ORGOVYX® (relugolix) 120 mg tablets

THE ONLY ORAL ADT

FOR ADULTS WITH ADVANCED PROSTATE CANCER (aPC)

THANKS TO YOU, TESTOSTERONE CAN BE CONTROLLED THROUGHOUT THE DIVE.

Not an actual patient.

The HERO study was a multinational, randomized, open-label, phase 3 trial in 930 men with aPC. Patients were randomized 2:1 to receive ORGOVYX (360 mg on the first day followed by daily doses of 120 mg orally [n=622]) or leuprolide acetate (22.5 mg injection [or 11.25 mg* in Japan and Taiwan per local guidelines] subcutaneously every 3 months [n=308]) for 48 weeks.[1]

The major efficacy outcome measured was the sustained testosterone suppression rate. 96.7% (95% CI: 94.9-97.9) of men treated with ORGOVYX and 88.8% (95% CI: 84.6-91.8)† of men treated with leuprolide achieved and maintained testosterone suppression to <50 ng/dL from Day 29 through Week 48.[1]

Please see additional information about ORGOVYX inside.

*11.25 mg is a dosage regimen that is not recommended for aPC in the United States.[1]
†The castration rate of the subgroup of patients receiving 22.5 mg leuprolide (n=264) was 88.0% (95% CI: 83.4%-91.4%).[1]
ADT=androgen deprivation therapy; CI=confidence interval.

INDICATION

ORGOVYX® (relugolix) is a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of adult patients with advanced prostate cancer.

IMPORTANT SAFETY INFORMATION

Contraindication

ORGOVYX is contraindicated in patients with severe hypersensitivity to relugolix or to any of the product components.

Warnings and Precautions

QT/QTc Interval Prolongation: Androgen deprivation therapy, such as ORGOVYX may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

ORGOVYX—MAKING AN IMPACT IN ADVANCED PROSTATE CANCER

5,000+ HEALTHCARE PROFESSIONALS LIKE YOU HAVE PRESCRIBED ORGOVYX SINCE 2021[2]*

#1
PRESCRIBED GnRH RECEPTOR ANTAGONIST for advanced prostate cancer[2]
Since 09/22. Based on IQVIA NSP data; assessed on a recurring 3-month cycle.

60,000+ MEN HAVE STARTED TREATMENT with ORGOVYX since 2021[2†]

500,000+ PRESCRIPTIONS filled since 2021[2‡]

RECOMMENDED BY NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®)[3§]

NCCN Guidelines® recommend relugolix (ORGOVYX) as a NCCN Category 2A treatment option for patients with advanced prostate cancer‖

Some recommendations may fall outside of the ORGOVYX US Prescribing Information.

*Based on claims and specialty pharmacy data from healthcare professionals across specialties from June 2021 to May 2023.[2]

†Includes projections derived from specialty pharmacy and HUB patient data from January 2021 to June 2024.[2]

‡Based on internal demand data (specialty distribution, specialty pharmacy, and patient assistance program) as of June 2024. Total prescriptions since FDA approval is estimated based on the shipping quantity of ORGOVYX, with each bottle equivalent to one prescription.[2]

§NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

‖A Category 2A recommendation is based on lower-level evidence and indicates uniform NCCN consensus that the intervention is appropriate.[3]

NCCN=National Comprehensive Cancer Network®.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Hypersensitivity: Angioedema was reported in 0.2% of patients treated with ORGOVYX in HERO. Hypersensitivity reactions, including pharyngeal edema and other serious cases of angioedema, have been reported in post-marketing with ORGOVYX. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue ORGOVYX and promptly seek medical care. Discontinue ORGOVYX for severe hypersensitivity reactions and manage as clinically indicated.

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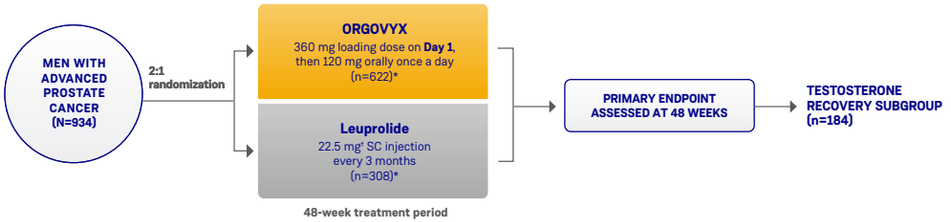
ORGOVYX® (relugolix) 120 mg tablets

HERO STUDY DESIGN

THE EFFICACY AND SAFETY OF ORGOVYX WERE EVALUATED IN A MULTINATIONAL, PHASE 3, RANDOMIZED, OPEN-LABEL, PARALLEL-GROUP STUDY[1,4]



*Two patients in each arm did not receive the study treatment and were not included.

†The dosage of leuprolide was 11.25 mg in Japan and Taiwan, per local guidelines, and is not recommended for advanced prostate cancer in the United States.

SC=subcutaneous.

PRIMARY ENDPOINT[1]

- Sustained testosterone suppression rate, defined as achieving and maintaining serum testosterone concentrations to <50 ng/dL by Day 29 through 48 weeks of treatment

KEY SECONDARY ENDPOINTS[4]

- Testosterone suppression rates on Day 4 and Day 15 (defined as testosterone concentrations <50 ng/dL)
- PSA response rate on Day 15 (>50% decrease from baseline), confirmed on Day 29
- Profound testosterone suppression rate on Day 15 (defined as testosterone concentrations <20 ng/dL)

TESTOSTERONE RECOVERY SUBSTUDY[4]

- Cumulative probability of testosterone recovery to 280 ng/dL at the 90-day follow-up in 184 patients who completed 48 weeks of treatment and who did not receive subsequent ADT for at least 90 days after discontinuation
- This endpoint was analyzed for exploratory purposes without formal testing

PSA=prostate-specific antigen.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Embryo-Fetal Toxicity: The safety and efficacy of ORGOVYX have not been established in females. Based on findings in animals and mechanism of action, ORGOVYX can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

PATIENT ENROLLMENT

THE HERO STUDY ENROLLED PATIENTS ACROSS DIFFERENT CLINICAL DISEASE PRESENTATIONS OF ADVANCED PROSTATE CANCER[1]

