FONDAPARINUX SODIUM- fondaparinux sodium injection
Sandoz Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FONDAPARINUX SODIUM INJECTION safely and effectively. See full prescribing information for FONDAPARINUX SODIUM INJECTION.

FONDAPARINUX SODIUM injection, for subcutaneous use
Initial U.S. Approval: 2001

WARNING:SPINAL/EPIDURAL HEMATOMAS

***See full prescribing information for complete boxed warning*.**

Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH), heparinoids, or fondaparinux sodium and are receiving neuraxial anesthesia or undergoing spinal puncture.
These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:
- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants**
- **a history of traumatic or repeated epidural or spinal puncture**
- **a history of spinal deformity or spinal surgery**

Monitor patients frequently for signs and symptoms of neurologic impairment. If neurologic compromise is noted, urgent treatment is necessary.
Consider the benefit and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis *[see Warnings and Precautions (5.1) and Drug Interactions (7)].*

INDICATIONS AND USAGE

Fondaparinux sodium injection is a Factor Xa inhibitor (anticoagulant) indicated for:
- Prophylaxis of deep vein thrombosis (DVT) in adult patients undergoing hip fracture surgery (including extended prophylaxis), hip replacement surgery, knee replacement surgery, or abdominal surgery. (1.1)
- Treatment of DVT or acute pulmonary embolism (PE) in adult patients when administered in conjunction with warfarin. (1.2, 1.3)
- Treatment of venous thromboembolism (VTE) in pediatric patients aged 1 year or older weighing at least 10 kg. (1.4)

DOSAGE AND ADMINISTRATION

- For subcutaneous use, do not mix with other injections or infusions. (2.1)
- Prophylaxis of deep vein thrombosis in adults: Fondaparinux sodium 2.5 mg subcutaneously once daily after hemostasis has been established. The initial dose should be given no earlier than 6 hours to 8 hours after surgery and continued for 5 days to 9 days. For patients undergoing hip fracture surgery, extended prophylaxis up to 24 additional days is recommended. (2.2, 2.3)
- Treatment of deep vein thrombosis and pulmonary embolism in adults: Fondaparinux sodium 5 mg (body weight less than 50 kg), 7.5 mg (50 kg to 100 kg), or 10 mg (greater than 100 kg) subcutaneously once daily. Treatment should continue for at least 5 days until INR 2 to 3 is achieved with warfarin sodium. (2.4)
- Treatment of venous thromboembolism in pediatric patients weighing at least 10 kg: Fondaparinux sodium 0.1 mg/kg subcutaneously once daily. (2.5)

DOSAGE FORMS AND STRENGTHS

Single-dose, prefilled syringes containing 2.5 mg, 5 mg, 7.5 mg, or 10 mg of fondaparinux sodium. (3)

CONTRAINDICATIONS

Fondaparinux sodium injection is contraindicated in the following conditions: (4) (4)
- Severe renal impairment (creatinine clearance less than 30 mL/min) in prophylaxis or treatment of venous thromboembolism.

- Active major bleeding.
- Bacterial endocarditis.
- Thrombocytopenia associated with a positive in vitro test for anti-platelet antibody in the presence of fondaparinux sodium.
- Body weight less than 50 kg (venous thromboembolism prophylaxis in adults only).
- History of serious hypersensitivity reaction (e.g., angioedema, anaphylactoid/anaphylactic reactions) to fondaparinux sodium.

WARNINGS AND PRECAUTIONS

• Spinal or epidural hematomas, which may result in long-term or permanent paralysis, can occur. (5.1) (5)
• Patients taking fondaparinux sodium with risk factors for bleeding are at increased risk of hemorrhage. (5.2) (5)
• Bleeding risk is increased in renal impairment and in adult patients with low body weight less than <50 kg. (5.3, 5.4) (5)
• Thrombocytopenia can occur with administration of fondaparinux sodium. (5.5) (5)
• Periodic routine complete blood counts (including platelet counts), serum creatinine level, and stool occult blood tests are recommended. (5.6) (5)

ADVERSE REACTIONS

The most serious adverse reactions associated with the use of fondaparinux sodium are bleeding complications. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Discontinue agents that may enhance the risk of hemorrhage prior to initiation of therapy with fondaparinux sodium unless essential. If co-administration is necessary, monitor patients closely for hemorrhage. (7) (7)

USE IN SPECIFIC POPULATIONS

- Because elderly patients are more likely to have reduced renal function, fondaparinux sodium should be used with caution in these patients. (8.5)
- The risk of bleeding is increased with reduced renal or hepatic function. (8.6, 8.7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 8/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: SPINAL/EPIDURAL HEMATOMAS

Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH), heparinoids, or fondaparinux sodium and are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants**
- **a history of traumatic or repeated epidural or spinal puncture**
- **a history of spinal deformity or spinal surgery**
- **Optimal timing between the administration of fondaparinux sodium and neuraxial procedures is not known.**

Monitor patients frequently for signs and symptoms of neurologic impairment. If neurologic compromise is noted, urgent treatment is necessary.

Consider the benefit and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis *[see Warnings and Precautions (5.1) and Drug Interactions (7)].*

1 INDICATIONS AND USAGE

1.1 Prophylaxis of Deep Vein Thrombosis in Adult Patients

Fondaparinux sodium injection is indicated for the prophylaxis of deep vein thrombosis (DVT in adults), which may lead to pulmonary embolism (PE):

- in patients undergoing hip fracture surgery, including extended prophylaxis;
- in patients undergoing hip replacement surgery;
- in patients undergoing knee replacement surgery;
- in patients undergoing abdominal surgery who are at risk for thromboembolic complications.

1.2 Treatment of Acute Deep Vein Thrombosis in Adult Patients

Fondaparinux sodium injection is indicated for the treatment of acute deep vein thrombosis in adults when administered in conjunction with warfarin sodium.

1.3 Treatment of Acute Pulmonary Embolism in Adult Patients

Fondaparinux sodium injection is indicated for the treatment of acute pulmonary embolism in adults when administered in conjunction with warfarin sodium when initial therapy is administered in the hospital.

1.4 Treatment of Venous Thromboembolism in Pediatric Patients

Fondaparinux sodium injection is indicated for the treatment of venous thromboembolism (VTE) in pediatric patients aged 1 year or older weighing at least 10 kg.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosing Information

Do not mix other medications or solutions with fondaparinux sodium injection. Administer fondaparinux sodium injection only subcutaneously. Discard unused portion.

Monitor routine complete blood counts (including platelet count), serum creatinine level, and stool occult blood periodically *[see Warnings and Precautions (5.6)].*

2.2 Deep Vein Thrombosis Prophylaxis Following Hip Fracture, Hip Replacement, and Knee Replacement Surgery in Adults

In adult patients undergoing hip fracture, hip replacement, or knee replacement surgery, the recommended dose of fondaparinux sodium injection is 2.5 mg administered by subcutaneous injection once daily after hemostasis has been established. Administer the initial dose no earlier than 6 hours to 8 hours after surgery. Administration of fondaparinux sodium injection earlier than 6 hours after surgery increases the risk of major bleeding. The usual duration of therapy is 5 days to 9 days; up to 11 days of therapy was administered in clinical trials.

In patients undergoing hip fracture surgery, an extended prophylaxis course of up to 24 additional days is recommended. In patients undergoing hip fracture surgery, a total of 32 days (peri-operative and extended prophylaxis) was administered in clinical trials *[see Warnings and Precautions (5.6), Adverse Reactions (6), and Clinical Studies (14)].*

2.3 Deep Vein Thrombosis Prophylaxis Following Abdominal Surgery in Adults

In adult patients undergoing abdominal surgery, the recommended dose of fondaparinux sodium injection is 2.5 mg administered by subcutaneous injection once daily after hemostasis has been established. Administer the initial dose no earlier than 6 hours to 8 hours after surgery. Administration of fondaparinux sodium injection earlier than 6 hours after surgery increases the risk of major bleeding. The usual duration of administration is 5 days to 9 days, and up to 10 days of fondaparinux sodium injection was administered in clinical trials.

2.4 Deep Vein Thrombosis and Pulmonary Embolism Treatment in Adults

In adult patients with acute symptomatic DVT and in patients with acute symptomatic PE, the recommended dose of fondaparinux sodium injection is 5 mg (body weight less than 50 kg), 7.5 mg (body weight 50 kg to 100 kg), or 10 mg (body weight greater than 100 kg) by subcutaneous injection once daily (fondaparinux sodium treatment regimen). Initiate concomitant treatment with warfarin sodium as soon as possible, usually within 72 hours. Continue treatment with fondaparinux sodium injection for at least 5 days and until a therapeutic oral anticoagulant effect is established (INR 2 to 3). The usual duration of administration of fondaparinux sodium injection is 5 days to 9 days; up to 26 days of fondaparinux sodium injection was administered in clinical trials *[see Warnings and*

Precautions (5.6), Adverse Reactions (6), and Clinical Studies (14)].

2.5 Venous Thromboembolism Treatment in Pediatric Patients Aged 1 Year or Older Weighing at Least 10 kg

For patients weighing 10 kg to 20 kg, the recommended initial dose is 0.1 mg/kg subcutaneously once daily. There is no available prefilled syringe for patients in this weight range, and a patient specific dose should be prepared (see section 2.8 Instructions for Preparation of Individual Pediatric Doses in Pharmacies). The dose should be exact and rounded to the nearest 0.1 mg (see Table 1).

Table 1: Recommended Initial Dose of Fondaparinux Sodium Injection for Treatment of VTE in Pediatric Patients Weighing 10 kg to 20 kg

Body Weight (kg)	Initial Dose
10 kg to 20 kg	Dosing should be exact and rounded to the nearest 0.1 mg

For patients weighing over 20 kg, the recommended initial dose is 0.1 mg/kg subcutaneously once daily with doses rounded to the nearest prefilled syringe according to Table 2.

There is no available information for dosing pediatric patients who weigh less than 10 kg.

Table 2: Recommended Prefilled Syringe Selection for Initial Dose of Fondaparinux Sodium Injection for Treatment of VTE in Pediatric Patients Weighing More Than 20 kg

Body Weight (kg)	**Prefilled Syringe Selection**
Greater than 20 kg to 40 kg*	2.5 mg/0.5 mL
Greater than 40 kg to 60 kg*	5 mg/0.4 mL
Greater than 60 kg*	7.5 mg/0.6 mL

*Whenever possible, patients weighing more than 20 kg should receive a full prefilled syringe for dosing. If therapeutic levels are not achievable using the prefilled syringe available strengths and dose adjustments are needed, a patient specific dose may be prepared (see section 2.8 Instructions for Preparation of Individual Pediatric Doses in Pharmacies).

Monitor fondaparinux levels 2 hours to 4 hours after the second or third dose and then

weekly for a month followed by every 1 month to 3 months for the duration of treatment using a fondaparinux-based anti-Xa assay with a therapeutic goal range of 0.5 mg/L to 1 mg/L.
Dosing adjustments may be necessary to achieve peak blood concentration within the therapeutic target of 0.5 mg/L to 1 mg/L (see Table 3). Do not exceed the maximum dose of 7.5 mg/day.

Table 3: Recommended Dose Adjustments

Fondaparinux-Based Anti-Xa Level (mg/L)	**Dose Adjustment**
Less than 0.3 mg/L	Increase dose by 0.03 mg/kg*
0.3 mg/L to 0.49 mg/L	Increase dose by 0.01 mg/kg*
0.5 mg/L to 1 mg/L	No change
1.01 mg/L to 1.2 mg/L	Decrease dose by 0.01 mg/kg*
Greater than 1.2 mg/L	Decrease dose by 0.03 mg/kg*

*Adjust the dose to the nearest 0.1 mg.

There is no adequate data to support the use of fondaparinux sodium injection in pediatric patients below 1 year of age.

2.6 Hepatic Impairment

No dose adjustment is recommended in patients with mild to moderate hepatic impairment, based upon single-dose pharmacokinetic data. Pharmacokinetic data are not available for patients with severe hepatic impairment. Patients with hepatic impairment may be particularly vulnerable to bleeding during fondaparinux sodium injection therapy. Observe these patients closely for signs and symptoms of bleeding *[see Clinical Pharmacology (12.4)]*.

2.7 Instructions for Use for Prefilled Syringe

Fondaparinux sodium injection is provided in a single-dose, prefilled syringe affixed with an automatic needle protection system. Fondaparinux sodium injection is administered by subcutaneous injection. It must not be administered by intramuscular injection. Fondaparinux sodium injection is intended for use under a physician's guidance. Patients may self-inject only if their physician determines that it is appropriate and the patients are trained in subcutaneous injection techniques.

Prior to administration, visually inspect fondaparinux sodium injection to ensure the solution is clear and free of particulate matter. **The following instructions are specific to the Hypak ™SCF ™injection system and may differ from the directions for other injection systems.**

To avoid the loss of drug when using the prefilled syringe, do not expel the air bubble from the syringe before the injection. Administration should be made in the fatty tissue, alternating injection sites (e.g., between the left and right anterolateral or the left and right posterolateral abdominal wall).

