

# **INQOVI- cedazuridine and decitabine tablet, film coated**

## **Taiho Pharmaceutical Co., Ltd.**

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### **HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

**INQOVI® (decitabine and cedazuridine) tablets, for oral use**  
**Initial U.S. Approval: 2020**

### **INDICATIONS AND USAGE**

INQOVI is a combination of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor, indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. (1)

### **DOSAGE AND ADMINISTRATION**

- The recommended dosage of INQOVI is 1 tablet (35 mg decitabine and 100 mg cedazuridine) taken orally once daily on Days 1 through 5 of each 28-day cycle. (2.2)
- Take INQOVI on an empty stomach. (2.2)

### **DOSAGE FORMS AND STRENGTHS**

Tablets: 35 mg decitabine and 100 mg cedazuridine. (3)

### **CONTRAINDICATIONS**

None. (4)

### **WARNINGS AND PRECAUTIONS**

- **Myelosuppression:** Fatal and serious myelosuppression and infectious complications can occur. Obtain complete blood cell counts prior to initiation of INQOVI, prior to each cycle, and as clinically indicated to monitor for response and toxicity. Delay the next cycle and resume at the same or reduced dose as recommended. (2.3, 5.1)
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.2, 8.1, 8.3)

### **ADVERSE REACTIONS**

Most common adverse reactions (incidence  $\geq$  20%) are fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and transaminase increased. The most common Grade 3 or 4 laboratory abnormalities ( $\geq$  50%) were leukocytes decreased, platelet count decreased, neutrophil count decreased, and hemoglobin decreased. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Taiho Oncology, Inc. at 1-844-878-2446 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### **DRUG INTERACTIONS**

Drugs Metabolized by Cytidine Deaminase: Avoid coadministration with INQOVI. (7)

### **USE IN SPECIFIC POPULATIONS**

- **Lactation:** Advise not to breastfeed. (8.2)
- **Infertility:** Can impair fertility. (8.3)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

**Revised: 3/2022**

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## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

INQOVI is indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Important Administration Information

Do NOT substitute INQOVI for an intravenous decitabine product within a cycle.

Consider administering antiemetics prior to each dose to minimize nausea and vomiting [see *Adverse Reactions (6.1)*].

### 2.2 Recommended Dosage

The recommended dosage of INQOVI is 1 tablet (containing 35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity. A complete or partial response may take longer than 4 cycles.

Instruct patients of the following:

- Take INQOVI at the same time each day.
- Swallow tablets whole. Do not cut, crush, or chew tablets.
- Do not consume food 2 hours before and 2 hours after each dose.
- Take one tablet a day for 5 days in each cycle. If the patient misses a dose within 12 hours of the time it is usually taken, instruct patients to take the missed dose as soon as possible and then to resume the normal daily dosing schedule. Extend the dosing period by one day for every missed dose to complete 5 daily doses for each cycle.
- Do not take an additional dose if vomiting occurs after INQOVI administration but continue with the next schedule dose.

INQOVI is a hazardous drug. Follow applicable special handling and disposal procedures.<sup>1</sup>

### 2.3 Monitoring and Dosage Modifications for Adverse Reactions

#### Hematologic Adverse Reactions

Obtain complete blood cell counts prior to initiating INQOVI and before each cycle. Delay the next cycle if absolute neutrophil count (ANC) is less than 1,000/ $\mu$ L and platelets are less than 50,000/ $\mu$ L in the absence of active disease. Monitor complete blood cell counts until ANC is 1,000/ $\mu$ L or greater and platelets are 50,000/ $\mu$ L or greater [see *Warnings and Precautions (5.1)*].

- If hematologic recovery occurs (ANC at least 1,000/ $\mu$ L and platelets at least 50,000/ $\mu$ L) within 2 weeks of achieving remission, continue INQOVI at the same dose.
- If hematologic recovery does not occur (ANC at least 1,000/ $\mu$ L and platelets at least 50,000/ $\mu$ L) within 2 weeks of achieving remission,
  - Delay INQOVI for up to 2 additional weeks AND
  - Resume at a reduced dose by administering INQOVI on Days 1 through 4. Consider further dose reductions in the order listed in Table 1 if myelosuppression persists after a dose reduction. Maintain or increase dose in subsequent cycles as clinically indicated.

**Table 1: Recommended INQOVI Dose**

## Reductions for Myelosuppression

Dose Reduction	Dosage
First	1 tablet orally once daily on Days 1 through 4
Second	1 tablet orally once daily on Days 1 through 3
Third	1 tablet orally once daily on Days 1, 3 and 5

Manage persistent severe neutropenia and febrile neutropenia with supportive treatment [see *Warnings and Precautions (5.1)*].

### Non-Hematologic Adverse Reactions

Delay the next cycle for the following non-hematologic adverse reactions and resume at the same or reduced dose upon resolution:

- Serum creatinine 2 mg/dL or greater
- Serum bilirubin 2 times upper limit of normal (ULN) or greater
- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) 2 times ULN or greater
- Active or uncontrolled infection

## 3 DOSAGE FORMS AND STRENGTHS

INQOVI tablets contain 35 mg decitabine and 100 mg cedazuridine. The tablets are biconvex, oval-shaped, film-coated, red and debossed with “H35” on one side.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Myelosuppression

Fatal and serious myelosuppression can occur with INQOVI. Based on laboratory values, new or worsening thrombocytopenia occurred in 82% of patients, with Grade 3 or 4 occurring in 76%. Neutropenia occurred in 73% of patients, with Grade 3 or 4 occurring in 71%. Anemia occurred in 71% of patients, with Grade 3 or 4 occurring in 55%. Febrile neutropenia occurred in 33% of patients, with Grade 3 or 4 occurring in 32%.

Myelosuppression (thrombocytopenia, neutropenia, anemia, and febrile neutropenia) is the most frequent cause of INQOVI dose reduction or interruption, occurring in 36% of patients. Permanent discontinuation due to myelosuppression (febrile neutropenia) occurred in 1% of patients. Myelosuppression and worsening neutropenia may occur more frequently in the first or second treatment cycles and may not necessarily indicate progression of underlying MDS.

Fatal and serious infectious complications can occur with INQOVI. Pneumonia occurred in 21% of patients, with Grade 3 or 4 occurring in 15%. Sepsis occurred in 14% of

patients, with Grade 3 or 4 occurring in 11%. Fatal pneumonia occurred in 1% of patients, fatal sepsis in 1%, and fatal septic shock in 1% [see *Adverse Reactions (6.1)*].

Obtain complete blood cell counts prior to initiation of INQOVI, prior to each cycle, and as clinically indicated to monitor response and toxicity. Administer growth factors and anti-infective therapies for treatment or prophylaxis as appropriate. Delay the next cycle and resume at the same or reduced dose as recommended [see *Dosage and Administration (2.3)*].

