FULL PRESCRIBING INFORMATION

INQOVI® Film-Coated Tablet

35 mg Decitabine and 100 mg Cedazuridine

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.

2.3 Monitoring and Dosage Modifications for Adverse Reactions

Monitoring

- Obtain liver chemistries and serum creatinine prior to initiation of treatment and repeat if liver/renal toxicities are suspected.

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/µL and platelets are less than 50,000/µL in the absence of active disease. Monitor complete blood cell counts until ANC is 1,000/µL or greater and platelets are 50,000/µL or greater *[see Warnings and Precautions (5.1)]*.

- If hematologic recovery occurs (ANC at least 1,000/µL and platelets at least 50,000/µL) within 2 weeks of achieving remission, continue INQOVI at the same dose.
- If hematologic recovery does not occur (ANC at least 1,000/µL and platelets at least 50,000/µL) 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

Pregnancy.

Hypersensitivity to the active substance or to any of the excipients.

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)]*.

5.3 Haemorrhage

Serious bleeding-related treatment-emergent adverse events (TEAEs) have been reported with INQOVI due to severe thrombocytopenia. Gastrointestinal haemorrhage was reported in 6.7% including Grade ≥ 3 in 2.4%. Intracranial haemorrhage was reported in 1.9% including Grade ≥ 3 in 1.4%. Monitor patients receiving INQOVI closely for signs and symptoms of serious bleeding related adverse reactions.

5.4 Cardiovascular

Patients with a history of severe congestive heart failure or clinically unstable cardiac disease were excluded from clinical studies and therefore the safety and efficacy of INQOVI in these patients has not been established. Patients with history of severe congestive heart failure or clinically unstable cardiac disease should be closely monitored.

5.5 Interstitial Lung Disease

Interstitial lung disease (ILD) (including pulmonary infiltrates, organising pneumonia and pulmonary fibrosis) without signs of infectious aetiology were reported in patients receiving intravenous decitabine. Assess patients with acute onset or unexplained worsening of pulmonary symptoms to exclude ILD. If ILD is confirmed, initiate appropriate treatment.

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 (12)]*.

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^2 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 (≥ 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 (≥ 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 (≥ 10%) in Patients Who Received INQOVI in Pooled Safety Population

	INQOVI Cycle 1 N=107		**Intravenous Decitabine Cycle 1 N=106**		**INQOVI† All Cycles N=208**	
Adverse Reactions	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
General disorders and administration site conditions						
Fatigue[1]	29	2	25	0	55	5
Hemorrhage[2]	24	2	17	0	43	3
Edema[3]	10	0	11	0	30	0.5
Pyrexia	7	0	7	0	19	1
Gastrointestinal disorders						
Constipation[4]	20	0	23	0	44	0
Mucositis[5]	18	1	24	2	41	4
Nausea	25	0	16	0	40	0.5
Diarrhea[6]	16	0	11	0	37	1
Transaminase increased[7]	12	1	3	0	21	3
Abdominal pain[8]	9	0	7	0	19	1
Vomiting	5	0	5	0	15	0
Musculoskeletal and connective tissue disorders						
Myalgia[9]	9	2	16	1	42	3
Arthralgia[10]	9	1	13	1	40	3
Respiratory, thoracic, and mediastinal disorders						

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 (%)
Dyspnea[11]	17	3	9	3	38	6
Cough[12]	7	0	8	0	28	0
Blood & lymphatic system disorders						
Febrile neutropenia	10	10	13	13	33	32
Skin and subcutaneous tissue disorders						
Rash[13]	12	1	11	1	33	0.5
Nervous system disorders						
Dizziness[14]	16	1	11	0	33	2
Headache[15]	22	0	13	0	30	0
Neuropathy[16]	4	0	8	0	13	0
Metabolism and nutritional disorders						
Decreased appetite	10	1	6	0	24	2
Infections and infestations						
Upper respiratory tract infection[17]	6	0	3	0	23	1
Pneumonia[18]	7	7	7	5	21	15
Sepsis[19]	6	6	2	1	14	11
Cellulitis[20]	4	1	3	2	12	5
Investigations						
Renal impairment[21]	9	0	8	1	18	0
Weight decreased	5	0	3	0	10	1
Injury, poisoning, and procedural complications						
Fall	4	0	1	0	12	1
Psychiatric disorders						
Insomnia	6	0	2	0	12	0.5
Vascular disorders						
Hypotension[22]	4	0	6	1	11	2