To administer fondaparinux sodium injection:

1. Wipe the surface of the injection site with an alcohol swab.

2. Hold the syringe with either hand and use your other hand to pull the rigid needle shield straight off the needle (**Figure 1**). Discard the needle shield.

3. Do not try to remove the air bubbles from the syringe before giving the injection.

4. Pinch a fold of skin at the injection site between your thumb and forefinger and hold it throughout the injection.

5. Hold the syringe with your thumb on the top pad of the plunger rod and your next 2 fingers on the finger grips on the syringe barrel. Pay attention to avoid sticking yourself with the exposed needle (**Figure 2**).

Figure 1

Figure 2

6. Insert the full length of the syringe needle perpendicularly into the skin fold held between the thumb and forefinger **(Figure 3)**.

7. Push the plunger to the bottom of the syringe. This will ensure you have injected all the contents of the syringe **(Figure 4)**.

Figure 3

Figure 4

8. Remove the syringe from the injection site keeping your finger on the plunger. Orient

the needle away from you and others, and activate the safety shield by firmly pushing the plunger (**Figure 5**). The protective sleeve will automatically cover the needle and an audible “click” will be heard to confirm shield activation (**Figure 6**). Once safety shield is activated, discard the syringe into the sharps container.

Figure 5

Figure 6

9. You will know that the syringe has worked when:
- The needle is pulled back into the security sleeve and the spring expands fully.
- You may also hear or feel a soft click when the plunger rod is released fully.

2.8 Instructions for Preparation of Individual Pediatric Doses in Pharmacies

For pediatric patients weighing 10 kg to 20 kg, a patient-specific dose may be prepared by a pharmacist under aseptic conditions per the instructions below.
These instructions may also be used to prepare pediatric patient-specific doses for patients weighing over 20 kg when dose adjustments are needed and therapeutic levels are not achievable using the prefilled syringe available strengths.
Prior to preparing fondaparinux sodium injection, visually inspect fondaparinux sodium prefilled syringe to ensure the solution is clear and free of particulate matter.
General Aseptic Preparation Practices
Strictly observe aseptic technique when preparing patient specific pediatric doses of fondaparinux sodium injection. To prevent accidental contamination, prepare fondaparinux sodium injection according to aseptic standards, including but not limited to:
• Prepare fondaparinux sodium injection in an ISO Class 5 laminar airflow (LAF) hood
• Ensure that the dose preparation area, including the LAF hood, has appropriate environmental specifications, confirmed by periodic monitoring.
• Ensure that personnel are appropriately trained in aseptic manipulations of sterile products.
• Ensure that personnel wear appropriate clothing and gloves.
• Ensure that gloves and surfaces are disinfected.
All steps should be completed in accordance with aseptic techniques:
1. Determine the total dose and volume per the duration, and the appropriate number of fondaparinux sodium injection prefilled syringes. One fondaparinux sodium injection prefilled syringe is used in cases where the total required dose is less than 0.5 mL. Where the total dose required is greater than or equal to 0.5 mL, only two fondaparinux

sodium injection prefilled syringes may be pooled together. The maximum number of fondaparinux sodium injection prefilled syringes that may be pooled together is two. Do not combine fondaparinux sodium injection prefilled syringes of different concentrations in one injection to give the prescribed dose.
2. Gather the required supplies including the appropriate fondaparinux sodium injection prefilled syringe(s), a sterile, closed/sealed, empty glass vial (recommended 5 mL), and required number of suitable sized graduated tuberculin sterile syringes with 27 gauge x ½" staked needles or sterile needles (if not pre-attached to syringe).
3. Verify the required supplies are correct and within expiry date. Ensure only the materials required for the preparation are present in the work area.
4. While wearing sterile gloves, clean the LAF hood and wipe it down with sterile 70% alcohol. Ensure the LAF hood is within specification and continually monitored.
5. Ensure equipment and consumables are cleaned with isopropyl alcohol (IPA).
6. Before transferring into the LAF hood, clean all supplies including ancillary items (such as vial holder jigs, syringe cap holder jigs, sharps containers) with IPA.
7. Perform all the dose preparation steps within the LAF hood.
8. Pre-sterilize gloves with IPA. While wearing sterile gloves, hold the fondaparinux sodium injection prefilled syringe with either gloved hand and use your other gloved hand to twist the rigid needle guard (covers the needle) counter-clockwise. Pull the rigid needle guard straight off the needle. Discard the needle guard.
9. Dispense the full contents of the fondaparinux sodium injection prefilled syringe into the vial by fully depressing the plunger.
10. When you have injected all the contents of the fondaparinux sodium injection prefilled syringe, the plunger should be released. The plunger will then rise automatically while the needle retracts into the security sleeve. Discard the fondaparinux sodium injection prefilled syringe into a sharps container.
11. Take an empty graduated tuberculin sterile syringe and attach a suitable sterile needle if not already supplied pre-attached.
12. Remove needle cap.
13. Withdraw required dose from vial into the tuberculin syringe.
14. Replace needle cap over the needle. Clean the external surfaces of the filled tuberculin syringe with IPA.
15. Repeat steps 11 to 14 as required for the appropriate number of tuberculin syringes necessary for the patient.
16. Label each fondaparinux sodium injection tuberculin syringe with patient specific information (e.g., dosing instructions, patient information), storage information (e.g., store refrigerated between 36°F to 46°F (2°C to 8°C), do not freeze, and the beyond use date). The beyond use date should be the earlier of the product expiration date of the fondaparinux sodium injection prefilled syringe or 30 days after preparation of the tuberculin syringe.
17. Prepared tuberculin syringes may be dispensed in an empty plastic bag. Include Patient Information and Instructions for Use for the tuberculin syringe within the plastic bag to be dispensed to patients. They may be stored at refrigerated temperatures between 36°F to 46°F (2°C to 8°C) for up to the beyond use date. Do not freeze.
Do not store the pediatric preparations at room temperature as they are growth promoting at room temperature.
Discard unused portion.

3 DOSAGE FORMS AND STRENGTHS

Injection: Single-dose, prefilled syringes containing clear and colorless to slightly yellow

liquid containing either 2.5 mg/0.5 mL, 5 mg/0.4 mL, 7.5 mg/0.6 mL, or 10 mg/0.8 mL of fondaparinux sodium.

4 CONTRAINDICATIONS

Fondaparinux sodium injection is contraindicated in the following conditions:

• Severe renal impairment (creatinine clearance [CrCl] less than 30 mL/min) *[see Warnings and Precautions (5.3) and Use in Specific Populations (8.6)].*

• Active major bleeding.

• Bacterial endocarditis.

• Thrombocytopenia associated with a positive in vitro test for anti-platelet antibody in the presence of fondaparinux sodium.

• Body weight less than 50 kg (venous thromboembolism [VTE] prophylaxis in adults only) *[see Warnings and Precautions (5.4)]*.

• History of serious hypersensitivity reaction (e.g., angioedema, anaphylactoid/anaphylactic reactions) to fondaparinux sodium.

5 WARNINGS AND PRECAUTIONS

5.1 Neuraxial Anesthesia and Post-operative Indwelling Epidural Catheter Use

Spinal or epidural hematomas, which may result in long-term or permanent paralysis, can occur with the use of anticoagulants and neuraxial (spinal/epidural) anesthesia or spinal puncture. The risk of these events may be higher with post-operative use of indwelling epidural catheters or concomitant use of other drugs affecting hemostasis such as NSAIDs *[see Boxed Warning]*. In the postmarketing experience, epidural or spinal hematoma has been reported in association with the use of fondaparinux sodium by subcutaneous (SC) injection. Optimal timing between the administration of fondaparinux sodium and neuraxial procedures is not known. Monitor patients undergoing these procedures for signs and symptoms of neurologic impairment such as midline back pain, sensory and motor deficits (numbness, tingling, or weakness in lower limbs), and bowel or bladder dysfunction. Consider the potential risks and benefits before neuraxial intervention in patients anticoagulated or who may be anticoagulated for thromboprophylaxis.

5.2 Hemorrhage

Fondaparinux sodium increases the risk of hemorrhage in patients at risk for bleeding, including conditions such as congenital or acquired bleeding disorders, active ulcerative and angiodysplastic gastrointestinal disease, hemorrhagic stroke, uncontrolled arterial hypertension, diabetic retinopathy, or shortly after brain, spinal, or ophthalmological surgery. Cases of elevated aPTT temporally associated with bleeding events have been reported following administration of fondaparinux sodium (with or without concomitant administration of other anticoagulants) *[see Adverse Reactions (6.2)].*

Conditions associated with increased bleeding in pediatric patients include systemic lupus erythematosus, Wilms tumor, antiphospholipid syndrome, antithrombin III deficiency, Factor V Leiden, malignancy, pancytopenia, indwelling chest tubes,

thoracotomy, invasive infections, hypertensive encephalopathy, intestinal lymphangiectasia and von Willebrand disease.

Do not administer agents that enhance the risk of hemorrhage with fondaparinux sodium unless essential for the management of the underlying condition, such as vitamin K antagonists for the treatment of VTE. If co-administration is essential, closely monitor patients for signs and symptoms of bleeding.

Do not administer the initial dose of fondaparinux sodium earlier than 6 to 8 hours after surgery. Administration earlier than 6 hours after surgery increases risk of major bleeding *[see Dosage and Administration (2) and Adverse Reactions (6.1)]*.

5.3 Renal Impairment and Bleeding Risk in Adult Patients

Fondaparinux sodium increases the risk of bleeding in adult patients with impaired renal function due to reduced clearance *[see Clinical Pharmacology (12.4)].*

The incidence of major bleeding by renal function status reported in clinical trials of adult patients receiving fondaparinux sodium for VTE surgical prophylaxis is provided in Table 4. In these patient populations, the following is recommended:

• Do not use fondaparinux sodium for VTE prophylaxis and treatment in patients with CrCl less than 30 mL/min *[see Contraindications (4)]*.

• Fondaparinux sodium may cause prolonged anticoagulation in patients with CrCl 30 mL/min to 50 mL/min.

Table 4: Incidence of Major Bleeding in Adult Patients Treated with Fondaparinux Sodium by Renal Function Status for Surgical Prophylaxis and Treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

Population	**Timing of Dose**	**Degree of Renal Impairment**			
		Normal % (n/N)	**Mild % (n/N)**	**Moderate % (n/N)**	**Severe % (n/N)**
CrCl (mL/min)		**Greaterthan or equal to 80**	**Greaterthan or equal to 50 to less than 80**	**Greaterthan or equal to 30 to less than 50**	**Less than 30**
Orthopedic surgery [a]	Overall	1.6% (25/1,565)	2.4% (31/1,288)	3.8% (19/504)	4.8% (4/83)
	6 hours to 8 hours after surgery	1.8% (16/905)	2.2% (15/675)	2.3% (6/265)	0% (0/40)
Abdominal surgery	Overall	2.1% (13/606)	3.6% (22/613)	6.7% (12/179)	7.1% (1/14)
	6 hours to 8 hours after surgery	2.1% (10/467)	3.3% (16/481)	5.8% (8/137)	7.7% (1/13)
DVT and PE Treatment		0.4% (4/1,132)	1.6% (12/733)	2.2% (7/318)	7.3% (4/55)

CrCl = creatinine clearance.
[a] Hip fracture, hip replacement, and knee replacement surgery prophylaxis.

CrCl=creatinine clearance.

[a]Hip fracture, hip replacement, and knee replacement surgery prophylaxis.

Assess renal function periodically in patients receiving fondaparinux sodium. Discontinue the drug immediately in patients who develop severe renal impairment while on therapy. After discontinuation of fondaparinux sodium, its anticoagulant effects may persist for 2 days to 4 days in patients with normal renal function (i.e., at least 3 to 5 half-lives). The anticoagulant effects of fondaparinux sodium may persist even longer in patients with renal impairment *[see Clinical Pharmacology (12.4)]*.

5.4 Body Weight Less than 50 kg and Bleeding Risk in Adults

Fondaparinux sodium increases the risk for bleeding in adults who weigh less than 50 kg, compared to adults with higher weights.

In adults who weigh less than 50 kg:

• Do not administer fondaparinux sodium as prophylactic therapy for adults undergoing hip fracture, hip replacement, or knee replacement surgery and abdominal surgery *[see Contraindications (4)].*

In randomized clinical trials of VTE prophylaxis in adults during the peri-operative period following hip fracture, hip or knee replacement surgery, and abdominal surgery, major bleeding occurred at a higher rate among adults with a body weight less than 50 kg compared to those with a body weight greater than 50 kg (5.4% versus 2.1% in adults undergoing hip fracture, hip replacement, or knee replacement surgery; 5.3% versus 3.3% in adults undergoing abdominal surgery).