KEY INCLUSION CRITERIA[4,5]

- **Men ≥18 years of age** with confirmed adenocarcinoma of the prostate
- **Requiring at least 1 year of continuous ADT** with one of the following clinical disease presentations:
  - Evidence of biochemical (PSA) or clinical relapse following local primary intervention with curative intent
  - Newly diagnosed androgen-sensitive metastatic disease
  - Advanced localized disease unlikely to be cured by local primary intervention with curative intent
- Serum testosterone ≥150 ng/dL
- Serum PSA >2.0 ng/mL*
- ECOG score 0/1

KEY EXCLUSION CRITERIA[5]

- **Patients likely to require chemotherapy or surgical therapy** for symptomatic disease management within 2 months of initiating ADT
- **Previously received GnRH analog** or other form of ADT for >18 months total duration
  - If ADT was received for ≤18 months total duration, then patients must have completed treatment >3 months prior to baseline, or at least as long as the dosing interval of the depot formulation received
- **Significant cardiovascular risk conditions**
  - Myocardial infarction or thromboembolic events within 6 months
  - Arrhythmias
  - Uncontrolled hypertension

*When applicable, post radical prostatectomy of >0.2 ng/mL or post radiotherapy, cryotherapy, or high-frequency ultrasound >2.0 ng/mL above the post-interventional nadir.[5]

ECOG=Eastern Cooperative Oncology Group; GnRH=gonadotropin-releasing hormone.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Laboratory Testing: Therapy with ORGOVYX results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after ORGOVYX may be affected. The therapeutic effect of ORGOVYX should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

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PATIENT POPULATION

BASELINE CHARACTERISTICS WERE WELL BALANCED BETWEEN TREATMENT ARMS

SELECT BASELINE CHARACTERISTICS[4,6]	ORGOVYX (n=622)	Leuprolide (n=308)
Age		
≤75 years	71.4%	71.4%
Median age (range), years	72 (48-91)	71 (47-97)
Race		
White	69.8%	65.6%
Asian	20.4%	23.1%
Black or African American	4.8%	5.2%
Other	5.0%	6.2%
Clinical disease presentation		
Evidence of biochemical or clinical relapse after local primary intervention with curative intent*	49.7%	51.3%
Newly diagnosed androgen-sensitive metastatic disease	22.7%	22.7%
Advanced localized disease not suitable for primary surgical intervention with curative intent	27.7%	26.0%
Mean testosterone level, ng/dL (±SD)	436.1 (±159.0)	410.0 (±149.1)
Mean PSA level, ng/mL (±SD)	104.2 (±416.0)	68.6 (±244.0)
ECOG performance status†		
0	88.1%	88.0%
1	11.9%	11.7%
3‡	0%	0.3%
Previous androgen deprivation therapy	13.0%	9.7%
Cardiovascular risk factors§	91.6%	94.2%
Lifestyle risk factors‖	67.8%	65.6%
Cardiovascular or cerebrovascular risk factors¶	78.5%	82.5%
History of major adverse cardiovascular events#	13.5%	14.6%

CARDIOVASCULAR RISK FACTORS AT BASELINE[4]:

- **80% of patients had cardiovascular or cerebrovascular risk factors,** such as diabetes or hypertension
- **67% of patients had lifestyle risk factors,** such as a history of smoking or obesity
- **14% of patients had a history of myocardial infarction or stroke**

See previous page for exclusion criteria about cardiovascular risk conditions.

*Biochemical relapse was defined by a rising PSA level.[4]

†ECOG performance status ranges from 0 to 5, with higher scores reflecting greater disability.[4]

‡One patient in the leuprolide group had a surgical vascular procedure on his leg and was given an ECOG score of 3 at screening because of the use of crutches. By the baseline Day 1 visit, the patient no longer used crutches, and his ECOG score had improved to 0.[4]

§Patients with multiple risk factors were counted only once.[4]

‖Included current/past tobacco smoking, heavy alcohol use, and a BMI >30 kg/m^2.[4]

¶Included hypertension; dyslipidemia; diabetes; a history of myocardial infarction or cardiovascular disease; a history of stroke, transient ischemic attack, or cerebral hemorrhage; peripheral arterial disease; atrial fibrillation and other arrhythmias; heart-valve disease; chronic obstructive pulmonary disease; chronic kidney disease; chronic liver disease; carotid artery stenosis or occlusion; venous thromboembolic events; and heart failure.[4]

#Search criteria included "myocardial infarction" (broad standardized MedDRA query) and "central nervous system hemorrhages and cerebrovascular conditions" (broad standardized MedDRA query).[4]

BMI=body mass index; MedDRA=Medical Dictionary for Regulatory Activities; SD=standard deviation.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

THANKS TO YOU, PATIENTS CAN HAVE AN ORAL ADT AS AN OPTION.

IN THE HERO STUDY, ORGOVYX WAS ASSESSED ACROSS MULTIPLE KEY ENDPOINTS

PRIMARY ENDPOINT

SUSTAINED TESTOSTERONE SUPPRESSION

The major efficacy outcome measured was the sustained testosterone suppression rate (cumulative probability of testosterone suppression to <50 ng/dL from Day 29 through Week 48).[1]

SECONDARY ENDPOINT

TESTOSTERONE SUPPRESSION AT DAY 4 AND DAY 15

A key secondary endpoint studied included cumulative probability of testosterone suppression (<50 ng/dL) at Day 4 and Day 15.[1,4]

Not an actual patient.