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 (%)
Cardiac Disorders						
Arrhythmia[23]	3	0	2	0	11	1

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

1 Includes fatigue, asthenia, and lethargy

2 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

3 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

4 Includes constipation and feces hard

5 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

6 Includes diarrhea and feces soft

7 Includes alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, gamma-glutamyltransferase increased, liver function test increased, and transaminases increased

8 Includes abdominal pain, abdominal pain upper, abdominal pain lower, epigastric discomfort, and abdominal discomfort

9 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

10 Includes arthralgia, back pain, neck pain, joint stiffness, pain in jaw, joint swelling, bursitis, joint range of motion decreased, and joint injury

11 Includes dyspnea, dyspnea exertional, hypoxia, wheezing, chronic obstructive pulmonary disease, and tachypnoea

12 Includes cough and productive cough

13 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

14 Includes dizziness, vertigo, postural dizziness, and positional vertigo

15 Includes headache, sinus pain, and sinus headache

16 Includes hypoesthesia, paresthesia, neuropathy peripheral, gait disturbance, peripheral sensory neuropathy, ataxia, balance disorder, brachial plexopathy, carpal tunnel syndrome, and radicular pain

17 Includes upper respiratory tract infection, nasopharyngitis, sinusitis, and viral upper respiratory tract infection

18 Includes pneumonia, pneumonitis, atypical pneumonia, and lung infection

19 Includes sepsis, bacteremia, septic shock, endocarditis, pseudomonal bacteremia, and staphylococcal bacteremia

20 Includes cellulitis, catheter site cellulitis, and infected bite

21 Includes blood creatinine increased, acute kidney injury, blood urea increased, blood creatine increased, and renal failure

22 Includes hypotension, blood pressure decreased, and cardiogenic shock

23 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 (%)
Hematology						
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
Chemistry						
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.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext. 1079
Website: https://e-meso.pom.go.id/ADR

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 (10.3)]*. Avoid coadministration of INQOVI with drugs that are metabolized by CDA.

Gastric pH Modifying Enzymes

Cedazuridine is converted to its epimer prior to absorption and its bioavailability may be affected by gastric PH. Based on a population pharmacokinetic analysis, no effect on cedazuridine or decitabine PK was shown with gastric pH modifying drugs as long as they are not administered within 4 hours of Inqovi administration.

CYP Enzymes

Decitabine is not a substrate for P450 and did not inhibit or induce cytochrome P450 enzymes in vitro. Cedazuridine did not induce or inhibit CYP1A, CYP3A, CYP2B6 or CYP2C9 and did not inhibit CYP1A, CYP3A, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP2E1 enzymes; therefore, CYP450-mediated drug-drug interactions are unlikely with Inqovi.

Transporter Systems

Decitabine is a weak inhibitor of P-glycoprotein (P-gp), and cedazuridine is neither a substrate nor an inhibitor of transporters including P-gp, MDR1, BCRP, MATE and OAT, therefore, Inqovi is not expected to affect P-gp mediated transport of coadministered medicinal products.

Drug-Food Interactions

Inqovi should be taken with water on an empty stomach. The oral bioavailability of decitabine is decreased in the presence of food.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

INQOVI is contraindicated in pregnancy. Based on findings from human data, animal studies, and its mechanism of action *[see Clinical Pharmacology (10.1)]*, 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 (mg/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 18^{th} 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 mg/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 mg/m^2 and decreased fetal weight was observed at both dose levels. The 3 mg/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 mg/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 mg/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^2. Increased incidence of foredigit defects was seen in fetuses at doses greater than 3.6 mg/m^2. Reduced size and ossification of long bones of the fore-limb and hind-limb were noted at 6 mg/m^2.