5.5 Thrombocytopenia

Thrombocytopenia can occur with the administration of fondaparinux sodium. Thrombocytopenia of any degree should be monitored closely. Discontinue fondaparinux sodium if the platelet count falls below 100,000/mm3. Moderate thrombocytopenia (platelet counts between 100,000/mm3 and 50,000/mm3) occurred at a rate of 3% in patients given fondaparinux sodium 2.5 mg in the peri-operative hip fracture, hip replacement, or knee replacement surgery and abdominal surgery clinical trials. Severe thrombocytopenia (platelet counts less than 50,000/mm3) occurred at a rate of 0.2% in patients given fondaparinux sodium 2.5 mg in these clinical trials. During extended prophylaxis, no cases of moderate or severe thrombocytopenia were reported.

Moderate thrombocytopenia occurred at a rate of 0.5% in patients given the fondaparinux sodium treatment regimen in the DVT and PE treatment clinical trials. Severe thrombocytopenia occurred at a rate of 0.04% in patients given the fondaparinux sodium treatment regimen in the DVT and PE treatment clinical trials.

Occurrences of thrombocytopenia with thrombosis that manifested similar to heparin-induced thrombocytopenia have been reported with the use of fondaparinux sodium in postmarketing experience *[see Adverse Reactions (6.2)].*

5.6 Monitoring: Laboratory Tests

Routine coagulation tests such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) are relatively insensitive measures of the activity of fondaparinux sodium and international standards of heparin or LMWH are not

calibrators to measure anti-Factor Xa activity of fondaparinux sodium. If unexpected changes in coagulation parameters or major bleeding occur during therapy with fondaparinux sodium, discontinue fondaparinux sodium. In postmarketing experience, occurrences of aPTT elevations have been reported following administration of fondaparinux sodium *[see Adverse Reactions (6.2)].*

Periodic routine complete blood counts (including platelet count), serum creatinine level, and stool occult blood tests are recommended during the course of treatment with fondaparinux sodium.

The anti-Factor Xa activity of fondaparinux sodium can be measured by anti-Xa assay using the appropriate calibrator (fondaparinux). The activity of fondaparinux sodium is expressed in milligrams (mg) of the fondaparinux and cannot be compared with activities of heparin or low molecular weight heparins *[see Clinical Pharmacology (12.2, 12.3)].*

6 ADVERSE REACTIONS

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

- Spinal or epidural hematomas *[see Warnings and Precautions (5.1)]*
- Hemorrhage *[see Warnings and Precautions (5.2)]*
- Renal impairment and bleeding risk *[see Warnings and Precautions (5.3)]*
- Body weight less than 50 kg and bleeding risk *[see Warnings and Precautions (5.4)]*
- Thrombocytopenia *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

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

Clinical Trials Experience in Adults

The adverse reaction information below is based on data from 8,877 patients exposed to fondaparinux sodium in controlled trials of hip fracture, hip replacement, major knee, or abdominal surgeries, and DVT and PE treatment.

Hemorrhage

During administration of fondaparinux sodium, the most common adverse reactions were bleeding complications *[see Warnings and Precautions (5.2)].*

Hip Fracture, Hip Replacement, and Knee Replacement Surgery

The rates of major bleeding events reported during 3 active-controlled peri-operative VTE prophylaxis trials with enoxaparin sodium in hip fracture, hip replacement, or knee replacement surgery (N = 3,616) and in an extended VTE prophylaxis trial (n = 327) with fondaparinux sodium 2.5 mg are provided in Table 5.

Table 5: Bleeding Across Randomized, Controlled Hip Fracture, Hip Replacement, and Knee Replacement Surgery Studies

	Peri-Operative Prophylaxis (Day 1 to Day 7 ± 1 post- surgery)		Extended Prophylaxis (Day 8 to Day 28 ± 2 post- surgery)	
	Fondaparinux Sodium 2.5 mg subcutaneously once daily N = 3,616	**EnoxaparinSodium [a, b]** N = 3,956	**Fondaparinux Sodium 2.5 mg subcutaneously once daily** N = 327	**Placebo subcutaneouslyonce daily** N = 329
Major bleeding [c]	96 (2.7%)	75 (1.9%)	8 (2.4%)	2 (0.6%)
Hip fracture	18/831 (2.2%)	19/842 (2.3%)	8/327 (2.4%)	2/329 (0.6%)
Hip replacement	67/2,268 (3.0%)	55/2,597 (2.1%)	—	—
Knee replacement	11/517 (2.1%)	1/517 (0.2%)	—	—
Fatal bleeding	0 (0%)	1 (less than 0.1%)	0 (0%)	0 (0%)
Non-fatal bleeding at critical site	0 (0%)	1 (less than 0.1%)	0 (0%)	0 (0%)
Re-operation due to bleeding	12 (0.3%)	10 (0.3%)	2 (0.6%)	2 (0.6%)
BI greater than or equal to 2 [d]	84 (2.3%)	63 (1.6%)	6 (1.8%)	0 (0%)
Minor bleeding [e]	109 (3%)	116 (2.9%)	5 (1.5%)	2 (0.6%)

[a] Enoxaparin sodium dosing regimen: 30 mg every 12 hours or 40 mg once daily.

[b] Not approved for use in patients undergoing hip fracture surgery.

[c] Major bleeding was defined as clinically overt bleeding that was (1) fatal, (2) bleeding at critical site (e.g., intracranial, retroperitoneal, intraocular, pericardial, spinal, or into adrenal gland), (3) associated with re-operation at operative site, or (4) with a bleeding index (BI) greater than or equal to 2.

[d] BI greater than or equal to 2: Overt bleeding associated only with a bleeding index (BI) greater than or equal to 2 calculated as [number of whole blood or packed red blood cell units transfused + [(pre-bleeding) – (post-bleeding)] hemoglobin (g/dL) values].

[e] Minor bleeding was defined as clinically overt bleeding that was not major.

A separate analysis of major bleeding across all randomized, controlled, peri-operative, prophylaxis clinical studies of hip fracture, hip replacement, or knee replacement surgery according to the time of the first injection of fondaparinux sodium after surgical closure was performed in patients who received fondaparinux sodium only post-operatively. In this analysis, the incidences of major bleeding were as follows: less than 4 hours was 4.8% (5/104), 4 to 6 hours was 2.3% (28/1,196), 6 to 8 hours was 1.9% (38/1,965). In all studies, the majority (greater than or equal to 75%) of the major

bleeding events occurred during the first 4 days after surgery.

Abdominal Surgery

In a randomized study of patients undergoing abdominal surgery, fondaparinux sodium 2.5 mg once daily (n = 1,433) was compared with dalteparin 5,000 IU once daily (n = 1,425). Bleeding rates are shown in Table 6.

Table 6: Bleeding in the Abdominal Surgery Study

	Fondaparinux Sodium2.5 mg subcutaneously once daily	**Dalteparin Sodium 5,000 IU subcutaneously once daily**
	N = 1,433	N = 1,425
Major bleeding [a]	49 (3.4%)	34 (2.4%)
Fatal bleeding	2 (0.1%)	2 (0.1%)
Non-fatal bleeding at critical site	0 (0%)	0 (0%)
Other non-fatal major bleeding Surgical site Non-surgical site	38 (2.7%) 9 (0.6%)	26 (1.8%) 6 (0.4%)
Minor bleeding [b]	31 (2.2%)	23 (1.6%)

[a] Major bleeding was defined as bleeding that was (1) fatal, (2) bleeding at the surgical site leading to intervention, (3) non-surgical bleeding at a critical site (e.g. intracranial, retroperitoneal, intraocular, pericardial, spinal, or into adrenal gland), or leading to an intervention, and/or with a bleeding index (BI) greater than or equal to 2.

[b] Minor bleeding was defined as clinically overt bleeding that was not major.

The rates of major bleeding according to the time interval following the first injection of fondaparinux sodium were as follows: less than 6 hours was 3.4% (9/263) and 6 hours to 8 hours was 2.9% (32/1,112).

Treatment of Deep Vein Thrombosis and Pulmonary Embolism

The rates of bleeding events reported during a dose-response trial (n = 111) and an active- controlled trial with enoxaparin sodium in DVT treatment (n = 1,091) and an active-controlled trial with heparin in PE treatment (n = 1,092) with fondaparinux sodium are provided in Table 7.

Table 7: Bleeding [a] in Deep Vein Thrombosis and Pulmonary Embolism Treatment Studies

	Fondaparinux Sodium N = 2,294	**Enoxaparin Sodium** N = 1,101	**HeparinaPTT adjusted IV** N = 1,092
Major bleeding [b]	28 (1.2%)	13 (1.2%)	12 (1.1%)
Fatal bleeding	3 (0.1%)	0 (0%)	1 (0.1%)
Non-fatal bleeding at a critical site	3 (0.1%)	0 (0%)	2 (0.2%)
Intracranial bleeding	3 (0.1%)	0 (0%)	1 (0.1%)
Retro-peritoneal bleeding	0 (0%)	0 (0%)	1 (0.1%)

Other clinically overt bleeding [c]	22 (1%)	13 (1.2%)	10 (0.9%)
Minor bleeding [d]	70 (3.1%)	33 (3%)	57 (5.2%)

[a] Bleeding rates are during the study drug treatment period (approximately 7 days). Patients were also treated with vitamin K antagonists initiated within 72 hours after the first study drug administration.

[b] Major bleeding was defined as clinically overt: – and/or contributing to death – and/or in a critical organ including intracranial, retroperitoneal, intraocular, spinal, pericardial, or adrenal gland – and/or associated with a fall in hemoglobin level greater than or equal to 2 g/dL – and/or leading to a transfusion greater than or equal to 2 units of packed red blood cells or whole blood.

[c] Clinically overt bleeding with a 2 g/dL fall in hemoglobin and/or leading to transfusion of PRBC or whole blood greater than or equal to 2 units.

[d] Minor bleeding was defined as clinically overt bleeding that was not major.

Local Reactions

Local irritation (injection site bleeding, rash, and pruritus) has occurred following subcutaneous injection of fondaparinux sodium.

Elevations of Serum Aminotransferases

In the peri-operative prophylaxis randomized clinical trials of 7 ± 2 days, asymptomatic increases in aspartate (AST) and alanine (ALT) aminotransferase levels greater than 3 times the upper limit of normal were reported in 1.7% and 2.6% of patients, respectively, during treatment with fondaparinux sodium 2.5 mg once daily versus 3.2% and 3.9% of patients, respectively, during treatment with enoxaparin sodium 30 mg every 12 hours or 40 mg once daily enoxaparin sodium. These elevations are reversible and may be associated with increases in bilirubin. In the extended prophylaxis clinical trial, no significant differences in AST and ALT levels between fondaparinux sodium 2.5 mg and placebo-treated patients were observed.

In the DVT and PE treatment clinical trials, asymptomatic increases in AST and ALT levels greater than 3 times the upper limit of normal of the laboratory reference range were reported in 0.7% and 1.3% of patients, respectively, during treatment with fondaparinux sodium. In comparison, these increases were reported in 4.8% and 12.3% of patients, respectively, in the DVT treatment trial during treatment with enoxaparin sodium 1 mg/kg every 12 hours and in 2.9% and 8.7% of patients, respectively, in the PE treatment trial during treatment with aPTT adjusted heparin.

Since aminotransferase determinations are important in the differential diagnosis of myocardial infarction, liver disease, and pulmonary emboli, elevations that might be caused by drugs like fondaparinux sodium should be interpreted with caution.

Other Adverse Reactions

Other adverse reactions that occurred during treatment with fondaparinux sodium in clinical trials with patients undergoing hip fracture, hip replacement, or knee replacement surgery are provided in Table 8.

Table 8: Adverse Reactions Across Randomized, Controlled, Hip Fracture Surgery, Hip Replacement Surgery, and Knee Replacement Surgery Studies

Adverse Reactions	Peri-Operative Prophylaxis (Day 1 to Day 7 ± 1 post-surgery)		Extended Prophylaxis (Day 8 to Day 28 ± 2 post-surgery)	
	Fondaparinux Sodium 2.5 mg subcutaneously once daily	EnoxaparinSodium [a, b]	Fondaparinux Sodium 2.5 mg subcutaneously once daily	Placebo subcutaneouslyonce daily
	N = 3,616	N = 3,956	N = 327	N = 329
Anemia	707 (19.6%)	670 (16.9%)	5 (1.5%)	4 (1.2%)
Insomnia	179 (5%)	214 (5.4%)	3 (0.9%)	1 (0.3%)
Wound drainage increased	161 (4.5%)	184 (4.7%)	2 (0.6%)	0 (0%)
Hypokalemia	152 (4.2%)	164 (4.1%)	0 (0%)	0 (0%)
Dizziness	131 (3.6%)	165 (4.2%)	2 (0.6%)	0 (0%)
Purpura	128 (3.5%)	137 (3.5%)	0 (0%)	0 (0%)
Hypotension	126 (3.5%)	125 (3.2%)	1 (0.3%)	0 (0%)
Confusion	113 (3.1%)	132 (3.3%)	4 (1.2%)	1 (0.3%)
Bullous eruption [c]	112 (3.1%)	102 (2.6%)	0 (0%)	1 (0.3%)
Hematoma	103 (2.8%)	109 (2.8%)	7 (2.1%)	1 (0.3%)
Post-operative hemorrhage	85 (2.4%)	69 (1.7%)	2 (0.6%)	2 (0.6%)

[a] Enoxaparin sodium dosing regimen: 30 mg every 12 hours or 40 mg once daily.