SECONDARY ENDPOINT

PROFOUND TESTOSTERONE SUPPRESSION DEFINED AS TESTOSTERONE CONCENTRATIONS <20 ng/dL

Another key secondary endpoint studied included cumulative probability of profound suppression (<20 ng/dL) at Day 15.[1,4]

ADDITIONAL EFFICACY AND SAFETY EVALUATIONS

EXPLORATORY ANALYSIS

RECOVERY OF TESTOSTERONE LEVELS 90 DAYS AFTER DISCONTINUATION

An exploratory endpoint studied was cumulative testosterone recovery, defined as recovery to at least 280 ng/dL at the 90-day follow-up in 184 patients who completed 48 weeks of treatment and who did not receive subsequent androgen deprivation therapy for at least 90 days after discontinuation.[4]

SAFETY EVALUATION

SAFETY OF ORGOVYX WAS ALSO EVALUATED

The most common adverse events during treatment with ORGOVYX (≥10%) in the study were hot flush, musculoskeletal pain, fatigue, constipation, and diarrhea.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions

Serious adverse reactions occurred in 12% of patients receiving ORGOVYX. Serious adverse reactions in ≥0.5% of patients included myocardial infarction (0.8%), acute kidney injury (0.6%), arrhythmia (0.6%), hemorrhage (0.6%), and urinary tract infection (0.5%). Fatal adverse reactions occurred in 0.8% of patients receiving ORGOVYX including metastatic lung cancer (0.3%), myocardial infarction (0.3%), and acute kidney injury (0.2%). Fatal and non-fatal myocardial infarction and stroke were reported in 2.7% of patients receiving ORGOVYX.

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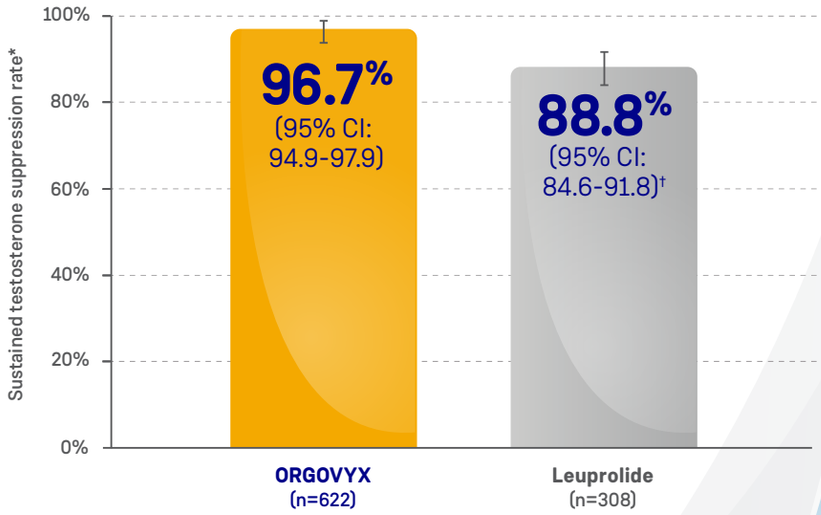
Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

PRIMARY ENDPOINT

ORGOVYX TESTOSTERONE CONTROL STARTS WITH SUSTAINED TESTOSTERONE SUPPRESSION TO <50 ng/dL[1]

- 96.7% of men achieved and maintained testosterone suppression to <50 ng/dL from Day 29 through Week 48 with ORGOVYX
- 88.8% of men treated with leuprolide achieved and maintained testosterone suppression from Day 29 through Week 48

MAJOR EFFICACY OUTCOME MEASURE: SUSTAINED TESTOSTERONE SUPPRESSION RATE (TESTOSTERONE LEVELS <50 ng/dL FROM DAY 29 THROUGH WEEK 48)[1]



*Kaplan-Meier estimates within each group.[1]

†The testosterone suppression rate of the subgroup of patients receiving leuprolide 22.5 mg (n=264) was 88.0% (95% CI: 83.4-91.4).[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions (cont'd)

Most common adverse reactions (≥10%) and laboratory abnormalities (≥15%) in patients receiving ORGOVYX were hot flush (54%), glucose increased (44%), triglycerides increased (35%), musculoskeletal pain (30%), hemoglobin decreased (28%), alanine aminotransferase increased (27%), fatigue (26%), aspartate aminotransferase increased (18%), constipation (12%), and diarrhea (12%).

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

SECONDARY ENDPOINT

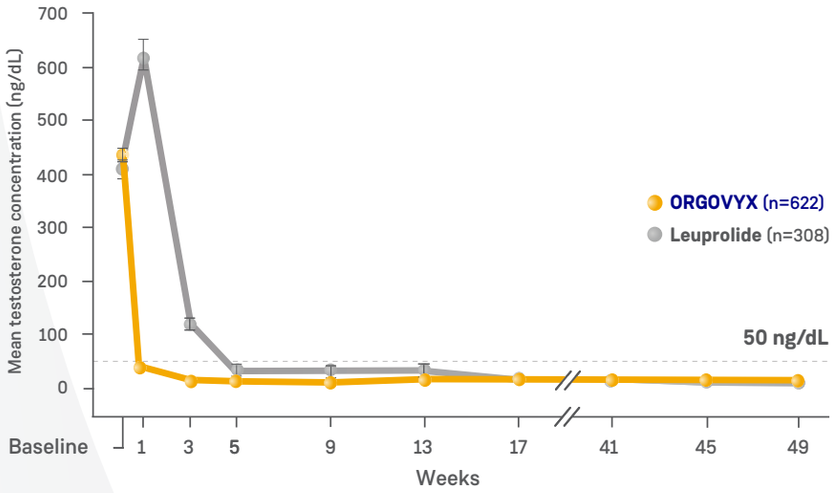
ORGOVYX TESTOSTERONE CONTROL ALSO INCLUDES

RAPID TESTOSTERONE SUPPRESSION

WITH NO INITIAL SURGE AND SUSTAINED SUPPRESSION THROUGHOUT THE STUDY[1]

- **On Day 4:** 56% of men treated with ORGOVYX achieved testosterone suppression to <50 ng/dL*
- 0% of men treated with leuprolide had testosterone levels <50 ng/dL on Day 4[1]

MEAN TESTOSTERONE CONCENTRATIONS FROM BASELINE THROUGH WEEK 48[1,4]



Adapted with permission from *The New England Journal of Medicine.*

- **On Day 15:** 99% of men treated with ORGOVYX achieved testosterone suppression to <50 ng/dL*
- 12% of men treated with leuprolide had testosterone levels <50 ng/dL on Day 15[1]

*Kaplan-Meier estimates within each group.[1]