## **5.2 Embryo-Fetal Toxicity**

Based on findings from human data, animal studies, and its mechanism of action, INQOVI can cause fetal harm when administered to a pregnant woman. In nonclinical studies with decitabine in mice and rats, decitabine was teratogenic, fetotoxic, and embryotoxic at doses less than the recommended human dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with INQOVI and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with INQOVI and for 3 months after the last dose [see *Use in Specific Populations (8.1, 8.3)*].

## **6 ADVERSE REACTIONS**

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Myelosuppression [see *Warnings and Precautions (5.1)*]

### **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely variable conditions, adverse event rates observed in clinical trials of a drug cannot be directly compared with rates of clinical trials of another drug and may not reflect the rates observed in practice.

#### Myelodysplastic Syndrome and Chronic Myelomonocytic Leukemia

The safety of INQOVI was evaluated in a pooled safety population that includes patients enrolled in Study ASTX727-01-B and Study ASTX727-02 [see *Clinical Studies (14)*].

Patients were randomized to receive INQOVI (35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 in Cycle 1 and decitabine 20 mg/m<sup>2</sup> intravenously on Days 1 through 5 in Cycle 2, or the reverse sequence, and then INQOVI (35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 of each 28-day cycle in Cycles 3 and beyond. Patients were allowed to have one prior cycle of decitabine or azacitidine and there was no limit for body weight or surface area. Among the patients who received INQOVI, 61% of patients were exposed for 6 months or longer and 24% were exposed to INQOVI for greater than 1 year.

Serious adverse reactions occurred in 68% of patients who received INQOVI. Serious adverse reactions in > 5% of patients included febrile neutropenia (30%), pneumonia (14%), and sepsis (13%). Fatal adverse reactions occurred in 6% of patients. These included sepsis (1%), septic shock (1%), pneumonia (1%), respiratory failure (1%), and one case each of cerebral hemorrhage and sudden death.

Permanent discontinuation due to an adverse reaction occurred in 5% of patients who received INQOVI. The most frequent adverse reactions resulting in permanent discontinuation were febrile neutropenia (1%) and pneumonia (1%).

Dose interruptions due to an adverse reaction occurred in 41% of patients who received INQOVI. Adverse reactions requiring dosage interruptions in > 5% of patients who received INQOVI included neutropenia (18%), febrile neutropenia (8%), thrombocytopenia (6%), and anemia (5%).

Dose reductions due to an adverse reaction occurred in 19% of patients who received INQOVI. Adverse reactions requiring dosage reductions in > 2% of patients who received INQOVI included neutropenia (12%), anemia (3%), and thrombocytopenia (3%).

The most common adverse reactions ( $\geq 20\%$ ) were fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and transaminase increased. The most common Grade 3 or 4 laboratory abnormalities ( $\geq 50\%$ ) were leukocytes decreased, platelet count decreased, neutrophil count decreased, and hemoglobin decreased.

Table 2 summarizes the adverse reactions in the pooled safety population.

**Table 2: Adverse Reactions ( $\geq 10\%$ ) in Patients Who Received INQOVI in Pooled Safety Population**

Adverse Reactions	INQOVI Cycle 1 N=107		Intravenous Decitabine Cycle 1 N=106		INQOVI* All Cycles N=208	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
<b>General disorders and administration site conditions</b>						
Fatigue <sup>†</sup>	29	2	25	0	55	5
Hemorrhage <sup>‡</sup>	24	2	17	0	43	3
Edema <sup>§</sup>	10	0	11	0	30	0.5
Pyrexia	7	0	7	0	19	1
<b>Gastrointestinal disorders</b>						
Constipation <sup>¶</sup>	20	0	23	0	44	0
Mucositis <sup>#</sup>	18	1	24	2	41	4
Nausea	25	0	16	0	40	0.5
Diarrhea <sup>Ⓟ</sup>	16	0	11	0	37	1
Transaminase increased <sup>Ⓛ</sup>	12	1	3	0	21	3
Abdominal pain <sup>ⓐ</sup>	9	0	7	0	19	1
Vomiting	5	0	5	0	15	0
<b>Musculoskeletal and connective tissue disorders</b>						
Myalgia <sup>ⓔ</sup>	9	2	16	1	42	3
Arthralgia <sup>ⓓ</sup>	9	1	13	1	40	3
<b>Respiratory, thoracic, and mediastinal disorders</b>						

Dyspnea <sup>ø</sup>	17	3	9	3	38	6
Cough <sup>ý</sup>	7	0	8	0	28	0
<b>Blood &amp; lymphatic system disorders</b>						
Febrile neutropenia	10	10	13	13	33	32
<b>Skin and subcutaneous tissue disorders</b>						
Rash <sup>£</sup>	12	1	11	1	33	0.5
<b>Nervous system disorders</b>						
Dizziness <sup>¥</sup>	16	1	11	0	33	2
Headache <sup>CE</sup>	22	0	13	0	30	0
Neuropathy <sup>œ</sup>	4	0	8	0	13	0
<b>Metabolism and nutritional disorders</b>						
Decreased appetite	10	1	6	0	24	2
<b>Infections and infestations</b>						
Upper respiratory tract infection <sup>D</sup>	6	0	3	0	23	1
Pneumonia <sup>A</sup>	7	7	7	5	21	15
Sepsis <sup>B</sup>	6	6	2	1	14	11
Cellulitis <sup>C</sup>	4	1	3	2	12	5
<b>Investigations</b>						
Renal impairment <sup>D</sup>	9	0	8	1	18	0
Weight decreased	5	0	3	0	10	1
<b>Injury, poisoning, and procedural complications</b>						
Fall	4	0	1	0	12	1
<b>Psychiatric disorders</b>						
Insomnia	6	0	2	0	12	0.5
<b>Vascular disorders</b>						
Hypotension <sup>E</sup>	4	0	6	1	11	2
<b>Cardiac Disorders</b>						
Arrhythmia <sup>F</sup>	3	0	2	0	11	1

\* Includes adverse reactions that occurred during all cycles, including during treatment with 1 cycle of intravenous decitabine.