[b] Not approved for use in patients undergoing hip fracture surgery.

[c] Localized blister coded as bullous eruption.

The most common adverse reaction in the abdominal surgery trial was post-operative wound infection (4.9%), and the most common adverse reaction in the VTE treatment trials was epistaxis (1.3%).

Clinical Trials Experience in Pediatric Patients

Safety data for use of fondaparinux sodium in the treatment of VTE in pediatric patients aged 1 year or older is available from Study FDPX-IJS-7001. In Study FDPX-IJS-7001 (n = 366), the median duration of treatment with fondaparinux sodium injection, including fondaparinux sodium, was 85 days (range 1 day to 3,768 days).

The incidence of major bleeding events, defined as per the ISTH criteria, was the primary safety outcome of interest in Study FDPX-IJS-7001. Seven patients (1.9%) had composite major bleeding events: 1 patient (0.3%) had clinically overt bleeding (associated with a decrease in hemoglobin of at least 20 g/L (2 g/dL) in a 24-hour period), 3 patients (0.8%) had bleeding that was retroperitoneal, pulmonary, intracranial, or otherwise involved the central nervous system, and 3 patients (0.8%) had major bleeding that required surgical intervention in an operating suite. Major bleeding events resulted in the interruption of fondaparinux sodium injection treatment for 4 patients and the discontinuation of fondaparinux sodium injection for 3 patients. All major

bleeding events were reported in patients between the ages of greater than or equal to 2 years to less than 18 years.

Eleven patients (3%) had non-major bleeding events: 8 patients (2.2%) had overt bleeding for which a blood product was administered, and which was not directly attributable to the patient's underlying medical condition and 4 patients (1.1%) had bleeding that required medical or surgical intervention to restore hemostasis other than in an operating room. All non-major bleeding events warranted either interruption or withdrawal of fondaparinux sodium injection treatment except for 1 patient for whom the action taken with fondaparinux was not reported. All non-major bleeding events were reported in patients between the ages of greater than or equal to 2 years to less than 18 years.

Overall, 65 patients (18%) had composite minor bleeding events: 64 patients (18%) had overt or macroscopic evidence of bleeding that did not fulfill the criteria for either major bleeding or clinically relevant, non-major bleeding and two patients (0.5%) had non-major menstrual bleeding which resulted in a medical consultation and/or intervention.

Other Adverse Reactions

Other adverse reactions that occurred during treatment with fondaparinux sodium injection in pediatric studies included: anemia, thrombocytopenia, allergic reactions, generalized skin associated events, abnormal liver function, hypokalemia, and hypotension.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of fondaparinux sodium. 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.

In the postmarketing experience, epidural or spinal hematoma has been reported in association with the use of fondaparinux sodium by subcutaneous (SC) injection *[see Warnings and Precautions (5.1)]*. Occurrences of thrombocytopenia with thrombosis that manifested similar to heparin- induced thrombocytopenia have been reported in the postmarketing experience and cases of elevated aPTT temporally associated with bleeding events have been reported following administration of fondaparinux sodium (with or without concomitant administration of other anticoagulants) *[see Warnings and Precautions (5.5)]*.

Serious allergic reactions, including angioedema, anaphylactoid/anaphylactic reactions have been reported with the use of fondaparinux sodium *[see Contraindications (4)]*.

Elevations of hepatic transaminases have been reported in pediatric patients with elevations greater than 10x ULN.

7 DRUG INTERACTIONS

In clinical studies performed with fondaparinux sodium, the concomitant use of oral anticoagulants (warfarin sodium), platelet inhibitors (acetylsalicylic acid), NSAIDs (piroxicam), and digoxin did not significantly affect the pharmacokinetics/pharmacodynamics of fondaparinux sodium. In addition, fondaparinux sodium neither influenced the pharmacodynamics of warfarin sodium, acetylsalicylic acid, piroxicam, and digoxin, nor the pharmacokinetics of digoxin at

steady state.

Agents that may enhance the risk of hemorrhage should be discontinued prior to initiation of therapy with fondaparinux sodium unless these agents are essential. If co-administration is necessary, monitor patients closely for hemorrhage *[see Warnings and Precautions (5.2)]*.

In an in vitro study in human liver microsomes, inhibition of CYP2A6 hydroxylation of coumarin by fondaparinux (200 micromolar i.e., 350 mg/L) was 17% to 28%. Inhibition of the other isozymes evaluated (CYPs 1A2, 2C9, 2C19, 2D6, 3A4, and 3E1) was 0% to 16%. Since fondaparinux does not markedly inhibit CYP450s (CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A4) in vitro, fondaparinux sodium is not expected to significantly interact with other drugs in vivo by inhibition of metabolism mediated by these isozymes.

Since fondaparinux sodium does not bind significantly to plasma proteins other than ATIII, no drug interactions by protein-binding displacement are expected.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from published literature and postmarketing reports have not reported a clear association with fondaparinux sodium and adverse developmental outcomes. Fondaparinux sodium plasma concentrations obtained from four women treated with fondaparinux sodium during pregnancy and their newborn infants demonstrated low placental transfer of fondaparinux sodium *(see Data)*. There are risks to the mother associated with untreated venous thromboembolism in pregnancy and a risk of hemorrhage in the mother and fetus associated with use of anticoagulants *(see Clinical Considerations)*. In animal reproduction studies, there was no evidence of adverse developmental outcomes when fondaparinux sodium was administered to pregnant rats and rabbits during organogenesis at doses 32 times and 65 times, respectively, the recommended human dose based on body surface area.

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.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Pregnancy confers an increased risk for thromboembolism that is higher for women with underlying thromboembolic disease and certain high-risk pregnancy conditions. Published data describe that women with a previous history of venous thrombosis are at high risk for recurrence during pregnancy.

Fetal/Neonatal Adverse Reactions

Fondaparinux sodium has been demonstrated to cross the placenta in humans *(see Data)*. Use of anticoagulants, including fondaparinux sodium, may increase the risk of

bleeding in the fetus and neonate. Monitor neonates for bleeding *[see Warnings and Precautions (5.2, 5.4, 5.6)]*.

Labor or Delivery

All patients receiving anticoagulants, including pregnant women, are at risk for bleeding. Fondaparinux sodium use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Pregnant women receiving fondaparinux sodium should be carefully monitored for evidence of bleeding or unexpected changes in coagulation parameters. Consideration for use of a shorter acting anticoagulant should be specifically addressed as delivery approaches *[see Warnings and Precautions (5.1, 5.6)]*.

Human Data

In a study of five pregnant women treated with fondaparinux sodium during the third trimester of pregnancy at a dose of 2.5 mg/day, four of the women had elevated anti-factor Xa activity noted in the cord blood. Anti-factor Xa clotting times in these four cases were between 37.5 seconds and 50.9 seconds. The patient who did not have elevated anti-factor Xa activity had received only one dose of fondaparinux sodium 22 hours prior to delivery. The concentration of fondaparinux sodium in umbilical cord plasma was approximately 1/10th the level of fondaparinux sodium in maternal plasma. None of the infants experienced adverse effects.

Animal Data

Embryo-fetal development studies have been conducted with fondaparinux sodium in pregnant rats at subcutaneous doses up to 10 mg/kg/day (about 32 times the recommended human dose based on body surface area) administered from days 6 to 17 of gestation and pregnant rabbits at subcutaneous doses up to 10 mg/kg/day (about 65 times the recommended human dose based on body surface area) administered from days 6 to 18 of gestation. These studies have revealed no evidence of adverse developmental outcomes when fondaparinux sodium was administered to pregnant rats and rabbits during organogenesis. Additionally, there were no effects on pre- and postnatal development in a study conducted in rats at subcutaneous doses up to 10 mg/kg/day (about 32 times the recommended human dose based on body surface area).

8.2 Lactation

Risk Summary

There are no data on the presence of fondaparinux sodium in human milk, or the effects on milk production. Limited clinical data during lactation preclude a clear determination of the risk of fondaparinux sodium to an infant during lactation; therefore, the developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for fondaparinux sodium and any potential adverse effects on the breastfed infant from fondaparinux sodium or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of fondaparinux sodium for the treatment of venous thromboembolism have been established in pediatric patients aged 1 year and older weighing at least 10 kg. Use of fondaparinux sodium for this indication is supported by evidence from adequate and well-controlled studies in adults with additional

pharmacokinetic, pharmacodynamic, safety, and efficacy data in pediatric patients aged 0.3 years and older *[see Adverse Reactions (6.1), Clinical Pharmacology (12.4), and Clinical Studies (14.8)]*. The frequency, type, and severity of adverse reactions observed were generally consistent with those observed in adults.

The safety and effectiveness of fondaparinux sodium have not been established in pediatric patients for the treatment of venous thromboembolism who are younger than 1 year old, weigh less than 10 kg, or with any category of renal or hepatic impairment.

The safety and effectiveness of fondaparinux sodium have not been established in pediatric patients for the prophylaxis of DVT and treatment of DVT or PE in conjunction with warfarin sodium.

8.5 Geriatric Use

Over 3,000 patients 65 years and older have received fondaparinux sodium in randomized clinical trials for the treatment or prophylaxis of DVT and PE. There were over 2,000 patients 65 years of age and older in the orthopedic surgery clinical studies for prophylaxis of DVT and PE *[see Clinical Studies (14)]*. Of the total number of fondaparinux sodium-treated patients in these orthopedic surgery studies, 1,111 (30.9%) were 65 years of age to 74 years of age, while 1,227 (34.2%) were 75 years of age and older. No overall differences in effectiveness of fondaparinux sodium have been observed between patients 65 years of age and older and younger adult patients. Serious adverse events were more frequent in patients 65 years of age and older. When using fondaparinux sodium in elderly patients, pay particular attention to dosing directions and concomitant medications (especially anti-platelet medication) *[see Warnings and Precautions (5.2)]*.

Fondaparinux sodium is substantially excreted by the kidney, and the risk of adverse reactions to fondaparinux sodium may be greater in patients with impaired renal function. Because geriatric patients are more likely to have decreased renal function, assess renal function prior to fondaparinux sodium administration *[see Contraindications (4), Warnings and Precautions (5.3), and Clinical Pharmacology (12.4)].*

In the peri-operative hip fracture, hip replacement, or knee replacement surgery clinical trials with patients receiving fondaparinux sodium 2.5 mg, serious adverse events increased with age for patients receiving fondaparinux sodium. The incidence of major bleeding in clinical trials of fondaparinux sodium by age is provided in Table 9.

Table 9: Incidence of Major Bleeding in Patients Treated with Fondaparinux Sodium Injection by Age

	Age		
	Less than 65 years % (n/N)	**65 years to 74 years % (n/N)**	**Greater than or equal to 75 years % (n/N)**
Orthopedic surgery [a] Extended prophylaxis	1.8% (23/1,253) 1.9% (1/52)	2.2% (24/1,111) 1.4% (1/71)	2.7% (33/1,277) 2.9% (6/204)
Abdominal surgery	3% (19/644)	3.2% (16/507)	5% (14/282)
DVT and PE	0.6% (7/1,151)	1.6% (9/560)	2.1% (12/583)

treatment			

[a]Includes hip fracture, hip replacement, and knee replacement surgery prophylaxis.

8.6 Renal Impairment

Patients with impaired renal function are at increased risk of bleeding due to reduced clearance of fondaparinux sodium *[see Contraindications (4) and Warnings and Precautions (5.3)]*. Assess renal function periodically in patients receiving fondaparinux sodium. Discontinue fondaparinux sodium immediately in patients who develop severe renal impairment while on therapy. After discontinuation of fondaparinux sodium, its anticoagulant effects may persist for 2 days to 4 days in patients with normal renal function (i.e., at least 3 to 5 half-lives). The anticoagulant effects of fondaparinux sodium may persist even longer in patients with renal impairment *[see Clinical Pharmacology (12.4)]*.

There is no adequate data to support safe and effective use of fondaparinux sodium in pediatric patients with renal impairment.