SECONDARY ENDPOINT

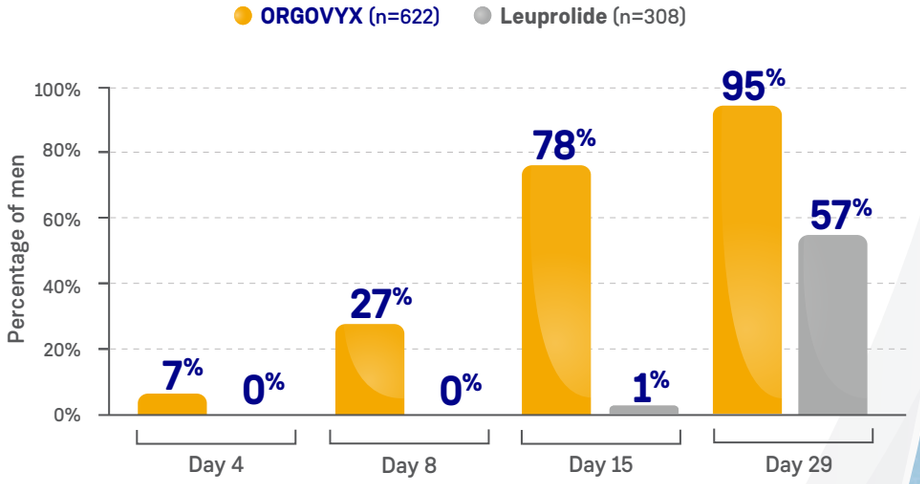
ORGOVYX TESTOSTERONE CONTROL ALSO INCLUDES

PROFOUND TESTOSTERONE SUPPRESSION

DEFINED AS TESTOSTERONE CONCENTRATIONS <20 ng/dL[1]

- **On Day 15:** 78% of men treated with ORGOVYX achieved profound testosterone suppression to <20 ng/dL
- 1% of men treated with leuprolide had testosterone levels <20 ng/dL on Day 15

PERCENTAGE OF MEN WITH TESTOSTERONE CONCENTRATIONS <20 ng/dL[1]*



*Kaplan-Meier estimates within each group.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Drug Interactions

Co-administration of ORGOVYX with a P-gp inhibitor increases the area under the curve (AUC) and maximum concentration (C_{max}) of ORGOVYX, which may increase the risk of adverse reactions associated with ORGOVYX. Avoid co-administration of ORGOVYX with oral P-gp inhibitors. If co-administration is unavoidable, take ORGOVYX first, separate dosing by at least 6 hours, and monitor patients more frequently for adverse reactions. Treatment with ORGOVYX may be interrupted for up to 2 weeks for a short course of treatment with certain P-gp inhibitors. If treatment with ORGOVYX is interrupted for more than 7 days, resume administration of ORGOVYX with a 360 mg loading dose on the first day, followed by 120 mg once daily.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

IMPORTANT SAFETY INFORMATION (cont'd)

Drug Interactions (cont'd)

Co-administration of ORGOVYX with a combined P-gp and strong CYP3A inducer decreases the AUC and C_{max} of ORGOVYX, which may reduce the effects of ORGOVYX. Avoid co-administration of ORGOVYX with combined P-gp and strong CYP3A inducers. If co-administration is unavoidable, increase the ORGOVYX dose to 240 mg once daily. After discontinuation of the combined P-gp and strong CYP3A inducer, resume the recommended ORGOVYX dose of 120 mg once daily.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

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SECONDARY ENDPOINT

PSA REDUCTION

ORGOVYX LOWERED PSA LEVELS AT 2 WEEKS AND MAINTAINED PSA SUPPRESSION THROUGH 48 WEEKS[1]

ORGOVYX DEMONSTRATED PSA REDUCTIONS FROM BASELINE AVERAGE OF 104.2 ng/mL[1,4]

AT 2 WEEKS	AT 4 WEEKS	AT 3 MONTHS
65% average PSA reductions	**83%** average PSA reductions	**92%** average PSA reductions

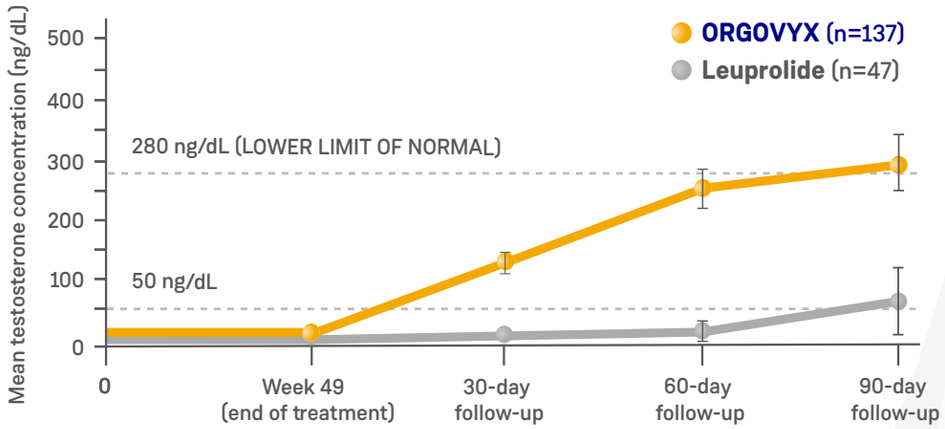
PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline is related to a clinical benefit.[1]

EXPLORATORY ANALYSIS

TESTOSTERONE RECOVERY

90 DAYS AFTER TREATMENT DISCONTINUATION[1,4]

TESTOSTERONE CONCENTRATIONS IN TESTOSTERONE RECOVERY SUBSTUDY (N=184)[4]



Adapted with permission from *The New England Journal of Medicine.*

- Testosterone recovery was evaluated in a substudy of 184 patients who completed 48 weeks of treatment[4]
- 90 days after treatment discontinuation, 55% of 137 men treated with ORGOVYX had their testosterone levels return to above the lower limit of the normal range (>280 ng/dL) or baseline values[1]*
- 3% of 47 men treated with leuprolide had their testosterone levels return to above the lower limit of the normal range (>280 ng/dL) or baseline values 90 days after discontinuation[4]
- **This endpoint was analyzed for exploratory purposes without formal testing. The data from the leuprolide arm were not included in the US Prescribing Information for ORGOVYX**

*Kaplan-Meier estimates within each group.[1]

INDICATION

ORGOVYX® (relugolix) is a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of adult patients with advanced prostate cancer.