The effect of decitabine on postnatal development and reproductive capacity was evaluated in mice administered a single 3 mg/m^2 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 (11.1)]*.

Infertility

Based on findings of decitabine and cedazuridine in animals, INQOVI may impair male fertility *[see Nonclinical Toxicology (11.1)]*. 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 (10.3)]*.

9 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies of the effects on the ability to drive or use machines have been performed. Patients should be advised that they may experience undesirable effects, such as fatigue and dizziness due to anaemia, during treatment. Therefore, caution should be recommended when driving a car or operating machines.

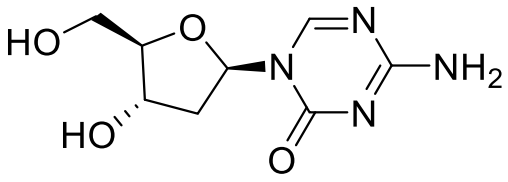
10 OVERDOSE

There is no known antidote for overdosage with INQOVI. Overdosage could cause increased myelosuppression, and neutropenia-related infections such as pneumonia and sepsis. For patients who experience overdose, closely monitor, and provide appropriate supportive treatment. For information on the management of overdose, contact your regional poison control centre.

11 DESCRIPTION

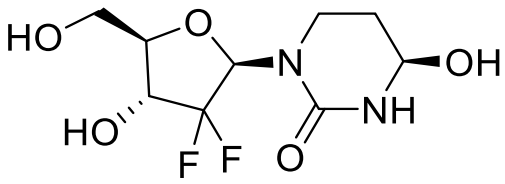
Decitabine

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-[(2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2(1*H*)-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 (4*R*)-1-[(2*R*,4*R*,5*R*)-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**
General Information		
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%)
Absorption		
Bioavailability	Cedazuridine increases oral decitabine exposure	20% (23%)
T_{max}, hours‡	1 (0.3 to 3.0)	3 (1.5 to 6.1)
Distribution		
V/F at steady state, L	417 (54%)	296 (51%)

Fraction unbound, in vitro	96% (4%) to 94% (2%) between 17 ng/mL to 342 ng/mL	66% (6%) to 62% (2%) between 1000 ng/mL and 50000 ng/mL
Elimination		
Half-life at steady state†, hours	1.5 (27%)	6.7 (19%)
CL/F at steady state, L/hours	197 (53%)	30.3 (46%)
Metabolism		
Primary Pathways	Primarily by cytidine deaminase (CDA) and by physicochemical degradation	Conversion to epimer by physicochemical degradation
Excretion§		
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)
† Mean (SD)
‡ Median (range)
§ 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^2), 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^2 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 ≥ 0.3 mg/m^2. In females mated to males dosed with ≥ 0.3 mg/m^2 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 ≥ 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^2 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

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

Characteristic	N=80
Prior Decitabine	4
Transfusion Dependence[†] (%)	
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

Efficacy Endpoint	INQOVI N=80
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^2 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

Characteristic	**N=133**
Age (years)	
Median (min, max)	71 (44, 88)
Sex (%)	
Male	65
Female	35
Race (%)	
White	91
Black or African American	3
Asian	2
Other or Not Reported	4
ECOG Performance Score (%)	
0	41
1	59
Disease Category / IPSS (%)	
MDS INT-1	44
MDS INT-2	20
MDS High Risk	16
MDS Low Risk	8
CMML	12
Prior HMA Therapy[*] (%)	
Prior Azacitidine	5
Prior Decitabine	3
Transfusion Dependence[†] (%)	
RBC Transfusion Dependence	39
Platelet Transfusion Dependence	8

[*] 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.