8.7 Hepatic Impairment

Following a single, subcutaneous dose of 7.5 mg of fondaparinux sodium in patients with moderate hepatic impairment (Child-Pugh Category B) compared to subjects with normal liver function, changes from baseline in aPTT, PT/INR, and antithrombin III were similar in the two groups. However, a higher incidence of hemorrhage was observed in subjects with moderate hepatic impairment than in normal subjects, especially mild hematomas at the blood sampling or injection site. The pharmacokinetics of fondaparinux have not been studied in patients with severe hepatic impairment *[see Dosage and Administration (2.6) and Clinical Pharmacology (12.4)]*. There is no adequate data to support safe and effective use of fondaparinux sodium in pediatric patients with hepatic impairment.

10 OVERDOSAGE

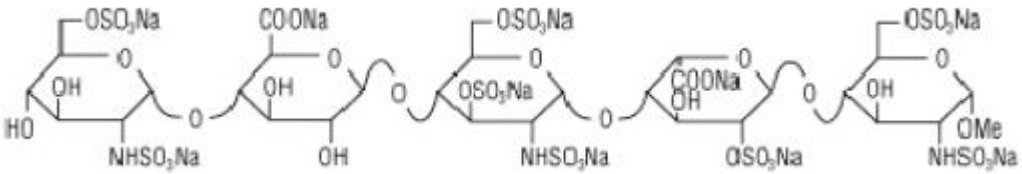
Overdose of fondaparinux sodium may lead to hemorrhagic complications. Discontinue treatment and initiate appropriate therapy if bleeding complications associated with overdosage occur. There is no known antidote for fondaparinux sodium.

Data obtained in patients undergoing chronic intermittent hemodialysis suggest that clearance of fondaparinux sodium can increase by 20% during hemodialysis.

11 DESCRIPTION

Fondaparinux sodium injection, USP is a sterile solution containing fondaparinux sodium. It is a synthetic and specific inhibitor of activated Factor X (Xa). Fondaparinux sodium is methyl O-2-deoxy-6-O-sulfo-2-(sulfoamino)-α-D-glucopyranosyl-(1→4)-O-β-D-glucopyranuronosyl-(1→4)-O-2-deoxy-3,6-di-O-sulfo-2-(sulfoamino)-α-D-glucopyranosyl-(1→4)-O-2-O- sulfo-α-L-idopyranuronosyl-(1→4)-2-deoxy-6-O-sulfo-2-(sulfoamino)-α-D-glucopyranoside, decasodium salt.

The molecular formula of fondaparinux sodium is C31H43N3Na10O49S8 and its molecular weight is 1728. The structural formula is provided below:



Fondaparinux sodium injection, USP is supplied as a sterile, preservative-free injectable solution for subcutaneous use.

Each single-dose, prefilled syringe of fondaparinux sodium injection, USP, affixed with an automatic needle protection system, contains 2.5 mg of fondaparinux sodium in 0.5 mL, 5 mg of fondaparinux sodium in 0.4 mL, 7.5 mg of fondaparinux sodium in 0.6 mL, or 10 mg of fondaparinux sodium in 0.8 mL of an isotonic solution of sodium chloride and water for injection. May also contain sodium hydroxide and/or hydrochloric acid as pH adjusters. The final drug product is a clear and colorless to slightly yellow liquid with a pH between 5 and 8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The antithrombotic activity of fondaparinux sodium is the result of antithrombin III (ATIII)-mediated selective inhibition of Factor Xa. By selectively binding to ATIII, fondaparinux sodium potentiates (about 300 times) the innate neutralization of Factor Xa by ATIII. Neutralization of Factor Xa interrupts the blood coagulation cascade and thus inhibits thrombin formation and thrombus development.

Fondaparinux sodium does not inactivate thrombin (activated Factor II) and has no known effect on platelet function. At the recommended dose, fondaparinux sodium does not affect fibrinolytic activity or bleeding time.

12.2 Pharmacodynamics

Anti-Xa Activity

The pharmacodynamics/pharmacokinetics of fondaparinux sodium are derived from fondaparinux plasma concentrations quantified via anti-Factor Xa activity. Only fondaparinux can be used to calibrate the anti-Xa assay. (The international standards of heparin or LMWH are not appropriate for this use.) As a result, the activity of fondaparinux sodium is expressed as milligrams (mg) of the fondaparinux calibrator. The anti-Xa activity of the drug increases with increasing drug concentration, reaching maximum values in approximately three hours.

12.3 Pharmacokinetics

Absorption: Fondaparinux sodium administered by subcutaneous injection is rapidly and completely absorbed (absolute bioavailability is 100%). Following a single subcutaneous dose of fondaparinux sodium 2.5 mg in young male subjects, Cmax of 0.34 mg/L is reached in approximately 2 hours. In patients undergoing treatment with fondaparinux sodium injection 2.5 mg, once daily, the peak steady-state plasma concentration is, on average, 0.39 mg/L to 0.5 mg/L and is reached approximately 3 hours post-dose. In these patients, the minimum steady-state plasma concentration is 0.14 mg/L to 0.19 mg/L. In patients with symptomatic deep vein thrombosis and pulmonary embolism

undergoing treatment with fondaparinux sodium injection 5 mg (body weight less than 50 kg), 7.5 mg (body weight 50 kg to 100 kg), and 10 mg (body weight greater than 100 kg) once daily, the body-weight-adjusted doses provide similar mean steady-state peaks and minimum plasma concentrations across all body weight categories. The mean peak steady-state plasma concentration is in the range of 1.20 mg/L to 1.26 mg/L. In these patients, the mean minimum steady-state plasma concentration is in the range of 0.46 mg/L to 0.62 mg/L.

Distribution:In healthy adults, intravenously or subcutaneously administered fondaparinux sodium distributes mainly in blood and only to a minor extent in extravascular fluid as evidenced by steady state and non-steady state apparent volume of distribution of 7 L to 11 L. Similar fondaparinux distribution occurs in patients undergoing elective hip surgery or hip fracture surgery. In vitro, fondaparinux sodium is highly (at least 94%) and specifically bound to antithrombin III (ATIII) and does not bind significantly to other plasma proteins (including platelet Factor 4 [PF4]) or red blood cells.

Metabolism:In vivo metabolism of fondaparinux has not been investigated since the majority of the administered dose is eliminated unchanged in urine in individuals with normal kidney function.

Elimination:In individuals with normal kidney function, fondaparinux is eliminated in urine mainly as unchanged drug. In healthy individuals up to 75 years of age, up to 77% of a single subcutaneous or intravenous fondaparinux dose is eliminated in urine as unchanged drug in 72 hours. The elimination half-life is 17 hours to 21 hours.

12.4 Special Populations

Renal Impairment:Fondaparinux elimination is prolonged in patients with renal impairment since the major route of elimination is urinary excretion of unchanged drug. In patients undergoing prophylaxis following elective hip surgery or hip fracture surgery, the total clearance of fondaparinux is approximately 25% lower in patients with mild renal impairment (CrCl 50 mL/min to 80 mL/min), approximately 40% lower in patients with moderate renal impairment (CrCl 30 mL/min to 50 mL/min), and approximately 55% lower in patients with severe renal impairment (less than 30 mL/min) compared to patients with normal renal function. A similar relationship between fondaparinux clearance and extent of renal impairment was observed in DVT treatment patients *[see Contraindications (4) and Warnings and Precautions (5.3)]*.

Hepatic Impairment:Following a single, subcutaneous dose of 7.5 mg of fondaparinux sodium in patients with moderate hepatic impairment (Child-Pugh Category B), Cmax and AUC were decreased by 22% and 39%, respectively, compared to subjects with normal liver function. The changes from baseline in pharmacodynamic parameters, such as aPTT, PT/INR, and antithrombin III, were similar in normal subjects and in patients with moderate hepatic impairment. Based on these data, no dosage adjustment is recommended in these patients. However, a higher incidence of hemorrhage was observed in subjects with moderate hepatic impairment than in normal subjects *[see Use in Specific Populations (8.7)]*. The pharmacokinetics of fondaparinux have not been studied in patients with severe hepatic impairment *[see Dosage and Administration (2.6)].*

Pediatric:Study FDPX-IJS-7001 characterized the fondaparinux peak level of once-daily subcutaneous fondaparinux sodium injection in 336 pediatric patients by measuring anti-Factor Xa activity. Of these patients, 93% achieved a therapeutic blood concentration of

fondaparinux (0.5 mg/L to 1 mg/L) during the course of their treatment following the recommended dose adjustments, as necessary. The median time to reach therapeutic levels across all age groups was approximately 3 days, with an interquartile range of 2 days to 6 days. Less than 3% of patients remained in subtherapeutic levels and 5% of patients remained in supratherapeutic levels during the course of their treatment. Approximately 55% of patients did not require any dose adjustment to reach a therapeutic blood concentration of fondaparinux during the course of their treatment; nearly 20% required one dose adjustment, 11% required 2 dose adjustments, and approximately 10% required more than two dose adjustments during the course of treatment to reach therapeutic concentrations of fondaparinux *[see Contraindications (4), Warnings and Precautions (5.4), and Use in Specific Populations (8.4)].*

Geriatric:Fondaparinux elimination is prolonged in patients older than 75 years. In studies evaluating fondaparinux sodium 2.5 mg prophylaxis in hip fracture surgery or elective hip surgery, the total clearance of fondaparinux was approximately 25% lower in patients older than 75 years as compared to patients younger than 65 years. A similar relationship between fondaparinux clearance and age was observed in DVT treatment patients *[see Use in Specific Populations (8.5)].*

Patients Weighing Less than 50 kg:Total clearance of fondaparinux sodium is decreased by approximately 30% in patients weighing less than 50 kg *[see Dosage and Administration (2.4) and Contraindications (4)]*.

Gender:The pharmacokinetic properties of fondaparinux sodium are not significantly affected by gender.

Race:Pharmacokinetic differences due to race have not been studied prospectively. However, studies performed in Asian (Japanese) healthy subjects did not reveal a different pharmacokinetic profile compared to Caucasian healthy subjects. Similarly, no plasma clearance differences were observed between black and Caucasian patients undergoing orthopedic surgery.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been performed to evaluate the carcinogenic potential of fondaparinux sodium.

Fondaparinux sodium was not genotoxic in the Ames test, the mouse lymphoma cell (L5178Y/TK $^{+/-}$) forward mutation test, the human lymphocyte chromosome aberration test, the rat hepatocyte unscheduled DNA synthesis (UDS) test, or the rat micronucleus test.

At subcutaneous doses up to 10 mg/kg/day (about 32 times the recommended human dose based on body surface area), fondaparinux sodium was found to have no effect on fertility and reproductive performance of male and female rats.

14 CLINICAL STUDIES

14.1 Prophylaxis of Thromboembolic Events Following Hip Fracture Surgery in Adult Patients

In a randomized, double-blind, clinical trial in patients undergoing hip fracture surgery, fondaparinux sodium 2.5 mg subcutaneously once daily was compared to enoxaparin sodium 40 mg subcutaneously once daily, which is not approved for use in patients undergoing hip fracture surgery. A total of 1,711 patients were randomized and 1,673 were treated. Patients ranged in age from 17 years to 101 years (mean age 77 years) with 25% men and 75% women. Patients were 99% Caucasian, 1% other races. Patients with multiple traumas affecting more than one organ system, serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from the trial. Fondaparinux sodium was initiated after surgery in 88% of patients (mean 6 hours) and enoxaparin sodium was initiated after surgery in 74% of patients (mean 18 hours). For both drugs, treatment was continued for 7 ± 2 days. The primary efficacy endpoint, venous thromboembolism (VTE), was a composite of documented deep vein thrombosis (DVT) and/or documented symptomatic pulmonary embolism (PE) reported up to Day 11. The efficacy data are provided in Table 10 and demonstrate that under the conditions of the trial fondaparinux sodium was associated with a VTE rate of 8.3% compared with a VTE rate of 19.1% for enoxaparin sodium for a relative risk reduction of 56% (95% CI: 39%, 70%; P <0.001).

Major bleeding episodes occurred in 2.2% of patients receiving fondaparinux sodium and 2.3% of enoxaparin sodium patients *[see Adverse Reactions (6.1)].*

Table 10: Efficacy of Fondaparinux Sodium Injection in the Peri-operative Prophylaxis of Thromboembolic Events Following Hip Fracture Surgery

Endpoint	**Peri-operative Prophylaxis**			
	(Day 1 to Day 7 ± 2 post-surgery)			
	Fondaparinux Sodium 2.5 mg subcutaneously once daily		**Enoxaparin Sodium 40 mg subcutaneously once daily**	
	n/N [a]	**% (95% CI)**	**n/N [a]**	**% (95% CI)**
VTE	52/626	8.3% [b](6.3, 10.8)	119/624	19.1% (16.1, 22.4)
All DVT	49/624	7.9% [b](5.9, 10.2)	117/623	18.8% (15.8, 22.1)
Proximal DVT	6/650	0.9% [b](0.3, 2)	28/646	4.3% (2.9, 6.2)
Symptomatic PE	3/831	0.4% [c](0.1, 1.1)	3/840	0.4% (0.1, 1)

[a]N = all evaluable hip fracture surgery patients. Evaluable patients were those who were treated and underwent the appropriate surgery (i.e., hip fracture surgery of the upper third of the femur), with an adequate efficacy assessment up to Day 11.
[b]P value versus enoxaparin sodium <0.001.
[c]P value versus enoxaparin sodium: NS.