† Includes fatigue, asthenia, and lethargy

‡ Includes contusion, epistaxis, petechiae, hematuria, conjunctival hemorrhage, mouth hemorrhage, purpura, angina bullosa hemorrhagica, gingival bleeding, hematoma, hemoptysis, eye contusion, hemorrhagic diathesis, increased tendency to bruise, vaginal hemorrhage, abdominal wall hematoma, blood blister, bone contusion, catheter site bruise, ecchymosis, genital hemorrhage, intra-abdominal hematoma, oral mucosa hematoma, periorbital hemorrhage, procedural hemorrhage, pulmonary alveolar hemorrhage, retinal hemorrhage, scleral hemorrhage, thrombotic thrombocytopenic purpura, tongue hemorrhage, and vessel puncture site hemorrhage

§ Includes edema peripheral, peripheral swelling, swelling face, fluid overload, localized edema, face edema, edema, eye swelling, eyelid edema, fluid retention, periorbital swelling, scrotal edema, scrotal swelling, and swelling

¶ Includes constipation and feces hard

# Includes oropharyngeal pain, stomatitis, mouth ulceration, proctalgia, oral pain, gingivitis, oral disorder, gingival pain, colitis, glossodynia, mouth swelling, pharyngitis, proctitis, duodenitis, enteritis, gingival discomfort, gingival swelling, lip disorder, lip ulceration, mucosal ulceration, nasal ulcer, noninfective gingivitis, oral mucosal blistering, oral mucosal erythema, pharyngeal erythema, pharyngeal ulceration, tongue ulceration, and vulvitis

þ Includes diarrhea and feces soft

ß Includes alanine aminotransferase increased, aspartate aminotransferase increased, blood

- alkaline phosphatase increased, gamma-glutamyltransferase increased, liver function test increased, and transaminases increased
- à Includes abdominal pain, abdominal pain upper, abdominal pain lower, epigastric discomfort, and abdominal discomfort
  - è Includes myalgia, pain in extremity, muscle spasms, pain, musculoskeletal pain, non-cardiac chest pain, muscular weakness, musculoskeletal chest pain, flank pain, musculoskeletal stiffness, muscle strain, and musculoskeletal discomfort
  - ð Includes arthralgia, back pain, neck pain, joint stiffness, pain in jaw, joint swelling, bursitis, joint range of motion decreased, and joint injury
  - ø Includes dyspnea, dyspnea exertional, hypoxia, wheezing, chronic obstructive pulmonary disease, and tachypnoea
  - ý Includes cough and productive cough
  - £ Includes maculo-papular rash, rash, erythema, skin lesion, folliculitis, dermatitis, dermatitis acneiform, eczema, erythema multiforme, rash erythematous, seborrheic keratosis, skin ulcer, dermatitis allergic, dermatitis contact, eczema nummular, genital erythema, rash papular, rash pruritic, rash pustular, seborrheic dermatitis, skin exfoliation, skin irritation, stasis dermatitis, and ulcerative keratitis
  - ¥ Includes dizziness, vertigo, postural dizziness, and positional vertigo
  - ⌘ Includes headache, sinus pain, and sinus headache
  - œ Includes hypoesthesia, paresthesia, neuropathy peripheral, gait disturbance, peripheral sensory neuropathy, ataxia, balance disorder, brachial plexopathy, carpal tunnel syndrome, and radicular pain
  - Ð Includes upper respiratory tract infection, nasopharyngitis, sinusitis, and viral upper respiratory tract infection
  - A Includes pneumonia, pneumonitis, atypical pneumonia, and lung infection
  - B Includes sepsis, bacteremia, septic shock, endocarditis, pseudomonal bacteremia, and staphylococcal bacteremia
  - C Includes cellulitis, catheter site cellulitis, and infected bite
  - D Includes blood creatinine increased, acute kidney injury, blood urea increased, blood creatine increased, and renal failure
  - E Includes hypotension, blood pressure decreased, and cardiogenic shock
  - F Includes sinus tachycardia, atrial fibrillation, bradycardia, tachycardia, atrial flutter, sinus bradycardia, and conduction disorder

Clinically relevant adverse reactions in < 10% of patients who received INQOVI included:

- Acute febrile neutrophilic dermatosis (Sweet's syndrome) (1%)
- Tumor lysis syndrome (0.5%)

**Table 3: Select Laboratory Abnormalities (> 20%) Worsening from Baseline in Patients Who Received INQOVI in Pooled Safety Population**

Lab Abnormality*	INQOVI Cycle 1†		Intravenous Decitabine Cycle 1†		INQOVI All Cycles†	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
<b>Hematology</b>						
Leukocytes decreased	79	65	77	59	87	81
Platelet count decreased	79	65	77	67	82	76
Neutrophil count decreased	70	65	62	59	73	71
Hemoglobin decreased	58	41	59	36	71	55
<b>Chemistry</b>						



Glucose increased	19	0	11	0	54	7
Albumin decreased	22	1	20	0	45	2
Alkaline phosphatase increased	22	1	12	0	42	0.5
Glucose decreased	14	0	17	0	40	1
Alanine aminotransferase increased	13	1	7	0	37	2
Sodium decreased	9	2	8	0	30	4
Calcium decreased	16	0	12	0	30	2
Aspartate aminotransferase increased	6	1	2	0	30	2
Creatinine increased	7	0	8	0	29	0.5

\* Includes any lab abnormalities that worsened by one or more grades. Grade 3-4 includes any lab abnormalities that worsened to Grade 3 or Grade 4.

† The denominator used to calculate the rate varied from 103 to 107 for INQOVI Cycle 1, from 102 to 106 for Intravenous Decitabine Cycle and from 203 to 208 for INQOVI All Cycles based on the number of patients with a baseline value and at least one post-treatment value.

## 6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of intravenous decitabine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Blood and Lymphatic System Disorders:* Differentiation syndrome

*Respiratory, Thoracic and Mediastinal Disorders:* Interstitial lung disease

*Cardiac Disorders:* Cardiomyopathy

## 7 DRUG INTERACTIONS

### 7.1 Effects of INQOVI on Other Drugs

#### Drugs Metabolized by Cytidine Deaminase

Cedazuridine is an inhibitor of the cytidine deaminase (CDA) enzyme. Coadministration of INQOVI with drugs that are metabolized by CDA may result in increased systemic exposure with potential for increased toxicity of these drugs [see *Clinical Pharmacology (12.3)*]. Avoid coadministration of INQOVI with drugs that are metabolized by CDA.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

Based on findings from human data, animal studies, and its mechanism of action [see *Clinical Pharmacology (12.1)*], INQOVI can cause fetal harm when administered to a

pregnant woman. A single published case report of intravenous decitabine use throughout the first trimester during pregnancy describes adverse developmental outcomes, including major birth defects (structural abnormalities). In animal reproduction studies, intravenous administration of decitabine to pregnant mice and rats during organogenesis at doses approximately 7% of the recommended human dose on a body surface area ( $\text{mg}/\text{m}^2$ ) basis caused adverse developmental outcomes, including increased embryo-fetal mortality, alterations to growth, and structural abnormalities (see *Data*). Advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

## Data

### *Human Data*

There are no available data on INQOVI use in pregnant women.