IMPORTANT SAFETY INFORMATION

Contraindication

ORGOVYX is contraindicated in patients with severe hypersensitivity to relugolix or to any of the product components.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

QT/QTc Interval Prolongation: Androgen deprivation therapy, such as ORGOVYX may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

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HERO STUDY ADVERSE EVENTS

ADVERSE EVENTS[4]*	ORGOVYX (n=622)		Leuprolide (n=308)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any adverse event, n (%)	578 (92.9)	112 (18.0)	288 (93.5)	63 (20.5)
Serious adverse event, n (%)	76 (12.2)	61 (9.8)	47 (15.3)	35 (11.4)
Fatal adverse event, n (%)	7 (1.1)	-	9 (2.9)	-
Major adverse cardiovascular event, n (%)†	18 (2.9)	8 (1.3)	19 (6.2)	4 (1.3)

- In a prespecified analysis, major adverse cardiovascular events were defined as nonfatal myocardial infarction, nonfatal stroke, and all-cause death[4]
- In a separate analysis reported in the US Prescribing Information, fatal and nonfatal myocardial infarction and stroke were reported in 2.7% of patients receiving ORGOVYX. Fatal adverse events, excluding prostate cancer–related deaths, were reported in 0.8% of patients receiving ORGOVYX[1,2‡]

AMONG PATIENTS WHO RECEIVED ORGOVYX, 91% WERE EXPOSED FOR AT LEAST 48 WEEKS[1]

- 99 patients (16%) received concomitant radiotherapy, and 17 patients (3%) received concomitant enzalutamide with ORGOVYX

ADVERSE REACTIONS (≥10%) OF PATIENTS WITH ADVANCED PROSTATE CANCER WHO RECEIVED ORGOVYX IN HERO[1]

ADVERSE REACTIONS	ORGOVYX (n=622)		Leuprolide (n=308)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Hot flush	54%	0.6%	52%	0%
Musculoskeletal pain§	30%	1.1%	29%	1.6%
Fatigue‖	26%	0.3%	24%	0%
Diarrhea¶	12%	0.2%	7%	0%
Constipation	12%	0%	10%	0%

- Most common laboratory abnormalities (≥15%, all grades) in patients receiving ORGOVYX vs leuprolide were glucose increased (44% vs 54%), triglycerides increased (35% vs 36%), hemoglobin decreased (28% vs 29%), alanine aminotransferase increased (27% vs 28%), and aspartate aminotransferase increased (18% vs 19%)[1]
- Permanent discontinuation of ORGOVYX due to an adverse reaction occurred in 3.5% of patients[1]

*Shown are the numbers of patients with an event, rather than the number of events. Adverse events were evaluated with the use of MedDRA, version 22.0, and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.[4]
†Search criteria included "myocardial infarction" (broad standardized MedDRA query), "central nervous system hemorrhages and cerebrovascular conditions" (broad standardized MedDRA query), and deaths from any cause.[4]
‡Reported in 2.3% of patients treated with leuprolide.[2]
§Includes arthralgia, back pain, pain in extremity, musculoskeletal pain, myalgia, bone pain, neck pain, arthritis, musculoskeletal stiffness, noncardiac chest pain, musculoskeletal chest pain, spinal pain, and musculoskeletal discomfort.[1]
‖Includes fatigue and asthenia.[1]
¶Includes diarrhea and colitis.[1]

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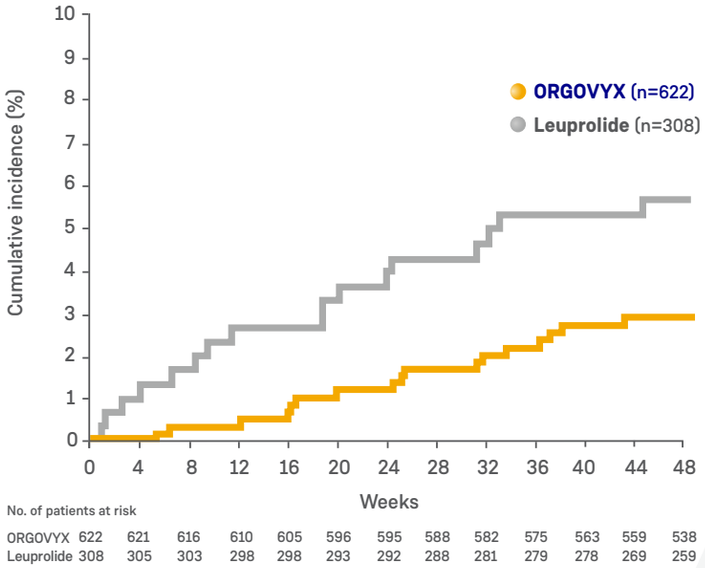
Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

MAJOR ADVERSE CARDIOVASCULAR EVENT DATA

CUMULATIVE INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS THROUGH WEEK 48 IN A POST-HOC ANALYSIS[4]

- In a prespecified analysis, major adverse cardiovascular events were defined as nonfatal myocardial infarction, nonfatal stroke, and all-cause death[4]

CUMULATIVE INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS[4]



Adapted with permission from *The New England Journal of Medicine*.

NCCN GUIDELINES FOR PROSTATE CANCER RECOMMEND MONITORING CARDIOVASCULAR DISEASE, AMONG OTHER FACTORS, WHEN PRESCRIBING ANDROGEN DEPRIVATION THERAPY[3]

The incidence of major adverse cardiovascular events was a prespecified safety analysis. This was not a prospective efficacy endpoint in the study, the events were not adjudicated, and only descriptive analyses were performed.[4]

For these reasons, the FDA did not include the incidence of major adverse cardiovascular events for leuprolide in the label. The major adverse cardiovascular event data for ORGOVYX and leuprolide should be interpreted with caution and in this context.[4]

The study excluded patients with myocardial infarction or thromboembolic events within 6 months, arrhythmias, and uncontrolled hypertension.[4]

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

HERO POST-HOC SUBGROUP ANALYSIS 1

SUSTAINED CASTRATION RATE FOR ORGOVYX USED CONCOMITANTLY WITH ENZALUTAMIDE OR DOCETAXEL (N=24)[7]

- In HERO, patients were randomized 2:1 to receive relugolix or leuprolide for 48 weeks. The addition of enzalutamide or docetaxel was allowed in case of a confirmed PSA progression*†
- Efficacy analysis was performed in the HERO study primary analysis population

SUSTAINED CASTRATION RATE
(Kaplan-Meier estimated cumulative probability of testosterone values <50 ng/dL from Day 29 through Week 48)

CONCOMITANT ORGOVYX AND ENZALUTAMIDE (n=17) OR DOCETAXEL (n=8)‡

95.8%

This subgroup analysis is post hoc and does not assess a prespecified endpoint, was not adjusted for multiplicity, and comprises a small sample size. The efficacy and safety of ORGOVYX used concomitantly with enzalutamide or docetaxel has not been established. The HERO study was neither designed nor powered to analyze these subgroups. No conclusions can be made; results are descriptive and not intended to demonstrate efficacy. Information presented on this page is not part of the ORGOVYX US Prescribing Information.