The primary outcome measure was comparison of the 5-day cumulative decitabine AUC between INQOVI and intravenous decitabine *[see Clinical Pharmacology (10.3)]*. 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

Efficacy Endpoints	**INQOVI (N=133)**
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 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 5 tablets in one blister card in a child-resistant carton

Storage and Handling

Store below 30°C Dispense medication in the original packaging.

INQOVI is a hazardous drug. Follow applicable special handling and disposal procedures.

16 PATIENT COUNSELING INFORMATION

Advise the patient to read the BPOM-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 (11.1)]*.

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)]*.

17 MARKETING AUTHORISATION HOLDER

PT Sydna Farma

Jl. RC Veteran No. 89, Kelurahan Bintaro, Kecamatan Pesanggrahan, Kota Jakarta Selatan, Provinsi DKI Jakarta, 12330

Under Authorization of:

Taiho Pharmaceutical Co., Ltd., Japan

18 MARKETING AUTHORISATION NUMBER(S)

Reg. No.: XXXXXXXXXXXXXXX

Box, 1 blister @ 5 film-coated tablets

19 MANUFACTURER

BSP Pharmaceuticals S.p.A.

Via Appia Km 65,561 (Loc. Latina Scalo) – 04013, Latina, Italy

20 DATE OF AUTHORISATION

16 June 2025

21 DATE OF REVISION OF THE TEXT

June 2025

HARUS DENGAN RESEP DOKTER

***Leaflet* kemasan: Informasi untuk pasien**

INQOVI

(35 mg Decitabine and 100 mg Cedazuridine)

Nama Obat	: **INQOVI**
Bentuk Sediaan	: Tablet Salut Selaput
Deskripsi	: Tablet salut selaput cembung, oval, salut selaput, merah dan tercantum “H35” pada satu sisi
Komposisi	: INQOVI Tablet Salut Selaput mengandung 35 mg decitabine dan 100 mg cedazuridine

Apa itu INQOVI dan apa kegunaannya?

INQOVI mengandung bahan aktif decitabine dan cedazuridine.

INQOVI adalah obat anti kanker dan bekerja dengan mencegah pertumbuhan sel kanker. INQOVI digunakan untuk mengobati *myelodysplastic syndromes* (MDS) atau *chronic myelomonocytic leukemia* (CMML) pada dewasa. Kedua penyakit ini adalah jenis kanker darah dimana sumsum tulang belakang tidak dapat bekerja dengan baik untuk menghasilkan sel darah yang dewasa. Hal ini menyebabkan tubuh kekurangan sel darah yang sehat.

Dokter Anda akan menentukan apakah INQOVI dapat mengobati tipe MDS Anda.

Bagaimana mengonsumsi INQOVI?

- Konsumsilah INQOVI tepat seperti yang diberitahukan oleh dokter Anda.
- Jangan mengubah dosis Anda atau menghentikan mengonsumsi INQOVI jika dokter Anda tidak memberitahukannya.
- Dokter Anda dapat menurunkan dosis obat Anda, menghentikan sementara, atau menghentikan permanen pemberian INQOVI jika Anda mendapat efek samping tertentu.
- Konsumsilah INQOVI satu kali sehari pada waktu yang sama setiap harinya.
- Konsumsilah INQOVI pada perut kosong. Jangan makan minimal 2 jam sebelum dan 2 jam sesudah meminum INQOVI.
- Telan tablet INQOVI dengan utuh. Tablet jangan dibelah, dihancurkan atau dikunyah

- Jika Anda lupa mengonsumsi INQOVI, minumlah dosis Anda sesegera mungkin jika masih dalam waktu 12 jam dari jadwal Anda meminum obat. Kemudian, lanjutkan mengonsumsi INQOVI sesuai jadwal Anda. Jika Anda lupa mengonsumsi INQOVI lebih dari 12 jam, jangan mengonsumsi dosis tambahan untuk menggantikan dosis yang terlewat. Konsumsi dosis selanjutnya pada hari berikutnya sesuai jadwal Anda.
- Jika Anda muntah setelah mengonsumsi INQOVI, jangan mengonsumsi dosis tambahan. Konsumsilah dosis selanjutnya sesuai jadwal Anda.