14.2 Extended Prophylaxis of Thromboembolic Events Following Hip Fracture Surgery in Adult Patients

In a noncomparative, unblinded manner, 737 patients undergoing hip fracture surgery were initially treated during the peri-operative period with fondaparinux sodium 2.5 mg once daily for 7 ± 1 days. Eighty-one (81) of the 737 patients were not eligible for randomization into the 3-week double-blind period. Three hundred twenty-six (326)

patients and 330 patients were randomized to receive fondaparinux sodium 2.5 mg once daily or placebo, respectively, in or out of the hospital for 21± 2 days. Patients ranged in age from 23 years to 96 years (mean age 75 years) and were 29% men and 71% women. Patients were 99% Caucasian and 1% other races. Patients with multiple traumas affecting more than one organ system or serum creatinine level more than 2 mg/dL (180 micromol/L) were excluded from the trial. The primary efficacy endpoint, venous thromboembolism (VTE), was a composite of documented deep vein thrombosis (DVT) and/or documented symptomatic pulmonary embolism (PE) reported for up to 24 days following randomization. The efficacy data are provided in Table 11 and demonstrate that extended prophylaxis with fondaparinux sodium was associated with a VTE rate of 1.4% compared with a VTE rate of 35% for placebo for a relative risk reduction of 95.9% (95% CI = [98.7; 87.1], P <0.0001).

Major bleeding rates during the 3-week extended prophylaxis period for fondaparinux sodium occurred in 2.4% of patients receiving fondaparinux sodium and 0.6% of placebo-treated patients *[see Adverse Reactions (6.1)].*

Table 11: Efficacy of Fondaparinux Sodium Injection in the Extended Prophylaxis of Thromboembolic Events Following Hip Fracture Surgery

Endpoint	**Extended Prophylaxis (Day 8 to Day 28 ± 2 post-surgery)**			
	Fondaparinux Sodium 2.5 mg subcutaneously once daily		**Placebo subcutaneously once daily**	
	n/N [a]	**% (95% CI)**	**n/N [a]**	**% (95% CI)**
VTE	3/208	1.4% [b](0.3, 4.2)	77/220	35% (28.7, 41.7)
All DVT	3/208	1.4% [b](0.3, 4.2)	74/218	33.9% (27.7, 40.6)
Proximal DVT	2/221	0.9% [b](0.1, 3.2)	35/222	15.8% (11.2, 21.2)
Symptomatic VTE (all)	1/326	0.3% [c](0, 1.7)	9/330	2.7% (1.3, 5.1)
Symptomatic PE	0/326	0% [d](0, 1.1)	3/330	0.9% (0.2, 2.6)

[a]N = all randomized evaluable hip fracture surgery patients. Evaluable patients were those who were treated in the post-randomization period, with an adequate efficacy assessment for up to 24 days following randomization.
[b]P value versus placebo <0.001
[c]P value versus placebo = 0.021.
[d]P value versus placebo = NS.

14.3Prophylaxis of Thromboembolic Events Following Hip Replacement Surgery in Adult Patients

In 2 randomized, double-blind, clinical trials in patients undergoing hip replacement surgery, fondaparinux sodium 2.5 mg subcutaneously once daily was compared to either enoxaparin sodium 30 mg subcutaneously every 12 hours (Study 1) or to enoxaparin sodium 40 mg subcutaneously once a day (Study 2). In Study 1, a total of 2,275 patients were randomized and 2,257 were treated.

Patients ranged in age from 18 years to 92 years (mean age 65 years) with 48% men and 52% women. Patients were 94% Caucasian, 4% black, less than 1% Asian, and 2%

others. In Study 2, a total of 2,309 patients were randomized and 2,273 were treated. Patients ranged in age from 24 years to 97 years (mean age 65 years) with 42% men and 58% women. Patients were 99% Caucasian, and 1% other races. Patients with serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from both trials. In Study 1, fondaparinux sodium was initiated 6 ± 2 hours (mean 6.5 hours) after surgery in 92% of patients and enoxaparin sodium was initiated 12 hours to 24 hours (mean 20.25 hours) after surgery in 97% of patients. In Study 2, fondaparinux sodium was initiated 6 ± 2 hours (mean 6.25 hours) after surgery in 86% of patients and enoxaparin sodium was initiated 12 hours before surgery in 78% of patients. The first post-operative enoxaparin sodium dose was given within 12 hours after surgery in 60% of patients and 12 hours to 24 hours after surgery in 35% of patients with a mean of 13 hours.

For both studies, both study treatments were continued for 7 ± 2 days. The efficacy data are provided in Table 12. Under the conditions of Study 1, fondaparinux sodium was associated with a VTE rate of 6.1% compared with a VTE rate of 8.3% for enoxaparin sodium for a relative risk reduction of 26% (95% CI: -11%, 53%; P=NS). Under the conditions of Study 2, fondaparinux sodium was associated with a VTE rate of 4.1% compared with a VTE rate of 9.2% for enoxaparin sodium for a relative risk reduction of 56% (95% CI: 33%, 73%; P <0.001). For the 2 studies combined, the major bleeding episodes occurred in 3% of patients receiving fondaparinux sodium and 2.1% of enoxaparin sodium patients *[see Adverse Reactions (6.1)].*

Table 12: Efficacy of Fondaparinux Sodium Injection in the Prophylaxis of Thromboembolic Events Following Hip Replacement Surgery

Endpoint	**Study 1 n/N [a] % (95% CI)**		**Study 2 n/N [a] % (95% CI)**	
	Fondaparinux Sodium 2.5 mg subcutaneously once daily	**Enoxaparin Sodium 30 mg subcutaneously every 12 hr**	**Fondaparinux Sodium 2.5 mg subcutaneously once daily**	**Enoxaparin Sodium 40 mg subcutaneously once daily**
VTE [b]	48/787 6.1% [c](4.5, 8)	66/797 8.3% (6.5, 10.4)	37/908 4.1% [e](2.9, 5.6)	85/919 9.2% (7.5, 11.3)
All DVT	44/784 5.6% [d](4.1, 7.5)	65/796 8.2% (6.4, 10.3)	36/908 4.0% [e](2.8, 5.4)	83/918 9.0% (7.3, 11.1)
Proximal DVT	14/816 1.7% [c](0.9, 2.9)	10/830 1.2% (0.6, 2.2)	6/922 0.7% [f](0.2, 1.4)	23/927 2.5% (1.6, 3.7)
Symptomatic PE	5/1,126 0.4% [c](0.1, 1)	1/1,128 0.1% (0, 0.5)	2/1,129 0.2% [c](0, 0.6)	2/1,123 0.2% (0, 0.6)

[a]N = all evaluable hip replacement surgery patients. Evaluable patients were those who were treated and underwent the appropriate surgery (i.e., hip replacement surgery), with an adequate efficacy assessment up to Day 11.
[b]VTE was a composite of documented DVT and/or documented symptomatic PE reported up to Day 11.
[c]P value versus enoxaparin sodium: NS.
[d]P value versus enoxaparin sodium in study 1: <0.05.
e P value versus enoxaparin sodium in study 2: <0.001.

[f]P value versus enoxaparin sodium in study 2: <0.01

14.4 Prophylaxis of Thromboembolic Events Following Knee Replacement Surgery Adult Patients

In a randomized, double-blind, clinical trial in patients undergoing knee replacement surgery (i.e., surgery requiring resection of the distal end of the femur or proximal end of the tibia), fondaparinux sodium 2.5 mg subcutaneously once daily was compared to enoxaparin sodium 30 mg subcutaneously every 12 hours. A total of 1,049 patients were randomized and 1,034 were treated. Patients ranged in age from 19 years to 94 years (mean age 68 years) with 41% men and 59% women. Patients were 88% Caucasian, 8% black, less 1% Asian, and 3% others. Patients with serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from the trial. Fondaparinux sodium was initiated 6 ± 2 hours (mean 6.25 hours) after surgery in 94% of patients, and enoxaparin sodium was initiated 12 hours to 24 hours (mean 21 hours) after surgery in 96% of patients. For both drugs, treatment was continued for 7 ± 2 days. The efficacy data are provided in Table 13 and demonstrate that under the conditions of the trial, fondaparinux sodium was associated with a VTE rate of 12.5% compared with a VTE rate of 27.8% for enoxaparin sodium for a relative risk reduction of 55% (95% CI: 36%, 70%; P <0.001). Major bleeding episodes occurred in 2.1% of patients receiving fondaparinux sodium and 0.2% of enoxaparin sodium patients *[see Adverse Reactions (6.1)]*.

Table 13: Efficacy of Fondaparinux Sodium Injection in the Prophylaxis of Thromboembolic Events Following Knee Replacement Surgery

Endpoint	**Fondaparinux Sodium 2.5 mg subcutaneously once daily**		**Enoxaparin Sodium 30 mg subcutaneously every 12 hours**	
	n/N [a]	**% (95% CI)**	**n/N [a]**	**% (95% CI)**
VTE [b]	45/361	12.5% [c](9.2, 16.3)	101/363	27.8% (23.3, 32.7)
All DVT	45/361	12.5% [c](9.2, 16.3)	98/361	27.1% (22.6, 32)
Proximal DVT	9/368	2.4% [d](1.1, 4.6)	20/372	5.4% (3.3, 8.2)
Symptomatic PE	1/517	0.2% [d](0, 1.1)	4/517	0.8% (0.2, 2)

[a]N = all evaluable knee replacement surgery patients. Evaluable patients were those who were treated and underwent the appropriate surgery (i.e., knee replacement surgery), with an adequate efficacy assessment up to Day 11.
[b]VTE was a composite of documented DVT and/or documented symptomatic PE reported up to Day 11.
[c]P value versus enoxaparin sodium <0.001.
[d]P value versus enoxaparin sodium: NS.

14.5 Prophylaxis of Thromboembolic Events Following Abdominal Surgery in Patients at Risk for Thromboembolic Complications in Adult Patients

Abdominal surgery patients at risk included the following: Those undergoing surgery under general anesthesia lasting longer than 45 minutes who are older than 60 years with or without additional risk factors; and those undergoing surgery under general anesthesia lasting longer than 45 minutes who are older than 40 years with additional risk factors. Risk factors included neoplastic disease, obesity, chronic obstructive

pulmonary disease, inflammatory bowel disease, history of deep vein thrombosis (DVT) or pulmonary embolism (PE), or congestive heart failure.

In a randomized, double-blind, clinical trial in patients undergoing abdominal surgery, fondaparinux sodium 2.5 mg subcutaneously once daily started postoperatively was compared to dalteparin sodium 5,000 IU subcutaneously once daily, with one 2,500 IU subcutaneously preoperative injection and a 2,500 IU subcutaneously first postoperative injection. A total of 2,927 patients were randomized and 2,858 were treated. Patients ranged in age from 17 years to 93 years (mean age 65 years) with 55% men and 45% women. Patients were 97% Caucasian, 1% black, 1% Asian, and 1% others. Patients with serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from the trial. Sixty-nine percent (69%) of study patients underwent cancer-related abdominal surgery. Study treatment was continued for 7 ± 2 days. The efficacy data are provided in Table 14 and demonstrate that prophylaxis with fondaparinux sodium was associated with a VTE rate of 4.6% compared with a VTE rate of 6.1% for dalteparin sodium (P = NS).

Table 14: Efficacy of Fondaparinux Sodium Injection in the Prophylaxis of Thromboembolic Events Following Abdominal Surgery

Endpoint	**Fondaparinux Sodium 2.5 mg subcutaneously once daily**		**Dalteparin Sodium 5,000 IU subcutaneously once daily**	
	n/N [a]	**% (95% CI)**	**n/N [a]**	**% (95% CI)**
VTE [b]	47/1,027	4.6% [c](3.4, 6)	62/1,021	6.1% (4.7, 7.7)
All DVT	43/1,024	4.2% (3.1, 5.6)	59/1,018	5.8% (4.4, 7.4)
Proximal DVT	5/1,076	0.5% (0.2, 1.1)	5/1,077	0.5% (0.2, 1.1)
Symptomatic VTE	6/1,465	0.4% (0.2, 0.9)	5/1,462	0.3% (0.1, 0.8)

[a]N = all evaluable abdominal surgery patients. Evaluable patients were those who were randomized and had an adequate efficacy assessment up to Day 10; non-treated patients and patients who did not undergo surgery did not get a VTE assessment.
[b]VTE was a composite of venogram positive DVT, symptomatic DVT, non-fatal PE and/or fatal PE reported up to Day 10.
[c]P value versus dalteparin sodium: NS.