A single published case report of intravenous decitabine pregnancy exposure in a 39-year-old woman with a hematologic malignancy described multiple structural abnormalities after 6 cycles of therapy in the 18th week of gestation. These abnormalities included holoprosencephaly, absence of nasal bone, mid-facial deformity, cleft lip and palate, polydactyly, and rocker-bottom feet. The pregnancy was terminated.

### *Animal Data*

No reproductive or developmental toxicity studies have been conducted with INQOVI or cedazuridine.

In utero exposure to decitabine causes temporal-related defects in the rat and/or mouse, which include growth suppression, exencephaly, defective skull bones, rib/sternabrae defects, phocomelia, digit defects, micrognathia, gastroschisis, and micromelia. Decitabine inhibits proliferation and increases apoptosis of neural progenitor cells of the fetal central nervous system (CNS) and induces palatal clefting in the developing murine fetus. Studies in mice have also shown that decitabine administration during osteoblastogenesis (Day 10 of gestation) induces bone loss in offspring.

In mice exposed to single intraperitoneal decitabine injections (0, 0.9 and 3.0  $\text{mg}/\text{m}^2$ , approximately 2% and 7% of the recommended daily clinical dose, respectively) over gestation Days 8, 9, 10 or 11, no maternal toxicity was observed, but reduced fetal survival was observed after treatment at 3  $\text{mg}/\text{m}^2$  and decreased fetal weight was observed at both dose levels. The 3  $\text{mg}/\text{m}^2$  dose elicited characteristic fetal defects for each treatment day, including supernumerary ribs (both dose levels), fused vertebrae and ribs, cleft palate, vertebral defects, hind-limb defects, and digital defects of fore- and hind-limbs.

In rats given a single intraperitoneal injection of 2.4, 3.6 or 6  $\text{mg}/\text{m}^2$  decitabine (approximately 5, 8, or 13% the daily recommended clinical dose, respectively) on gestation Days 9-12, no maternal toxicity was observed. No live fetuses were seen at any dose when decitabine was injected on gestation Day 9. A significant decrease in fetal survival and reduced fetal weight at doses greater than 3.6  $\text{mg}/\text{m}^2$  was seen when decitabine was given on gestation Day 10. Increased incidences of vertebral and rib

anomalies were seen at all dose levels, and induction of exophthalmia, exencephaly, and cleft palate were observed at 6.0 mg/m<sup>2</sup>. Increased incidence of foredigit defects was seen in fetuses at doses greater than 3.6 mg/m<sup>2</sup>. Reduced size and ossification of long bones of the fore-limb and hind-limb were noted at 6 mg/m<sup>2</sup>.

The effect of decitabine on postnatal development and reproductive capacity was evaluated in mice administered a single 3 mg/m<sup>2</sup> intraperitoneal injection (approximately 7% the recommended daily clinical dose) on Day 10 of gestation. Body weights of males and females exposed in utero to decitabine were significantly reduced relative to controls at all postnatal time points. No consistent effect on fertility was seen when female mice exposed in utero were mated to untreated males. Untreated females mated to males exposed in utero showed decreased fertility at 3 and 5 months of age (36% and 0% pregnancy rate, respectively). Follow up studies indicated that treatment of pregnant mice with decitabine on gestation Day 10 was associated with a reduced pregnancy rate resulting from effects on sperm production in the F1-generation.

## **8.2 Lactation**

### Risk Summary

There are no data on the presence of cedazuridine, decitabine, or their metabolites in human milk or on their effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with INQOVI and for 2 weeks after the last dose.

## **8.3 Females and Males of Reproductive Potential**

INQOVI can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

### Pregnancy Testing

Verify the pregnancy status in females of reproductive potential prior to initiating INQOVI.

### Contraception

#### *Females*

Advise females of reproductive potential to use effective contraception during treatment with INQOVI and for 6 months after the last dose.

#### *Males*

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with INQOVI and for 3 months after the last dose [*see Nonclinical Toxicology (13.1)*].

### Infertility

Based on findings of decitabine and cedazuridine in animals, INQOVI may impair male fertility [*see Nonclinical Toxicology (13.1)*]. The reversibility of the effect on fertility is unknown.

## **8.4 Pediatric Use**

The safety and effectiveness of INQOVI have not been established in pediatric patients.

## 8.5 Geriatric Use

Of the 208 patients in clinical studies who received INQOVI, 75% were age 65 years and older, while 36% were age 75 years and older. No overall differences in safety or effectiveness were observed between patients age 65 years and older, 75 years and older, and younger patients.

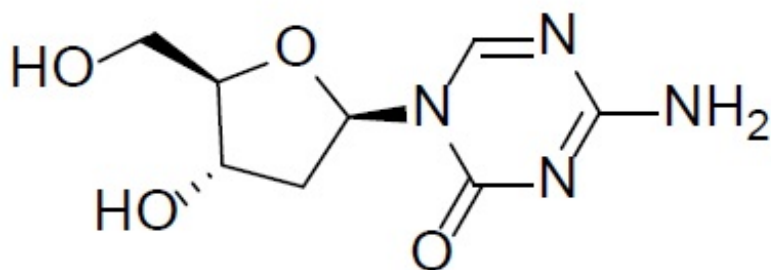
## 8.6 Renal Impairment

No dosage modification of INQOVI is recommended for patients with mild or moderate renal impairment (creatinine clearance [CLcr] of 30 to 89 mL/min based on Cockcroft-Gault). Due to the potential for increased adverse reactions, monitor patients with moderate renal impairment (CLcr 30 to 59 mL/min) frequently for adverse reactions. INQOVI has not been studied in patients with severe renal impairment (CLcr 15 to 29 mL/min) or end-stage renal disease (ESRD: CLcr <15 mL/min) [see *Clinical Pharmacology (12.3)*].