Sebelum mengonsumsi INQOVI, beritahu dokter Anda tentang semua kondisi kesehatan Anda, termasuk jika Anda:

- memiliki penyakit ginjal
- memiliki penyakit hati
    - Kelainan perdarahan. Kasus perdarahan serius telah dilaporkan pada pasien yang menerima INQOVI.
    - Jumlah sel darah yang rendah (trombosit, sel darah merah atau sel darah putih).
    - Penurunan jumlah darah sangat umum terjadi pada INQOVI dan dapat memburuk. Penurunan jumlah darah merupakan ciri khas dari penyakit Anda dan dapat diperbaiki dengan pengobatan. Dokter Anda akan menilai potensi manfaat dari pengobatan dibandingkan dengan risiko terjadinya infeksi atau gejala menyerupai flu. Infeksi serius dapat terjadi saat menggunakan INQOVI. Hal tersebut dapat menyebabkan kematian.
    - Penyakit paru. Kasus penyakit paru dilaporkan pada pasien yang mengonsumsi decitabine intravena.
    - Intoleransi terhadap laktosa yang berat. Hal ini dikarenakan INQOVI mengandung sejumlah kecil laktosa.
- sedang hamil atau merencanakan kehamilan. INQOVI dapat membahayakan janin Anda. Beritahu dokter Anda segera jika Anda hamil atau kemungkinan hamil selama pengobatan INQOVI.

Wanita yang dapat hamil:

- Dokter Anda akan memeriksa untuk melihat apakah Anda hamil sebelum memulai pengobatan dengan INQOVI.
- Anda harus menggunakan kontrasepsi dengan efektif selama pengobatan dengan INQOVI dan minimal 6 bulan setelah dosis terakhir INQOVI.

Pria yang memiliki pasangan wanita yang dapat hamil harus menggunakan kontrasepsi dengan efektif selama pengobatan dengan INQOVI dan minimal 3 bulan setelah dosis terakhir. Beritahu dokter Anda jika Anda memiliki pertanyaan mengenai pilihan kontrasepsi yang tepat bagi Anda.

- sedang menyusui atau mempunyai rencana untuk menyusui. Tidak diketahui apakah INQOVI dapat masuk ke dalam air susu. Jangan menyusui selama pengobatan dengan INQOVI dan selama 2 minggu setelah dosis terakhir INQOVI.

Beritahu dokter Anda mengenai semua pengobatan yang Anda konsumsi, termasuk obat resep, obat bebas, vitamin dan suplemen herbal. Ketahui obat yang Anda konsumsi. Simpan daftar obat Anda untuk ditunjukkan pada dokter dan apoteker Anda jika Anda menerima obat baru.

Pada keadaan apa Anda tidak diperbolehkan mengonsumsi obat ini?

Jangan mengonsumsi INQOVI jika:

- Anda memiliki alergi terhadap decitabine atau cedazuridine, atau salah satu bahan yang tercantum pada bagian akhir dari *leaflet* ini. Selalu periksa bahan-bahan tersebut untuk memastikan Anda dapat menggunakan obat ini
- Anda dalam kondisi hamil

Apa efek samping dari INQOVI?

INQOVI dapat menyebabkan efek samping serius, termasuk:

- **Jumlah sel darah yang rendah.** Jumlah sel darah yang rendah (sel darah putih, platelet, dan sel darah merah) adalah umum pada INQOVI namun dapat menjadi serius dan mengarah ke infeksi yang kemungkinan dapat mengancam nyawa. Jika

jumlah sel darah Anda terlalu rendah, dokter Anda mungkin perlu untuk menunda pengobatan dengan INQOVI, menurunkan dosis INQOVI, atau pada beberapa kasus memberikan Anda obat untuk mengobati jumlah sel darah yang rendah.