*Patients were allowed to receive enzalutamide or docetaxel in case of a confirmed PSA progression as defined by the PCWG3 criteria or other disease progression in the setting of testosterone suppression to castration levels (<50 ng/dL).[7]

†Enzalutamide (160 mg administered orally once daily) or docetaxel (75 mg/m^2 intravenous given in 21-day cycles) were dosed per their respective approved labels.[7]

‡1 patient received both enzalutamide and docetaxel throughout the course of the study.

PCWG3=Prostate Cancer Clinical Trials Working Group 3.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Hypersensitivity: Angioedema was reported in 0.2% of patients treated with ORGOVYX in HERO. Hypersensitivity reactions, including pharyngeal edema and other serious cases of angioedema, have been reported in post-marketing with ORGOVYX. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue ORGOVYX and promptly seek medical care. Discontinue ORGOVYX for severe hypersensitivity reactions and manage as clinically indicated.

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Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

HERO POST-HOC SUBGROUP ANALYSIS 1

SAFETY WAS EVALUATED IN PATIENTS WHO RECEIVED ORGOVYX WITH ENZALUTAMIDE (n=20) OR DOCETAXEL (n=17)[7]*

- Safety analysis was performed in the final analysis population, which included additional patients, including men with metastatic disease and those who were enrolled for other analyses as part of the HERO study

ADVERSE EVENTS FOR PATIENTS ADMINISTERED ORGOVYX WITH CONCOMITANT ENZALUTAMIDE OR DOCETAXEL†

PATIENTS TREATED WITH CONCOMITANT:

	ORGOVYX and enzalutamide (n=20)		ORGOVYX and docetaxel (n=17)	
	Any Grade n (%)	**Grade 3 or 4 n (%)**	**Any Grade n (%)**	**Grade 3 or 4 n (%)**
Any AE	20 (100%)	8 (40.0%)	17 (100%)	8 (47.1%)
Serious AE[a]	5 (25.0%)	-	5 (29.4%)	-
AEs that occurred in >10% of patients in either group in the overall safety population				
Hot flash	13 (65.0%)	0	12 (70.6%)	0
Fatigue	8 (40.0%)	0	6 (35.3%)	0
Constipation	3 (15.0%)	0	6 (35.3%)	0
Diarrhea	2 (10.0%)	0	2 (11.8%)	0
Arthralgia	5 (25.0%)	1 (5.0%)	2 (11.8%)	0
Hypertension	4 (20.0%)	4 (15.0%)	1 (5.9%)	1 (5.9%)

[a]Concomitant therapy with enzalutamide or docetaxel was associated with higher frequency of serious and fatal AEs, although patient numbers are too small to make any definitive conclusions.

This subgroup analysis is post hoc and does not assess a prespecified endpoint, was not adjusted for multiplicity, and comprises a small sample size. The efficacy and safety of ORGOVYX used concomitantly with enzalutamide or docetaxel has not been established. The HERO study was neither designed nor powered to analyze these subgroups. No conclusions can be made; results are descriptive and not intended to demonstrate efficacy. Information presented on this page is not part of the ORGOVYX US Prescribing Information.

*Patients were allowed to receive enzalutamide or docetaxel in case of a confirmed PSA progression as defined by the PCWG3 criteria or other disease progression in the setting of testosterone suppression to castration levels (<50 ng/dL).[7]

†Adverse events were evaluated with the use of MedDRA, version 22.0, and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.[7]

AE=adverse event.

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HERO POST-HOC SUBGROUP ANALYSIS 2

RESULTS OF ORGOVYX USED CONCOMITANTLY WITH RADIOTHERAPY[8]*

- A post hoc analysis of a treatment subset from the phase 3 HERO trial in patients with locally advanced, recurrent, or metastatic prostate cancer who received radiotherapy
- Patients were randomized 2:1 to receive ORGOVYX 120 mg once daily (n=99) after a single loading dose of 360 mg, or leuprolide acetate injections (n=58) every 12 weeks for 48 weeks
- Concomitant radiotherapy was permitted after 2 months following initiation of ADT

LIMITATIONS

- The radiotherapy subset analysis of the HERO phase 3 trial was unplanned, and complete details of radiotherapy dose and volume irradiated were not collected. Similarly, clinicopathological prognostic features to better define patients' disease state were not collected. Lastly, the HERO study included patients who received palliative and definitive postoperative radiotherapy

This subgroup analysis is post hoc and does not assess a prespecified endpoint, was not adjusted for multiplicity, and comprises a small sample size. The efficacy and safety of ORGOVYX used concomitantly with radiotherapy has not been established. The HERO study was neither designed nor powered to analyze these subgroups. No conclusions can be made; results are descriptive and not intended to demonstrate safety. Information presented on this page is not part of the ORGOVYX US Prescribing Information.

SELECT PATIENT CHARACTERISTICS AT BASELINE FROM THE POST HOC ANALYSIS

Characteristics	No. (%) ORGOVYX (n=99)
Age, mean (SD), y	69.9 (7.6)
Disease state presentation	
Evidence of biochemical (PSA) or clinical relapse following local primary intervention with curative intent	23 (23)
Newly diagnosed androgen-sensitive metastatic disease	16 (16)
Advanced localized disease not suitable for primary surgical intervention with curative intent	60 (61)
Had prior radiotherapy†	5 (5)
Radiotherapy treatment intent†	
Primary	60 (61)
Salvage	15 (15)
Palliative	24 (24)
Unknown	1 (1)
Total Gleason score‡	
≤6	16 (16)
7	35 (35)
8-10	47 (48)
Unknown	1 (1)
ECOG performance status§	
0	87 (88)
1	12 (12)
Unknown	0
PSA level, mean (SD), ng/mL	100.4 (436.2)

*Radiotherapy was prescribed, as determined by the investigator. Types of radiation therapy: external beam, brachytherapy, or systemic.