## 11 DESCRIPTION

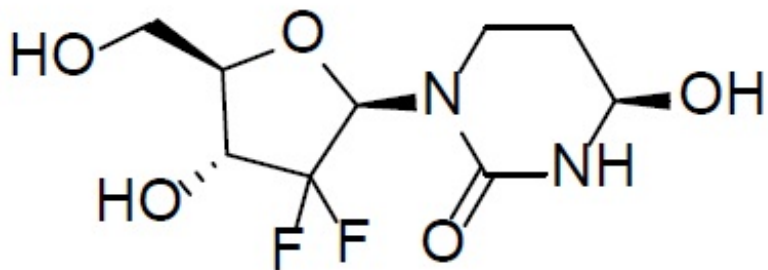
### Decitabine

Decitabine is a nucleoside metabolic inhibitor. Decitabine is a white to off-white solid with the molecular formula of  $C_8H_{12}N_4O_4$  and a molecular weight of 228.21 daltons. Its international union of pure and applied chemistry (IUPAC) chemical name is 4-amino-1-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2(1H)-one and it has the following structural formula:



### Cedazuridine

Cedazuridine is a cytidine deaminase inhibitor. Cedazuridine is a white to off-white solid with the molecular formula of  $C_9H_{14}F_2N_2O_5$  and a molecular weight of 268.21 daltons. Its IUPAC chemical name is (4R)-1-[(2R,4R,5R)-3,3-difluoro-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-4-hydroxy-1,3-diazinan-2-one and it has the following structural formula:



## INQOVI

INQOVI (decitabine and cedazuridine) tablets, for oral use contain 35 mg decitabine and 100 mg cedazuridine. The tablets are biconvex, oval-shaped, film-coated, red and debossed with “H35” on one side. Each film-coated tablet contains the following inactive ingredients: lactose monohydrate, hypromellose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate. The film coating material contains polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and iron oxide red.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

Decitabine is a nucleoside metabolic inhibitor that is believed to exert its effects after phosphorylation and direct incorporation into DNA and inhibition of DNA methyltransferase, causing hypomethylation of DNA and cellular differentiation and/or apoptosis. Decitabine inhibits DNA methylation in vitro, which is achieved at concentrations that do not cause major suppression of DNA synthesis. Decitabine-induced hypomethylation in cancer cells may restore normal function to genes that are critical for the control of cellular differentiation and proliferation. In rapidly dividing cells, the cytotoxicity of decitabine may also be attributed to the formation of covalent adducts between DNA methyltransferase and decitabine incorporated into DNA. Non-proliferating cells are relatively insensitive to decitabine.

Cytidine deaminase (CDA) is an enzyme that catalyzes the degradation of cytidine, including the cytidine analog decitabine. High levels of CDA in the gastrointestinal tract and liver degrade decitabine and limit its oral bioavailability. Cedazuridine is a CDA inhibitor. Administration of cedazuridine with decitabine increases systemic exposure of decitabine.

### **12.2 Pharmacodynamics**

Decitabine induced hypomethylation both in vitro and in vivo. In patients administered the recommended dosage of INQOVI, the maximum change from baseline in the long interspersed nucleotide elements-1 (LINE-1) demethylation was observed at Day 8, with less than complete recovery of LINE-1 methylation to baseline at the end of the treatment cycle.

Based on the exposure-response analyses, a relationship between an increase in 5-day cumulative daily decitabine exposure and a greater likelihood of some adverse reactions

(e.g., any grade neutropenias, thrombocytopenia) was observed in clinical studies.

### 12.3 Pharmacokinetics

The pharmacokinetics of decitabine and cedazuridine following administration of INQOVI at the recommended dosage in patients with MDS and CMML are shown in Table 4.

The geometric mean ratio (GMR) of decitabine area under the curve (AUC) following the first dose of INQOVI compared to that of intravenous decitabine on Day 1 was 60% (90% confidence intervals (CI): 55, 65) in patients with MDS and CMML [see *Dosage and Administration (2.1)*]. The GMR of decitabine AUC following 5 consecutive once daily doses of INQOVI compared to that of intravenous decitabine on Day 5 was 106% (90% CI: 98, 114) and the GMR of the 5-day cumulative decitabine AUC following 5 consecutive once daily doses of INQOVI compared to that of intravenous decitabine was 99% (90% CI: 93, 106).

An approximately dose-proportional increase in peak concentrations ( $C_{max}$ ) and AUC over the dosing interval was observed for decitabine following administration of oral decitabine at 20 mg to 40 mg once daily (0.6 to 1.1 times the recommended dose) in combination with 100 mg oral cedazuridine, and for cedazuridine following administration of oral cedazuridine at 40 to 100 mg once daily (0.4 to 1.0 times the recommended dose) in combination with 20 mg oral decitabine.

**Table 4: Pharmacokinetics of the Components of INQOVI\***

Parameter	Decitabine	Cedazuridine
<u>General Information</u>		
With the recommended dosage of INQOVI for 5 consecutive days:		
5-day cumulative AUC, ng.hr/mL	851 (50%)	--
Day 1 AUC, ng.hr/mL	103 (55%)	2950 (49%)
Steady state AUC, ng.hr/mL	178 (53%)	3291 (45%)
Time to steady state, days	2	2
Accumulation ratio based on AUC	1.7 (42%)	1.1 (63%)
$C_{max}$ , ng/mL	145 (55%)	371 (52%)
<u>Absorption</u>		
Bioavailability	Cedazuridine increases oral decitabine exposure	20% (23%)
$T_{max}$ , hours <sup>†</sup>	1 (0.3 to 3.0)	3 (1.5 to 6.1)
<u>Distribution</u>		
V/F at steady state, L	417 (54%)	296 (51%)
Fraction unbound,	96% (4%) to 94% (2%) between 17	66% (6%) to 62% (2%) between 1000

in vitro	(27%) between 17 ng/mL to 342 ng/mL	ng/mL and 50000 ng/mL
<u>Elimination</u>		
Half-life at steady state <sup>†</sup> , hours	1.5 (27%)	6.7 (19%)
CL/F at steady state, L/hours	197 (53%)	30.3 (46%)
<u>Metabolism</u>		
Primary Pathways	Primarily by cytidine deaminase (CDA) and by physicochemical degradation	Conversion to epimer by physicochemical degradation
<u>Excretion</u> <sup>§</sup>		
Total (% unchanged)	--	46% (21%) in urine and 51% (27%) in feces

$C_{max}$ = maximum plasma concentration;  $AUC_{0-24h}$ =area under the plasma concentration-time curve from time zero to 24 hours; CV=coefficient of variation; SD=standard deviation;  $T_{max}$ = Time to maximum concentration; V/F=apparent volume of distribution; CL/F=apparent clearance

\* Mean (%CV)

† Median (range)

‡ Mean (SD)

§ Healthy subjects

### Specific Populations

Age (32 to 90 years), sex, and mild hepatic impairment (total bilirubin > 1 to 1.5 × ULN or AST > ULN) did not have an effect on the pharmacokinetics of decitabine or cedazuridine after dosing with INQOVI.

Decitabine exposure (AUC) increased with decreasing body surface area or body weight, and cedazuridine exposure increased with decreasing CLcr; however, body surface area (1.3 to 2.9 m<sup>2</sup>), body weight (41 to 158 kg), and mild to moderate renal impairment (CLcr 30 to 89 mL/min based on Cockcroft Gault) did not have a clinically meaningful effect on the pharmacokinetics of decitabine and cedazuridine after dosing with INQOVI.

