of ZIIHERA was reported in 1.0% of patients. The median time to first occurrence of LVD was 6.0 months (range: 1.4 to 15.0 months). LVD resolved in 70% of patients.

Infusion-Related Reactions
ZIIHERA can cause infusion-related reactions (IRRs).

Prior to each dose of ZIIHERA, administer premedication to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use.

If an IRR occurs, slow or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr

An IRR was reported in 22% of 330 patients in clinical studies, including Grade 4 (0.3%), Grade 3 (1.2%), and Grade 2 (16%) despite use of prophylaxis. IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.3% of patients. IRRs occurred on the first day of dosing in 17% of patients. Of all patients who experienced IRRs, 60% of reactions resolved within the first day.

ZIIHERA in combination with chemotherapy

An IRR was reported in 24% of 395 patients in clinical studies, including Grade 4 (0.3%), Grade 3 (1.5%), and Grade 2 (18%) despite use of prophylaxis. IRRs leading to permanent discontinuation of ZIIHERA were reported in 1.3% of patients. IRRs occurred on the first day of dosing in 22% of patients. Of all patients who experienced IRRs, 83% of reactions resolved within the first day.

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IMPORTANT SAFETY INFORMATION (CONT.)

Adverse Reactions

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr

Serious adverse reactions occurred in 59% of 294 patients in HERIZON-GEA-01. Serious adverse reactions in > 2% of patients included diarrhea (17%), IRR (5%), vomiting (4.8%), hypokalemia (4.4%), acute kidney injury (3.7%), pneumonia (3.7%), nausea (2.4%), decreased appetite (2.4%), and anemia (2.4%). Fatal adverse reactions occurred in 2.4% of patients and included acute kidney injury (N=2), cardiac failure, diarrhea, dehydration, hypovolemic shock and intestinal obstruction (all N=1).

Permanent discontinuation of ZIIHERA occurred in 13% of patients. Adverse reactions that resulted in permanent discontinuation of ZIIHERA in ≥ 1% of patients included diarrhea (4.4%) and ejection fraction decreased (2.7%).

The most common adverse reactions (≥ 20%) were diarrhea (83%), nausea (56%), decreased appetite (46%), vomiting (44%), hypokalemia (39%), fatigue (37%), rash (36%), peripheral neuropathy (27%), and IRR (25%).

ZIIHERA in combination with chemotherapy

Serious adverse reactions occurred in 49% of 305 patients in HERIZON-GEA-01. Serious adverse reactions in > 2% of patients included diarrhea (11%), vomiting (3.3%), decreased appetite (2.6%), pneumonia (2.6%), sepsis (2.6%), hypokalemia (2.3%), and nausea (2.3%).

Permanent discontinuation of ZIIHERA occurred in 10% of patients. Adverse reactions that resulted in permanent discontinuation of ZIIHERA in ≥ 1% of patients included ejection fraction decreased (2.0%), IRR (1.6%), and diarrhea (1.6%).

The most common adverse reactions (≥ 20%) were diarrhea (79%), nausea (54%), vomiting (44%), decreased appetite (40%), fatigue (36%), hypokalemia (33%), peripheral neuropathy (32%), IRR (25%), and rash (22%).

Pediatric Use

Safety and efficacy of ZIIHERA have not been established in pediatric patients.

Geriatric Use

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr

Of 302 patients randomized to ZIIHERA in combination with chemotherapy and tislelizumab-jsgr in HERIZON-GEA-01, there were 139 (46%) patients aged ≥ 65 years. One hundred and six (35%) were aged 65-74 years and 33 (11%) were aged ≥ 75 years.

There was a higher incidence of Grade ≥ 3 adverse reactions observed in patients aged ≥ 65 years (87%) as compared to younger patients (80%). The incidence of Grade 3 or 4 diarrhea was higher in patients aged ≥ 65 years (32%) compared to younger patients (20%).

There was an increased incidence of fatal adverse reactions in patients aged ≥ 65 years (4.4%); including acute kidney injury (N=2), cardiac failure, dehydration, hypovolemic shock and intestinal obstruction (all N=1), compared to younger patients (0.6%), including diarrhea (N=1).

ZIIHERA in combination with chemotherapy

Of 304 patients randomized to ZIIHERA in combination with chemotherapy in HERIZON-GEA-01, there were 130 (43%) patients aged ≥ 65 years. One hundred (33%) were aged 65-74 years and 30 (10%) were aged ≥ 75 years.

No overall differences in safety were observed between patients aged ≥ 65 years and younger adult patients.

Please see full Prescribing Information, including BOXED WARNINGS and Medication Guide.

For more information about ZIIHERA, visit www.ZIIHERAhcp.com.

References: 1. ZIIHERA® (zanidatamab-hrii) Prescribing Information. Jazz Pharmaceuticals, Inc. **2.** CMS website. Centers for Medicare & Medicaid Services (CMS) Healthcare Common Procedure Coding System (HCPCS) Application Summaries and Coding Determinations. First quarter, 2025 coding cycle. www.cms.gov/files/document/2025-hcpcs-application-summary-quarter-1-2025-drugs-and-biologicals.pdf. April 7, 2025. Accessed April 3, 2026.

Jazz Pharmaceuticals

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