14.6 Treatment of Deep Vein Thrombosis in Adult Patients

In a randomized, double-blind, clinical trial in patients with a confirmed diagnosis of acute symptomatic DVT without PE, fondaparinux sodium 5 mg (body weight less than 50 kg), 7.5 mg (body weight 50 kg to 100 kg), or 10 mg (body weight greater than 100 kg) subcutaneously once daily (fondaparinux sodium treatment regimen) was compared to enoxaparin sodium 1 mg/kg subcutaneously every 12 hours. Almost all patients started study treatment in hospital. Approximately 30% of patients in both groups were discharged home from the hospital while receiving study treatment. A total of 2,205 patients were randomized and 2,192 were treated. Patients ranged in age from 18 years to 95 years (mean age 61 years) with 53% men and 47% women. Patients were 97% Caucasian, 2% black, and 1% other races. Patients with serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from the trial. For both groups, treatment continued for at least 5 days with a treatment duration range of 7 ± 2 days, and both treatment groups received vitamin K antagonist

therapy initiated within 72 hours after the first study drug administration and continued for 90 ± 7 days, with regular dose adjustments to achieve an INR of 2 to 3. The primary efficacy endpoint was confirmed, symptomatic, recurrent VTE reported up to Day 97. The efficacy data are provided in Table 15.

Table 15: Efficacy of Fondaparinux Sodium Injection in the Treatment of Deep Vein Thrombosis (All Randomized)

Endpoint	**Fondaparinux Sodium 5 mg, 7.5 mg, or 10 mg subcutaneously once daily N = 1,098**		**Enoxaparin Sodium 1 mg/kg subcutaneously every 12 hours N = 1,107**	
	n	**% (95% CI)**	**n**	**% (95% CI)**
Total VTE [a]	43	3.9% (2.8, 5.2)	45	4.1% (3, 5.4)
DVT only	18	1.6% (1, 2.6)	28	2.5% (1.7, 3.6)
Non-fatal PE	20	1.8% (1.1, 2.8)	12	1.1% (0.6, 1.9)
Fatal PE	5	0.5% (0.1, 1.1)	5	0.5% (0.1, 1.1)

[a]VTE was a composite of symptomatic recurrent non-fatal VTE or fatal PE reported up to Day 97. The 95% confidence interval for the treatment difference for total VTE was: (-1.8% to 1.5%).

During the initial treatment period, 18 (1.6%) of patients treated with fondaparinux sodium and 10 (0.9%) of patients treated with enoxaparin sodium had a VTE endpoint (95% CI for the treatment difference [fondaparinux sodium-enoxaparin sodium] for VTE rates: -0.2%; 1.7%).

14.7 Treatment of Pulmonary Embolism in Adult Patients

In a randomized, open-label, clinical trial in patients with a confirmed diagnosis of acute symptomatic PE, with or without DVT, fondaparinux sodium 5 mg (body weight less than 50 kg), 7.5 mg (body weight 50 kg to 100 kg), or 10 mg (body weight greater than 100 kg) subcutaneously once daily (fondaparinux sodium treatment regimen) was compared to heparin IV bolus (5,000 USP units) followed by a continuous IV infusion adjusted to maintain 1.5 to 2.5 times aPTT control value. Patients with a PE requiring thrombolysis or surgical thrombectomy were excluded from the trial. All patients started study treatment in hospital. Approximately 15% of patients were discharged home from the hospital while receiving fondaparinux sodium therapy. A total of 2,213 patients were randomized and 2,184 were treated. Patients ranged in age from 18 years to 97 years (mean age 62 years) with 44% men and 56% women. Patients were 94% Caucasian, 5% black, and 1% other races. Patients with serum creatinine level more than 2 mg/dL (180 micromol/L), or platelet count less than 100,000/mm3 were excluded from the trial. For both groups, treatment continued for at least 5 days with a treatment duration range 7 ± 2 days, and both treatment groups received vitamin K antagonist therapy initiated within 72 hours after the first study drug administration and continued for 90 ± 7 days, with regular dose adjustments to achieve an INR of 2 to 3. The primary efficacy endpoint was confirmed, symptomatic, recurrent VTE reported up to Day 97. The efficacy data are provided in Table 16.

Table 16: Efficacy of Fondaparinux Sodium Injection in the Treatment of Pulmonary Embolism (All Randomized)

Endpoint	Fondaparinux Sodium 5 mg, 7.5 mg, or 10 mg subcutaneously once daily N = 1,103		Heparin aPTT adjusted IV N = 1,110	
	n	% (95% CI)	n	% (95% CI)
Total VTE [a]	42	3.8% (2.8, 5.1)	56	5% (3.8, 6.5)
DVT only	12	1.1% (0.6, 1.9)	17	1.5% (0.9, 2.4)
Non-fatal PE	14	1.3% (0.7, 2.1)	24	2.2% (1.4, 3.2)
Fatal PE	16	1.5% (0.8, 2.3)	15	1.4% (0.8, 2.2)

[a]VTE was a composite of symptomatic recurrent non-fatal VTE or fatal PE reported up to Day 97. The 95% confidence interval for the treatment difference for total VTE was: (-3% to 0.5%).

During the initial treatment period, 12 (1.1%) of patients treated with fondaparinux sodium and 19 (1.7%) of patients treated with heparin had a VTE endpoint (95% CI for the treatment difference [fondaparinux sodium-heparin] for VTE rates: -1.6%; 0.4%).

14.8 Treatment of Venous Thromboembolism in Pediatric Patients

The efficacy of fondaparinux sodium for the treatment of VTE in pediatric patients aged 1 year and older is based on an open-label, single-arm retrospective clinical study (FDPX-IJS-7001) in 366 pediatric patients aged 0.3 years to 17 years with VTE who were treated with fondaparinux sodium injection, including fondaparinux sodium, at a single center in a tertiary care pediatric hospital. Out of these 366 patients, 325 patients with diagnosis of VTE were included in the efficacy analysis set.

Of the 325 total patients, 30 patients were less than 2 years, 65 patients were 2 years to less than 6 years, 78 patients were 6 years to less than 12 years, and 152 patients were 12 years to less than18 years. Patients were started on fondaparinux sodium injection 0.1 mg/kg once daily with doses rounded to the nearest prefilled syringe (2.5 mg, 5 mg, or 7.5 mg) for patients weighing over 20 kg. For patients weighing 10 kg to 20 kg, dosing was based on body weight without rounding to the nearest prefilled syringe. Fondaparinux levels were monitored after the second or third dose until therapeutic levels were achieved. Fondaparinux levels were then monitored weekly while patients were admitted within the hospital and, after approximately every 1 month to 3 months while outpatient for the duration of treatment. Dosing adjustments were made to achieve peak fondaparinux blood concentration within the therapeutic target of 0.5 mg/L to 1 mg/L.

Patients received an initial median dose of approximately 0.1 mg/kg body weight of fondaparinux sodium injection, which translates into a median dose of 1.37 mg in the less than 20 kg weight group, 2.5 mg in the 20 kg to less than 40 kg weight group, 5 mg in the 40 kg to less than 60 kg, and 7.5 mg in the greater than or equal to 60 kg weight group. Based on median values, it took approximately 3 days (range 1 day to 929 days) to achieve therapeutic levels across all age groups.

The efficacy of fondaparinux sodium was based on measuring the proportion of pediatric patients with complete clot resolution up to 3 months (±15 days). Among the 325 pediatric patients in the efficacy analysis set, 146 (44.9%; 95% CI: 39.6, 50.4) experienced complete resolution of at least one clot, while 143 (44%; 95% CI: 38.7,

49.4) had complete resolution of all clots. Summaries of complete clot resolution of patients' main VTEs at month 3 are provided by age group (*see*Table 17) and weight group (*see*Table 18).

Table 17: Summary of Complete Clot Resolution of Main VTEs Up to Month 3 by Age Group

Parameter	**Less than 2 years (N=30) n (%)**	**Greater than or equal to 2 years to less than 6 years (N=65) n (%)**	**Greater than or equal to 6 years to less than 12 years (N=78) n (%)**	**Greater than or equal to 12 years to less than 18 years (N=152)n (%)**
Complete Resolution of At Least One Clot, n (%) 95% Confidence Interval	14 (46.7) (30.2, 63.9)	26 (40) (29, 52.1)	40 (51.3) (40.4, 62.1)	66 (43.4) (35.8, 51.4)
Complete Resolution of All Clots, n (%) 95% Confidence Interval	14 (46.7) (30.2, 63.9)	25 (38.5) (27.6, 50.6)	39 (50) (39.2, 60.8)	65 (42.8) (35.2, 50.7)

Table 18: Summary of Complete Clot Resolution of Main VTEs Up to Month 3 by Weight Group

Parameter	**Less than 20 kg (N=95) n (%)**	**20 kg to less than 40 kg (N=84) n (%)**	**40 kg to less than 60 kg (N=72) n (%)**	**Greater than or equal to 60 kg (N=73) n (%)**
Complete Resolution of At Least One Clot, n (%) 95% Confidence Interval	42 (44.2) (34.6, 54.2)	45 (53.6) (43, 63.8)	30 (41.7) (31, 53.2)	28 (38.4) (28.1, 49.8)
Complete Resolution of All Clots, n (%) 95% Confidence Interval	41 (43.2) (33.7, 53.2)	45 (53.6) (43, 63.8)	29 (40.3) (29.7, 51.8)	27 (37) (26.8, 48.5)

16 HOW SUPPLIED/STORAGE AND HANDLING

Fondaparinux sodium injection, USP is available in single-dose, prefilled syringes containing clear and colorless to slightly yellow liquid in the following strengths:

2.5 mg/0.5 mL fondaparinux sodium injection, USP in single-dose prefilled syringe,

affixed with a 27-gauge x ½-inch needle and an automatic needle protection system with white plunger rod.

NDC 0781-3443-95 10 Single Unit Syringes

5 mg/0.4 mL fondaparinux sodium injection, USP in single-dose prefilled syringe, affixed with a 27-gauge x ½-inch needle and an automatic needle protection system with white plunger rod.

NDC 0781-3454-95 10 Single Unit Syringes

7.5 mg/0.6 mL fondaparinux sodium injection, USP in single-dose prefilled syringe, affixed with a 27-gauge x ½-inch needle and an automatic needle protection system with white plunger rod.

NDC 0781-3465-95 10 Single Unit Syringes

10 mg/0.8 mL fondaparinux sodium injection, USP in single-dose prefilled syringe, affixed with a 27-gauge x ½-inch needle and an automatic needle protection system with white plunger rod.

NDC 0781-3476-95 10 Single Unit Syringes

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) *[See USP Controlled Room Temperature].*

Discard unused portion.

PHARMACIST: Dispense a Patient Information Leaflet with each prescription.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling *(Patient Information and Instructions for Use).*

17.1 Patient Advice

If the patients have had neuraxial anesthesia or spinal puncture, and particularly, if they are taking concomitant NSAIDS, platelet inhibitors, or other anticoagulants, inform patients to watch for signs and symptoms of spinal or epidural hematomas, such as back pain, tingling, numbness (especially in the lower limbs), muscular weakness, and stool or urine incontinence. If any of these symptoms occur, advise patients to contact his or her physician immediately.

The use of aspirin and other NSAIDS may enhance the risk of hemorrhage. Advise patients to discontinue use prior to fondaparinux sodium injection therapy whenever possible; if co-administration is essential, the patient’s clinical and laboratory status should be closely monitored *[see Drug Interactions (7)].*

If patients must self-administer fondaparinux sodium injection or if administered by a caregiver, (e.g., if fondaparinux sodium injection is used at home), advise patients of the following:

• Advise patients that fondaparinux sodium injection should be given by subcutaneous injection. Instruct patients in the proper technique for administration.

• Instruct patients that if they miss a dose of fondaparinux sodium injection, to inject the dose as soon as they remember. Advise patients not to inject two doses at the same

time.

• The most important risk with fondaparinux sodium injection administration is bleeding. Counsel patients on signs and symptoms of possible bleeding.

• Advise patients that it may take them longer than usual to stop bleeding.

• Advise patients that they may bruise and/or bleed more easily when they are treated with fondaparinux sodium injection.

• Advise patients to report any unusual bleeding, bruising, or signs of thrombocytopenia (such as a rash of dark red spots under the skin) to their physician *[see Warnings and Precautions (5.2, 5.5)]*.

• Advise patients to tell their physicians and dentists they are taking fondaparinux sodium injection and/or any other product known to affect bleeding before any surgery is scheduled and before any new drug is taken *[see Warnings and Precautions (5.2)]*.

• Advise patients to tell their physicians and dentists of all medications they are taking, including those obtained without a prescription, such as aspirin or other NSAIDs *[see Drug Interactions (7)]*.

Manufactured by Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Lianyungang, Jiangsu 222047, China for

Sandoz Inc., Princeton, NJ 08540

PATIENT INFORMATION

Fondaparinux (fon-da-PEH-rih-nux) sodium injection

for subcutaneous use

What is the most important information I should know about fondaparinux sodium injection?