Dokter Anda mungkin perlu memberikan Anda obat antibiotik untuk mencegah atau mengobati infeksi atau demam saat jumlah sel darah Anda rendah. Dokter Anda akan memeriksa jumlah sel darah Anda sebelum Anda memulai pengobatan dan selama pengobatan menggunakan INQOVI secara rutin. **Hubungi dokter Anda segera jika Anda mengalami tanda dan gejala infeksi di bawah ini selama pengobatan menggunakan INQOVI:**

- demam
- mengigil
- pegal-pegal
- lebih mudah memar dari biasanya

Efek samping paling umum dari INQOVI termasuk:

- jumlah sel darah putih yang rendah (leukopenia)
- jumlah platelet darah yang rendah (trombositopenia)
- jumlah sel darah putih yang rendah (neutropenia)
- jumlah sel darah merah yang rendah (anemia)
- kelelahan
- konstipasi
- perdarahan
- nyeri otot
- nyeri atau sakit pada mulut atau tenggorokan
- nyeri sendi
- mual
- sesak napas
- diare
- kemerahan atau ruam
- pusing
- demam dengan jumlah sel darah putih yang rendah (febrile neutropenia)
- pembengkakan tangan atau kaki
- sakit kepala

- batuk
- penurunan nafsu makan
- infeksi saluran pernapasan atas
- pneumonia
- perubahan dalam tes fungsi hati

INQOVI dapat mempengaruhi kesuburan pada pria. Beritahu pada dokter Anda jika ini menjadi perhatian Anda.

Ini semua bukan keseluruhan efek samping dari INQOVI. Hubungi dokter Anda untuk saran pengobatan mengenai efek samping.

Bagaimana menyimpan INQOVI?

- Simpan di bawah suhu 30^{o}C
- Jangan menyimpan INQOVI tanpa blister aslinya.
- Bicarakan dengan dokter Anda mengenai bagaimana membuang INQOVI dengan aman.

Simpan INQOVI dan semua obat-obatan jauh dari jangkauan anak-anak.

Informasi umum mengenai keamanan dan efektifitas INQOVI

Jangan menggunakan INQOVI bila tidak diresepkan. Jangan memberikan INQOVI pada orang lain, bahkan jika mereka memiliki gejala yang sama dengan yang Anda miliki. Hal tersebut dapat membahayakan mereka. Anda dapat menanyakan pada apoteker atau dokter Anda mengenai informasi INQOVI yang ditulis untuk dokter.

Pelaporan Efek Samping

Jika Anda mengalami efek samping, hubungi dokter atau apoteker Anda. Hal ini termasuk kemungkinan adanya efek samping yang tidak tercantum pada *leaflet* ini. Dengan melaporkan efek samping kepada dokter Anda, Anda dapat membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

Menyetir dan Menggunakan Mesin

Saat menggunakan INQOVI, Anda mungkin merasa lemah, lelah, atau pusing. Sebelum mengemudikan kendaraan atau menggunakan mesin, tunggu beberapa saat untuk melihat bagaimana kondisi Anda setelah mengonsumsi INQOVI.

Overdosis

Jika Anda merasa telah mengonsumsi INQOVI terlalu banyak, segera hubungi petugas kesehatan, unit gawat darurat rumah sakit atau pusat kendali racun, meskipun tidak ada gejala.

Apa yang terkandung pada INQOVI?

Zat aktif: decitabine dan cedazuridine

Bahan tambahan: *lactose monohydrate, hypromellose, croscarmellose sodium, colloidal silicon dioxide* dan *magnesium stearate*. Bahan salut obat mengandung *polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc,* dan *iron oxide red*.

Nomor Ijin Edar:
Reg. No.: XXXXXXXXXXXXXXX
Dus, 1 blister @ 5 tablet salut selaput

Diproduksi oleh:
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Di bawah Otorisasi dari:
Taiho Pharmaceutical Co., Ltd., Japan

Tanggal Revisi:
Jun 2025

HARUS DENGAN RESEP DOKTER