The effects of moderate (total bilirubin > 1.5 to 3 × ULN and any AST) and severe hepatic impairment (total bilirubin > 3 × ULN and any AST) or severe renal impairment (CLcr 15 to <30 mL/min) and ESRD (CLcr <15 mL/min) on the pharmacokinetics of decitabine and cedazuridine are unknown.

### Drug Interaction Studies

#### *Clinical Studies*

Decitabine had no clinically meaningful effect on the pharmacokinetics of cedazuridine. Cedazuridine increased the exposure of decitabine.

The coadministration of INQOVI with proton pump inhibitors had no clinically meaningful effect on exposure to decitabine or cedazuridine.

## *In vitro Studies*

**CYP Enzymes:** Cedazuridine is not a substrate of cytochrome P450 (CYP) enzymes. Cedazuridine does not induce CYP1A, CYP2B6, CYP2C9, or CYP3A or inhibit CYP1A, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A.

**Transporter Systems:** Cedazuridine is not a substrate of P-glycoprotein (P-gp), MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OAPT1B3, OATP2B1, OCT1, or OCT2, and does not inhibit P-gp, BCRP, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, or OCT2.

## **13 NONCLINICAL TOXICOLOGY**

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

Carcinogenicity studies with decitabine, cedazuridine, or their combination have not been conducted.

INQOVI is genotoxic. Decitabine increased mutation frequency in L5178Y mouse lymphoma cells, and mutations were produced in an *E. coli* lac-I transgene in colonic DNA of decitabine-treated mice. Decitabine also caused chromosomal rearrangements in larvae of fruit flies. Cedazuridine was genotoxic in a reverse bacterial mutation assay (Ames assay) and in an in vitro chromosomal aberration study using human lymphocytes.

Fertility and repeat-dose toxicity studies in animals showed adverse outcomes on reproductive function and fertility. In male mice given intraperitoneal injections of 0.15, 0.3, or 0.45 mg/m<sup>2</sup> decitabine (approximately 0.3% to 1% the recommended clinical dose) 3 times a week for 7 weeks, testes weights were reduced, abnormal histology was observed, and significant decreases in sperm number were found at doses  $\geq$  0.3 mg/m<sup>2</sup>. In females mated to males dosed with  $\geq$  0.3 mg/m<sup>2</sup> decitabine, pregnancy rate was reduced, and preimplantation loss was significantly increased.

Decitabine was administered orally to rats at 0.75, 2.5, or 7.5 mg/kg/day in cycles of 5-days-on/23-days-off for a total of 90 days. Low testes and epididymis weights, abnormal histology, and reduced sperm number were observed at doses  $\geq$  0.75 mg/kg. The dose of 0.75 mg/kg resulted in exposures in animals that were approximately 3 times the exposure in patients at the recommended clinical dose based on AUC.

Cedazuridine was administered orally to mice at 100, 300, or 1,000 mg/kg/day in cycles of 7-days-on/21-days-off for a total of 91 days. Adverse findings in male and female reproductive organs were observed at the 1,000 mg/kg dose and included abnormal histology in the testes and epididymis, reduced sperm number, and abnormal histology in the ovary. The dose of 1,000 mg/kg/day resulted in exposures in animals that were approximately 108 times the exposure in patients at the recommended clinical dose. Adverse effects in male and female reproductive organs were reversible following a recovery period.

## **14 CLINICAL STUDIES**

### Study ASTX727-01-B

INQOVI was evaluated in Study ASTX727-01-B, an open-label, randomized, 2-cycle, 2-sequence crossover study (NCT02103478) that included 80 adult patients with MDS



(International Prognostic Scoring System [IPSS] Intermediate-1, Intermediate-2, or high-risk) or CMML. Patients were randomized 1:1 to receive INQOVI (35 mg decitabine and 100 mg cedazuridine) orally in Cycle 1 and decitabine 20 mg/m<sup>2</sup> intravenously in Cycle 2 or the reverse sequence. Both INQOVI and intravenous decitabine were administered once daily on Days 1 through 5 of the 28-day cycle. Starting with Cycle 3, all patients received INQOVI orally once daily on Days 1 through 5 of each 28-day cycle until disease progression or unacceptable toxicity. Randomization was stratified by IPSS risk level. Twelve (15%) of the 80 patients went on to stem cell transplantation following INQOVI treatment.

The baseline demographic and disease characteristics are shown in Table 5.

**Table 5: Demographics and Baseline Disease Characteristics for Study ASTX727-01-B**

<b>Characteristic</b>	<b>N=80</b>
<b>Age</b>	
Median (min, max) (years)	71 (32, 90)
<b>Sex (%)</b>	
Male	76
Female	24
<b>Race (%)</b>	
White	93
Black or African American	3
Asian	1
Other or Not Reported	4
<b>ECOG Performance Score (%)</b>	
0	44
1	48
2	9
<b>Disease Category / IPSS (%)</b>	
MDS INT-1	44
MDS INT-2	24
MDS High-Risk	11
CMML	21
<b>Prior HMA Therapy* (%)</b>	
Prior Azacitidine	4
Prior Decitabine	4
<b>Transfusion Dependence† (%)</b>	
RBC Transfusion Dependence	48
Platelet Transfusion Dependence	15

\* One cycle only, per the Exclusion Criteria.

† Defined as documentation of ≥ 2 units of transfusion within 56 days prior to the first day of study treatment.

Efficacy was established on the basis of complete response (CR) and the rate of conversion from transfusion dependence to transfusion independence. Efficacy results are shown in Table 6. The median follow-up time was 24.0 months (range: 12.0 to 28.8

months) and median treatment duration was 6.6 months (range < 0.1 to 27.9).

**Table 6: Efficacy Results in Patients with MDS or CMML from Study ASTX727-01-B**

<b>Efficacy Endpoint</b>	<b>INQOVI N=80</b>
Complete Response (%) (95% CI)	18 (10, 28)
Median Duration of CR - months (range)*	8.7 (1.1, 18.2)
Median Time to CR - months (range)	4.8 (1.7, 10.0)

\* From start of CR until relapse or death.

Among the 41 patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 20 (49%) became independent of RBC and platelet transfusions during any consecutive 56-day post-baseline period. Of the 39 patients who were independent of both RBC and platelet transfusions at baseline, 25 (64%) remained transfusion-independent during any consecutive 56-day post-baseline period.

#### Study ASTX727-02

INQOVI was evaluated in ASTX727-02, an open-label, randomized, 2-cycle, 2-sequence crossover study (NCT03306264) that included 133 adult patients with MDS or CMML, including all French-American-British (FAB) classification criteria and IPSS Intermediate-1, Intermediate-2, or high-risk prognostic scores. Patients were randomized 1:1 to receive INQOVI (35 mg decitabine and 100 mg cedazuridine) orally in Cycle 1 and decitabine 20 mg/m<sup>2</sup> intravenously in Cycle 2 or the reverse sequence. Both INQOVI and intravenous decitabine were administered once daily on Days 1 through 5 of the 28-day cycle. Starting with Cycle 3, all patients received INQOVI orally once daily on Days 1 through 5 of each 28-day cycle until disease progression or unacceptable toxicity. No stratification was performed. Twenty-seven (20%) of the 133 patients went on to stem cell transplantation following INQOVI treatment.