†Almost all patients in this study were receiving radiotherapy with neoadjuvant/adjuvant ADT as the primary (first-line) therapy for their prostate disease. Thus, there were very limited data regarding prior therapies relevant to this study.

‡Gleason score was determined by adding primary and secondary Gleason scores together.

§ECOG performance status score ranged from 0 to 5, with higher scores reflecting greater disability.

HERO POST-HOC SUBGROUP ANALYSIS 2

RESULTS OF ORGOVYX USED CONCOMITANTLY WITH RADIOTHERAPY[8]

POST-HOC ANALYSIS OF PRIMARY ENDPOINT

TESTOSTERONE SUPPRESSION (<50 ng/dL) OF PATIENTS RECEIVING ORGOVYX AND RADIOTHERAPY

96.9%

SUSTAINED CASTRATION RATE OVER 48 WEEKS IN PATIENTS RECEIVING ORGOVYX AND RADIOTHERAPY (95% CI: 90.6-99.0)

POST-HOC ANALYSIS OF SECONDARY ENDPOINTS

CUMULATIVE PROBABILITY OF TESTOSTERONE SUPPRESSION (<50 ng/dL)

- **59.6%** of patients receiving ORGOVYX and radiotherapy by Day 4
- **100%** of patients receiving ORGOVYX and radiotherapy by Day 15

PROPORTION OF PATIENTS WITH A PSA RESPONSE ON DAY 15 FOLLOWED BY CONFIRMATION ON DAY 29

- **75.8%** of patients receiving ORGOVYX and radiotherapy had a PSA response by Day 15

PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline is related to a clinical benefit.

ADVERSE EVENTS[8]

GRADE 3 OR HIGHER (≥2% OF POPULATION) AND MOST COMMON (≥10% OF POPULATION) AEs

	No. (%) ORGOVYX (n=99)
Grade 3 or higher in ≥2% of population	
Atrial fibrillation	2 (2)
Hypertension	2 (2)
Any grade in ≥10% of population	
Hot flash	54 (55)
Fatigue	29 (29)
Diarrhea*	25 (25)
Constipation*	22 (22)
Arthralgia	14 (14)

This subgroup analysis is post hoc and does not assess a prespecified endpoint, was not adjusted for multiplicity, and comprises a small sample size. The efficacy and safety of ORGOVYX used concomitantly with radiotherapy has not been established. The HERO study was neither designed nor powered to analyze these subgroups. No conclusions can be made; results are descriptive and not intended to demonstrate safety. Information presented on this page is not part of the ORGOVYX US Prescribing Information.

***Rates of diarrhea and constipation were higher in patients who received radiotherapy in this subgroup analysis than in the total study population.**

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Embryo-Fetal Toxicity: The safety and efficacy of ORGOVYX have not been established in females. Based on findings in animals and mechanism of action, ORGOVYX can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

Please see Important Safety Information throughout and accompanying full Prescribing Information for ORGOVYX.

ORAL DOSING

ONE PILL, ONCE A DAY, FITS INTO MEN'S LIVES[1]

- The only oral androgen deprivation therapy that offers **convenient and injection-free administration**[1,4]
- Mean effective half-life of ORGOVYX is 25 hours[1]

FIRST DAY OF TREATMENT[1]	EVERY DAY AFTER THAT[1]
• Take 3 pills • 360 mg loading dose	• Take 1 pill • 120 mg daily dose

Pills not shown at actual size. Actual size: ~10.7 mm x 7.5 mm x 5.2 mm[2]

AFTER THE INITIAL LOADING DOSE, PATIENTS TAKE ONE PILL, ONCE A DAY[1]

Can be taken with or without food

Should be taken around the same time each day

For oral administration only—should be swallowed whole, not crushed or chewed

- In patients treated with GnRH receptor agonists and antagonists for prostate cancer, treatment is usually continued upon development of nonmetastatic or metastatic castration-resistant prostate cancer[1]
- No dosage adjustment required in patients with mild to severe renal impairment or mild or moderate hepatic impairment[1]*
- Advise patients to take a missed dose of ORGOVYX as soon as they remember. If the dose was missed by more than 12 hours, patients should not take the missed dose and should resume with the next scheduled dose[1]
- Avoid co-administration of ORGOVYX with oral P-gp inhibitors. If co-administration is unavoidable, take ORGOVYX first and separate dosing by at least 6 hours. Treatment with ORGOVYX may be interrupted for up to 2 weeks if a short course of treatment with a P-gp inhibitor is required[1]
- If treatment with ORGOVYX is interrupted for more than 7 days, resume administration of ORGOVYX with a 360 mg loading dose on the first day, followed by 120 mg once a day[1]
- Avoid co-administration of ORGOVYX with combined P-gp and strong CYP3A inducers. If co-administration is unavoidable, increase the ORGOVYX dose to 240 mg once a day. After discontinuation of the combined P-gp and strong CYP3A inducer, resume the recommended ORGOVYX dose of 120 mg once a day[1]

*The effect of end-stage renal disease with or without hemodialysis or severe hepatic impairment on the pharmacokinetics of ORGOVYX has not been evaluated.[1]

CYP3A=cytochrome P450, family 3, subfamily A; P-gp=P-glycoprotein.

ORGOVYX® (relugolix) 120 mg tablets

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IMPORTANT SAFETY INFORMATION

INDICATION

ORGOVYX® (relugolix) is a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of adult patients with advanced prostate cancer.

IMPORTANT SAFETY INFORMATION

Contraindication

ORGOVYX is contraindicated in patients with severe hypersensitivity to relugolix or to any of the product components.