The baseline demographic and disease characteristics are shown in Table 7.

**Table 7: Demographics and Baseline Disease Characteristics for Study ASTX727-02**

<b>Characteristic</b>	<b>N=133</b>
<b>Age (years)</b>	
Median (min, max)	71 (44, 88)
<b>Sex (%)</b>	
Male	65
Female	35
<b>Race (%)</b>	
White	91
Black or African American	3
Asian	2

Other or Not Reported	4
<b>ECOG Performance Score (%)</b>	
0	41
1	59
<b>Disease Category / IPSS (%)</b>	
MDS INT-1	44
MDS INT-2	20
MDS High Risk	16
MDS Low Risk	8
CMML	12
<b>Prior HMA Therapy* (%)</b>	
Prior Azacitidine	5
Prior Decitabine	3
<b>Transfusion Dependence† (%)</b>	
RBC Transfusion Dependence	39
Platelet Transfusion Dependence	8

\* One cycle only, per the Exclusion Criteria.

† Defined as documentation of  $\geq 2$  units of transfusion within 56 days prior to the first day of study treatment.

The primary outcome measure was comparison of the 5-day cumulative decitabine AUC between INQOVI and intravenous decitabine [see *Clinical Pharmacology (12.3)*]. Efficacy was established on the basis of complete response (CR) and the rate of conversion from transfusion dependence to transfusion independence. Efficacy results are shown in Table 8. The median follow-up time was 12.6 months (range: 9.3 to 20.5) and median treatment duration was 8.2 months (range 0.2 to 19.7).

**Table 8: Efficacy Results in Patients with MDS or CMML from Study ASTX727-02**

<b>Efficacy Endpoints</b>	<b>INQOVI (N=133)</b>
Complete Response (%) (95% CI)	21 (15, 29)
Median Duration of CR - months (range)*	7.5 (1.6, 17.5)
Median Time to CR - months (range)	4.3 (2.1, 15.2)

\* From start of CR until relapse or death.

Among the 57 patients who were dependent on RBC and/or platelet transfusions at baseline, 30 (53%) became independent of RBC and platelet transfusions during any 56-day post-baseline period. Of the 76 patients who were independent of both RBC and platelet transfusions at baseline, 48 (63%) remained transfusion-independent during any 56-day post-baseline period.

## 15 REFERENCES

1. OSHA Hazardous Drugs. *OSHA*.  
<http://www.osha.gov/SLTC/hazardousdrugs/index.html>

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

### How Supplied

INQOVI tablets are biconvex, oval-shaped, film-coated, red, and debossed with “H35” on one side.

The tablets are packaged in blisters and supplied as follows:

- NDC: 64842-0727-9; 5 tablets in one blister card in a child-resistant carton

### Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Dispense medication in the original packaging.

INQOVI is a hazardous drug. Follow applicable special handling and disposal procedures.<sup>1</sup>

## **17 PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-approved patient labeling (Patient Information).

### Myelosuppression

Advise patients of the risk of myelosuppression and to report any symptoms of fever, infection, anemia, or bleeding to their healthcare provider as soon as possible. Advise patients for the need for laboratory monitoring [see *Warnings and Precautions (5.1)*].

### Embryo-Fetal Toxicity

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.2)*, *Use in Specific Populations (8.1)*].

Advise females of reproductive potential to use effective contraception during treatment with INQOVI and for 6 months after the last dose [see *Use in Specific Populations (8.3)*].

Advise males with female partners of reproductive potential to use effective contraception during treatment with INQOVI and for 3 months after the last dose [see *Use in Specific Populations (8.3)*, *Nonclinical Toxicology (13.1)*].

### Lactation

Advise women not to breastfeed during treatment with INQOVI and for 2 weeks after the last dose [see *Use in Specific Populations (8.2)*].

### Administration

Advise patients to take INQOVI at approximately the same time each day on an empty stomach. Instruct patients to avoid eating for at least 2 hours before and 2 hours after taking INQOVI. Advise patients on what to do when a dose is missed or vomited [see *Dosage and Administration (2.2)*].

### **Manufactured for:**

Otsuka Pharmaceutical Co., Ltd.

Japan

**Distributed by:**

Taiho Oncology, Inc.

Princeton, NJ 08540 USA

**PATIENT INFORMATION**  
**INQOVI® (IN KOE' VEE)**  
**(decitabine and cedazuridine)**  
**tablets**

**What is INQOVI?**

INQOVI is a prescription medicine used to treat adults with myelodysplastic syndromes (MDS), including chronic myelomonocytic leukemia (CMML). Your healthcare provider will determine if INQOVI can treat your type of MDS.

It is not known if INQOVI is safe or effective in children.

**Before taking INQOVI, tell your healthcare provider about all of your medical conditions, including if you:**

- have kidney problems
- have liver problems
- are pregnant or plan to become pregnant. INQOVI can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with INQOVI.

**Females who are able to become pregnant:**

- Your healthcare provider will check to see if you are pregnant before you start treatment with INQOVI.
- You should use effective birth control during treatment with INQOVI and for at least 6 months after your last dose of INQOVI.

**Males** with female partners who are able to become pregnant should use effective birth control during treatment with INQOVI and for 3 months after the last dose. Talk to your healthcare provider if you have questions about birth control options that are right for you.

- are breastfeeding or plan to breastfeed. It is not known if INQOVI passes into breast milk. Do not breastfeed during treatment with INQOVI and for 2 weeks after your last dose of INQOVI.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

**How should I take INQOVI?**

- Take INQOVI exactly as your healthcare provider tells you to.
- Do not change your dose or stop taking INQOVI unless your healthcare provider tells you to.
- Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking INQOVI if you get certain side effects.
- Take INQOVI one time a day at about the same time each day.
- Take INQOVI on an empty stomach. Do not eat for at least 2 hours before and 2 hours after taking INQOVI.
- Swallow INQOVI tablets whole. Do not cut, crush, or chew the tablet.

- If you miss a dose of INQOVI, take your dose as soon as possible if it is within 12 hours of your usual time. Then, continue taking INQOVI at your scheduled time. If you missed a dose by more than 12 hours, do not take additional doses to make up for the missed dose. Take your next scheduled dose on the following day at your usual time.
- If you vomit after taking a dose of INQOVI, do not take an additional dose. Take your next scheduled dose at your usual time.

### **What are the possible side effects of INQOVI?**

#### **INQOVI may cause serious side effects, including:**

- **Low blood cell counts.** Low blood counts (white blood cells, platelets, and red blood cells) are common with INQOVI but can also be serious and lead to infections that may be life-threatening. If your blood cell counts are too low, your healthcare provider may need to delay treatment with INQOVI, lower your dose of INQOVI, or in some cases give you a medicine to help treat low blood cell counts. Your healthcare provider may need to give you antibiotic medicines to prevent or treat infections or fever while your blood cell counts are low. Your healthcare provider will check your blood cell counts before you start treatment and regularly during treatment with INQOVI. **Call your healthcare provider right away if you get any of the following signs and symptoms of infection during treatment with INQOVI:**

- fever
- chills
- body aches
- bruising more easily than usual

#### **The most common side effects of INQOVI include:**

- low white blood cell count (leukopenia)
- low platelets in your blood (thrombocytopenia)
- low white blood cell count (neutropenia)
- low red blood cell count (anemia)
- tiredness
- constipation
- bleeding
- muscle pain
- pain or sores in your mouth or throat
- joint pain
- nausea
- shortness of breath
- diarrhea
- rash
- dizziness
- fever with low white blood cell count (febrile neutropenia)
- swelling of arms or legs
- headache
- cough
- decreased appetite
- upper respiratory tract infection
- pneumonia
- changes in liver function tests

INQOVI may affect fertility in men. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of INQOVI. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

#### **How should I store INQOVI?**

- Store INQOVI at room temperature between 68°F and 77°F (20°C and 25°C).
- Do not store INQOVI outside of the original blisters.
- Talk to your healthcare provider about how to safely throw away (dispose of) INQOVI.

**Keep INQOVI and all medicines out of the reach of children.**

**General information about the safe and effective use of INQOVI**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use INQOVI for a condition for which it was not prescribed. Do not give INQOVI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about INQOVI that is written for health professionals.

**What are the ingredients in INQOVI?**

**Active ingredients:** decitabine and cedazuridine

**Inactive ingredients:** lactose monohydrate, hypromellose, croscarmellose sodium, colloidal silicon dioxide and magnesium stearate. The film coating material contains polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and iron oxide red.

Manufactured for: Otsuka Pharmaceutical Co., Ltd., Japan

Distributed by: Taiho Oncology, Inc., Princeton, NJ 08540 USA

INQOVI is a registered trademark of Otsuka Pharmaceutical Company, Ltd.

For more information, go to [www.INQOVI.com](http://www.INQOVI.com) or call 1-844-878-2446.

This Patient Information has been approved by the  
U.S. Food and Drug Administration

Issued: 4/2022

**PRINCIPAL DISPLAY PANEL - 35 mg/100 mg Tablet Carton**

**NDC 64842-0727-9**

Rx Only

**INQOVI®  
(decitabine and cedazuridine) tablets**

**35 mg/100 mg per tablet**

**CAUTION: Hazardous Agent**

**One Blister card  
containing 5 tablets**

**TAIHO  
ONCOLOGY, INC.**

NDC 64842-0727-9

Rx Only

# INQOVI<sup>®</sup>

(decitabine and cedazuridine)  
tablets

**35 mg/100 mg per tablet**

**CAUTION: Hazardous Agent**



One Blister card  
containing 5 tablets

OPEN HERE

NDC 64842-0727-9

Rx Only

# INQOVI<sup>®</sup>

(decitabine and cedazuridine)  
tablets

**35 mg/100 mg per tablet**

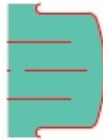
**CAUTION: Hazardous Agent**



One Blister card  
containing 5 tablets

Use thumb to push the button gently,  
and hold button.

While holding the button down,  
pull out card.

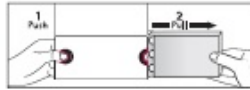


**1. Push and Hold**

**2. Pull**



To Open



Recommended Dosage: See Prescribing Information.  
Store at 20° to 25°C (68° to 77°F); excursions are permitted from  
15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].  
Dispense in the original packaging.  
Dispose of unused tablets in accordance with local requirements.  
Do not crush, cut or chew tablets. Tablets must be swallowed whole.

Each tablet contains:  
Decitabine ..... 35 mg and  
Cedazuridine ..... 100 mg

Manufactured for:  
Otsuka Pharmaceutical Co., Ltd.  
Japan  
Distributed by:  
Taiho Oncology, Inc.  
Princeton, NJ 08540 USA



GTIN: 01061619072794  
SN: 1246789043  
Exp: 2023 SEP 30  
Lot: 1704760

PS





## INQOVI

cedazuridine and decitabine tablet, film coated

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:64842-0727
<b>Route of Administration</b>	ORAL		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>CEDAZURIDINE</b> (UNII: 39IS23Q1EW) (CEDAZURIDINE - UNII:39IS23Q1EW)	CEDAZURIDINE	100 mg
<b>DECITABINE</b> (UNII: 776B62CQ27) (DECITABINE - UNII:776B62CQ27)	DECITABINE	35 mg

### Inactive Ingredients

Ingredient Name	Strength
<b>LACTOSE MONOHYDRATE</b> (UNII: EWQ57Q8I5X)	
<b>HYPROMELLOSE, UNSPECIFIED</b> (UNII: 3NXW29V3WO)	
<b>CROSCARMELLOSE SODIUM</b> (UNII: M28OL1HH48)	
<b>SILICON DIOXIDE</b> (UNII: ETJ7Z6XBU4)	
<b>MAGNESIUM STEARATE</b> (UNII: 70097M6I30)	
<b>POLYVINYL ALCOHOL, UNSPECIFIED</b> (UNII: 532B59J990)	
<b>TITANIUM DIOXIDE</b> (UNII: 15FIX9V2JP)	
<b>POLYETHYLENE GLYCOL, UNSPECIFIED</b> (UNII: 3WJQ0SDW1A)	
<b>TALC</b> (UNII: 7SEV7J4R1U)	
<b>FERRIC OXIDE RED</b> (UNII: 1K09F3G675)	

### Product Characteristics

<b>Color</b>	RED	<b>Score</b>	no score
<b>Shape</b>	OVAL	<b>Size</b>	14mm
<b>Flavor</b>		<b>Imprint Code</b>	H35
<b>Contains</b>			

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64842-0727-9	1 in 1 CARTON	08/25/2020	
1		5 in 1 BLISTER PACK; Type 0: Not a Combination Product		

**Marketing Information**

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA212576	07/07/2020	

**Labeler** - Taiho Pharmaceutical Co., Ltd. (690548730)

Revised: 5/2022

Taiho Pharmaceutical Co., Ltd.