Warnings and Precautions

QT/QTc Interval Prolongation: Androgen deprivation therapy, such as ORGOVYX may prolong the QT/QTc interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

Hypersensitivity: Angioedema was reported in 0.2% of patients treated with ORGOVYX in HERO. Hypersensitivity reactions, including pharyngeal edema and other serious cases of angioedema, have been reported in post-marketing with ORGOVYX. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue ORGOVYX and promptly seek medical care. Discontinue ORGOVYX for severe hypersensitivity reactions and manage as clinically indicated.

Embryo-Fetal Toxicity: The safety and efficacy of ORGOVYX have not been established in females. Based on findings in animals and mechanism of action, ORGOVYX can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of ORGOVYX.

Laboratory Testing: Therapy with ORGOVYX results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after ORGOVYX may be affected. The therapeutic effect of ORGOVYX should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

Adverse Reactions

Serious adverse reactions occurred in 12% of patients receiving ORGOVYX. Serious adverse reactions in ≥0.5% of patients included myocardial infarction (0.8%), acute kidney injury (0.6%), arrhythmia (0.6%), hemorrhage (0.6%), and urinary tract infection (0.5%). Fatal adverse reactions occurred in 0.8% of patients receiving ORGOVYX including metastatic lung cancer (0.3%), myocardial infarction (0.3%), and acute kidney injury (0.2%). Fatal and non-fatal myocardial infarction and stroke were reported in 2.7% of patients receiving ORGOVYX.

Most common adverse reactions (≥10%) and laboratory abnormalities (≥15%) in patients receiving ORGOVYX were hot flush (54%), glucose increased (44%), triglycerides increased (35%), musculoskeletal pain (30%), hemoglobin decreased (28%), alanine aminotransferase increased (27%), fatigue (26%), aspartate aminotransferase increased (18%), constipation (12%), and diarrhea (12%).

Drug Interactions

Co-administration of ORGOVYX with a P-gp inhibitor increases the area under the curve (AUC) and maximum concentration (C_{max}) of ORGOVYX, which may increase the risk of adverse reactions associated with ORGOVYX. Avoid co-administration of ORGOVYX with oral P-gp inhibitors. If co-administration is unavoidable, take ORGOVYX first, separate dosing by at least 6 hours, and monitor patients more frequently for adverse reactions. Treatment with ORGOVYX may be interrupted for up to 2 weeks for a short course of treatment with certain P-gp inhibitors. If treatment with ORGOVYX is interrupted for more than 7 days, resume administration of ORGOVYX with a 360 mg loading dose on the first day, followed by 120 mg once daily.

Co-administration of ORGOVYX with a combined P-gp and strong CYP3A inducer decreases the AUC and C_{max} of ORGOVYX, which may reduce the effects of ORGOVYX. Avoid co-administration of ORGOVYX with combined P-gp and strong CYP3A inducers. If co-administration is unavoidable, increase the ORGOVYX dose to 240 mg once daily. After discontinuation of the combined P-gp and strong CYP3A inducer, resume the recommended ORGOVYX dose of 120 mg once daily.

Please see accompanying full Prescribing Information for ORGOVYX.

References: 1. ORGOVYX (relugolix) [prescribing information]. Marlborough, MA: Sumitomo Pharma America, Inc.; 2023. **2.** Data on file. Sumitomo Pharma America, Inc. 2024. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed July 16, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **4.** Shore ND, Saad F, Cookson MS, et al. Oral relugolix for androgen-deprivation therapy in advanced prostate cancer. *N Engl J Med*. 2020;382(23):2187-2196. doi:10.1056/NEJMoa2004325 **5.** Protocol for: Shore ND, Saad F, Cookson MS, et al. Oral relugolix for androgen-deprivation therapy in advanced prostate cancer. *N Engl J Med*. 2020;382(23):2187-2196. doi:10.1056/NEJMoa2004325 **6.** Shore ND, Saad F, Cookson MS, et al. HERO phase 3 trial: results comparing relugolix, an oral GnRH receptor antagonist, versus leuprolide acetate for advanced prostate cancer. Presented at: American Society of Clinical Oncology Virtual Scientific Program; May 29-June 2, 2020; virtual. Abstract 5602. **7.** George DJ, Saad F, Cookson MS, et al. Impact of concomitant prostate cancer medications on efficacy and safety of relugolix versus leuprolide in men with advanced prostate cancer. *Clin Genitourin Cancer*. 2023;21(3):383-392.e2. doi:10.1016/j.clgc.2023.03.009 **8.** Spratt DE, George DJ, Shore ND, et al. Efficacy and safety of radiotherapy plus relugolix in men with localized or advanced prostate cancer. *JAMA Oncol*. 2024;10(5):594-602. doi:10.1001/jamaoncol.2023.7279

ORGOVYX—MAKING AN IMPACT IN ADVANCED PROSTATE CANCER

ORGOVYX® (relugolix) 120 mg tablets

THE ONLY ORAL ADT

5,000+ HEALTHCARE PROFESSIONALS LIKE YOU HAVE PRESCRIBED ORGOVYX SINCE 2021[2]*

#1
PRESCRIBED GnRH RECEPTOR ANTAGONIST for advanced prostate cancer[2]
Since 09/22. Based on IQVIA NSP data; assessed on a recurring 3-month cycle.

60,000+ MEN HAVE STARTED TREATMENT with ORGOVYX since 2021[2†]

500,000+ PRESCRIPTIONS filled since 2021[2‡]

RECOMMENDED BY NCCN GUIDELINES®[3§]

NCCN Guidelines recommend relugolix (ORGOVYX) as a NCCN Category 2A treatment option for patients with advanced prostate cancer‖

Some recommendations may fall outside of the ORGOVYX US Prescribing Information.

*Based on claims and specialty pharmacy data from healthcare professionals across specialties from June 2021 to May 2023.[2]
†Includes projections derived from specialty pharmacy and HUB patient data from January 2021 to June 2024.[2]
‡Based on internal demand data (specialty distribution, specialty pharmacy, and patient assistance program) as of June 2024. Total prescriptions since FDA approval is estimated based on the shipping quantity of ORGOVYX, with each bottle equivalent to one prescription.[2]
§NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
‖A Category 2A recommendation is based on lower-level evidence and indicates uniform NCCN consensus that the intervention is appropriate.[3]

INDICATION

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Sumitomo Pharma

Pfizer Oncology

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