Fondaparinux sodium injection may cause serious side effects, including:

• **Spinal or epidural blood clots (hematoma).**People who take a blood thinner medicine (anticoagulant) like fondaparinux sodium injection, and have medicine injected into their spinal and epidural area, or have a spinal puncture have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:

1. a thin tube called an epidural catheter is placed in your back to give you certain medicine
2. you take non-steroidal anti-inflammatory drugs (NSAIDs) or a medicine to help prevent blood from clotting
3. you have a history of difficult or repeated epidural or spinal punctures
4. you have a history of problems with your spine or have had surgery on your spine

If you use fondaparinux sodium injection and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have back pain, tingling, numbness, muscle weakness (especially in your legs and feet), and loss of control of your bowels or bladder (incontinence).

Because the risk of bleeding may be higher, tell your doctor before using fondaparinux sodium injection if you:

1. are also taking certain other medicines that affect blood clotting such as aspirin, an NSAID (for example, ibuprofen or naproxen), clopidogrel, or warfarin sodium
2. have bleeding problems
3. had problems in the past with pain medication given through the spine
4. have had surgery to your spine
5. have a spinal deformity

See "What are the possible side effects of fondaparinux sodium injection?" for more information about side effects.

What is fondaparinux sodium injection?

Fondaparinux sodium injection is a prescription medicine that is used to:

• help prevent blood clots from forming in adults who have had certain surgeries of the hip, knee, or the stomach-area (abdominal surgery).

• treat adults who have blood clots in their legs or blood clots that travel to their lungs, along with the blood thinner medicine called warfarin sodium.

• treat children 1 year of age or older weighing at least 22 pounds (10 kg) who have blood clots.

It is not known if fondaparinux sodium injection is safe and effective for use in children:

• younger than 1 year of age and weighing less than 22 pounds (10 kg) who have blood clots.

• younger than 1 year of age with kidney problems.

• for the prevention of blood clots in the legs and to treat blood clots in the legs or lungs when given with warfarin sodium.

• with liver problems.

Who should not use fondaparinux sodium injection?

Do not use fondaparinux sodium injection if you:

• have certain kidney problems

• have active bleeding problems

• have an infection in your heart

• have low platelet counts and if you test positive for a certain antibody during treatment with fondaparinux sodium injection

• weigh less than 110 pounds (50 kg) and fondaparinux sodium injection will be used to help prevent blood clots in adults undergoing certain surgery. See **"What are the possible side effects of fondaparinux sodium injection?"**

• had a serious allergic reaction to fondaparinux sodium injection

Before using fondaparinux sodium injection, tell your doctor about all of your medical conditions, including if you:

• have had any bleeding problems (such as stomach ulcers)

• have had a stroke

• have had recent surgeries, including eye surgery

• have diabetic eye disease

• have kidney or liver problems

• have uncontrolled high blood pressure

• are pregnant or plan to become pregnant. Fondaparinux sodium may harm your unborn baby. If you are pregnant, talk to your doctor about the best way for you to prevent or treat blood clots.

• are breastfeeding or plan to breastfeed. It is not known if fondaparinux sodium passes into breast milk. You and your doctor should decide if you will breastfeed during treatment with fondaparinux sodium injection.

Tell your doctor about all the medicines you takeincluding prescriptions and over-the-counter medicines, vitamins, and herbal supplements. Some medicines can increase your risk of bleeding.

See **"What is the most important information I should know about fondaparinux sodium injection?"**Do not start taking any new medicines without first talking to your doctor.

Tell all your doctors and dentist that you use fondaparinux sodium injection, especially if you need to have any kind of surgery or a dental procedure.

Keep a list of your medicines and show it to all your doctors and pharmacist before you start a new medicine.

How should I use fondaparinux sodium injection?

• Fondaparinux sodium injection is available in different types of syringes. Your doctor will decide which type of syringe is best for you or your child. See the Instructions for Use to confirm the prescribed syringe and how to give a fondaparinux sodium injection.

• If your doctor tells you that you may give yourself or your child injections of fondaparinux sodium injection at home, you will be shown how to give the injections first before you do them on your own.

• Use fondaparinux sodium injection exactly as your doctor tells you to.

• Fondaparinux sodium injection is given as an injection under your skin (subcutaneous injection).

• If you miss a dose of fondaparinux sodium injection, inject your dose as soon as you remember. Do not inject 2 doses at the same time.

• Your doctor may perform blood tests and test for blood in your stool as needed during treatment with fondaparinux sodium injection to check for side effects.

• If you inject too much fondaparinux sodium injection, call your doctor right away.

What are possible side effects of fondaparinux sodium injection?

Fondaparinux sodium injection can cause serious side effects. See "What is the most important information I should know about fondaparinux sodium injection?"

• **Severe bleeding.**Certain conditions can increase your risk for severe bleeding, including:

1. some bleeding problems
2. some gastrointestinal problems including ulcers
3. some types of strokes
4. uncontrolled high blood pressure
5. diabetic eye disease
6. soon after brain, spine, or eye surgery

In children, certain conditions that can increase risk of bleeding, include:

1. systemic lupus erythematous (also known as Lupus)
2. Wilms tumor
3. antiphospholipid syndrome
4. genetic conditions that affect blood clotting
5. cancer
6. decreased red blood cells, white blood cells and platelets (pancytopenia)
7. indwelling chest tubes
8. chest surgery
9. infection
10. severe high blood pressure that affects the brain
11. enlarged or blocked lymph vessels in the small intestine (intestinal lymphangiectasia)

• **Certain kidney problems can also increase your risk of bleeding with fondaparinux sodium injection.** Your doctor may check your kidney function during your treatment with fondaparinux sodium injection.

• **Increased bleeding risk in adults who weigh less than 110 pounds (50 kg) undergoing certain surgeries.**

• **Low blood platelets (thrombocytopenia).** Platelets are blood cells that help your blood to clot normally. Your doctor may check your platelet counts during your treatment with fondaparinux sodium injection.

You may bruise or bleed more easily during your treatment with fondaparinux sodium injection, and it may take longer than usual for bleeding to stop. Tell your doctor if you have any signs or symptoms of bleeding, bruising or rash of dark red spots under the skin during your treatment with fondaparinux sodium injection.

The most common side effects of fondaparinux sodium injection in adults include:

- bleeding problems
- bleeding, rash, and itching at the injection site (injection site reactions)
- increased blood levels of certain liver tests
- low red blood cell counts (anemia)
- sleep problems (insomnia)
- increased wound drainage
- purplish spots on skin (purpura)
- low blood pressure (hypotension)
- confusion
- fluid-filled blisters (bullous eruption)
- blood clots (hematoma)
- severe bleeding after surgery (post-operative hemorrhage)

- low potassium in your blood (hypokalemia)
- infection
- dizziness

The most common side effects of fondaparinux sodium injection in children include:

- bleeding problems
- skin problems
- low red blood cell counts (anemia)
- abnormal blood levels of certain liver tests
- low blood platelet counts
- low potassium in your blood (hypokalemia)
- allergic reaction, such as sudden swelling of your face, tongue, throat, or troubled swallowing
- low blood pressure (hypotension)

These are not all the possible side effects of fondaparinux sodium injection.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store fondaparinux sodium injection?

• See the product label for complete instructions on how to store fondaparinux sodium injection.

• Throw away (discard) fondaparinux sodium injection that is out of date (expired) or unused.

Keep fondaparinux sodium injection and all medicines out of the reach of children.

General information about the safe and effective use of fondaparinux sodium injection

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use fondaparinux sodium injection for a condition for which it was not prescribed. Do not give fondaparinux sodium injection to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or doctor for information about fondaparinux sodium injection that is written for healthcare professionals.

What are the ingredients in fondaparinux sodium injection?

Active ingredient:fondaparinux sodium

Inactive ingredients:sodium chloride and water for injection. May also contain sodium hydroxide and/or hydrochloric acid as pH adjusters.

For more information about fondaparinux sodium injection, contact Sandoz Inc. at 1-800-525-8747.

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

Revised: 02/2025

INSTRUCTIONS FOR USE

Fondaparinux (fon-da-PEH-rih-nux) sodiuminjection

for subcutaneoususe

This Instructions for Use contains information on how to inject fondaparinux sodium injection. Before you use fondaparinux sodium injection, read and follow the step-by-step instructions. Talk to your child’s doctor or pharmacist if you have any questions.

Important Information You Need to Know Before Injecting Fondaparinux Sodium Injection

• Fondaparinux sodium injection is available in different types of syringes. Confirm the syringe looks like the figure (Syring looks) below before you continue:

• Your healthcare provider should show you how to prepare and inject fondaparinux sodium injection. **Do not**inject your child until you have been shown how to inject fondaparinux sodium injection.

• Each fondaparinux sodium injection syringe is 1 dose of fondaparinux sodium injection. **The syringe is for a one-time use only.**

• Use fondaparinux sodium injection exactly as prescribed by your doctor.

How should I store fondaparinux sodium injection syringes?

• Store fondaparinux sodium injection syringes in a refrigerator between 36°F to 46°F (2°C to 8°C) for up to the beyond use date on the syringe.

• **Do not**freeze.

• Store syringes in a clean container in the refrigerator.

• **Do not**store fondaparinux sodium injection syringes at room temperature between 68°F to 77°F (20°C to 25°C).

• Take fondaparinux sodium injection syringe out of the refrigerator and allow it to reach room temperature. Inject right away after the syringe reaches room temperature.

• Throw away (dispose of) fondaparinux sodium injection syringes that has been left at room temperature for longer than 4 hours.

• Keep fondaparinux sodium injection syringes and all medicines out of the reach of children.

Do not use fondaparinux sodium injection if:

• the solution appears discolored (the solution should normally appear clear)

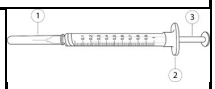
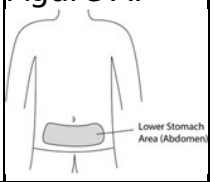
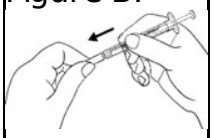
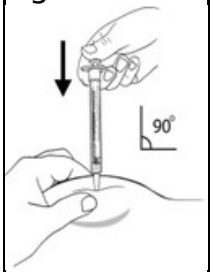
• you see any particles in the solution

• the syringe is damaged, including:
1. cracks, breaks, or bends in the syringe or the plunger
2. broken, bent, or detached needle
3. medicine leaking from the plunger or needle

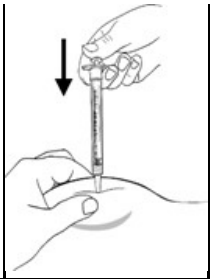
• past the beyond use date on the syringe labeled by the pharmacy

How should I give an injection of fondaparinux sodium injection?

Fondaparinux sodium injection is injected into a skin fold of the lower stomach-area (abdomen) as directed by your child's doctor. Do not inject fondaparinux sodium injection into muscle.

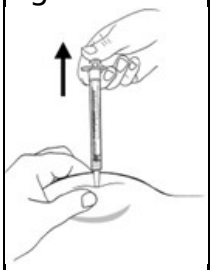
Instructions for injecting fondaparinux sodium injection	
Parts of the fondaparinux sodium injection syringe:	
1. Rigid needle guard 2. Finger-grip 3. Plunger	
1. Wash your hands well with soap and water, rinse, and towel dry.	
2. Instruct your child to sit or lie down in a comfortable position. Choose a spot on the lower stomach-area (abdomen), at least 2 inches below the belly button (Figure A). Change (alternate) between using the left and right side of the lower abdomen for each injection	Figure A. 
3. Clean the injection area with an alcohol swab.	
1. Remove the needle guard, by pulling it in a straight line away from the body of the syringe (Figure B). Throw away (discard) the needle guard. • **Do not touch the needle or let it come in contact with any surface before the injection.**A small air bubble in the syringe is normal. • To be sure that you do not lose any medicine from the syringe, do not try to remove air bubbles from the syringe before giving the injection.	Figure B. 
5. Gently pinch the skin that has been cleaned to make a fold. Hold the fold between the thumb and the forefinger of one hand during the entire injection (Figure C).	Figure C. 
6. Hold the syringe firmly in your other hand using the finger grip. Insert the full length of the needle straight down into your skinfold (at an angle of 90°) (Figure D).	Figure D. 
7. Inject all of the medicine in the syringe by using your thumb to firmly	Figure E.

press down on the plunger as far as it goes (Figure E).



8. Pull out the needle at the same angle you inserted in (Figure F).

Figure F.



9. Throw away (dispose of) used and unused fondaparinux sodium injection needles and syringes:

- Put your used fondaparinux sodium injection needles and syringes in an FDA-cleared sharps disposal container right away after use. **Do not**throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

1. made of a heavy-duty plastic,
2. can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
3. upright and stable during use,
4. leak-resistant, and
5. properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

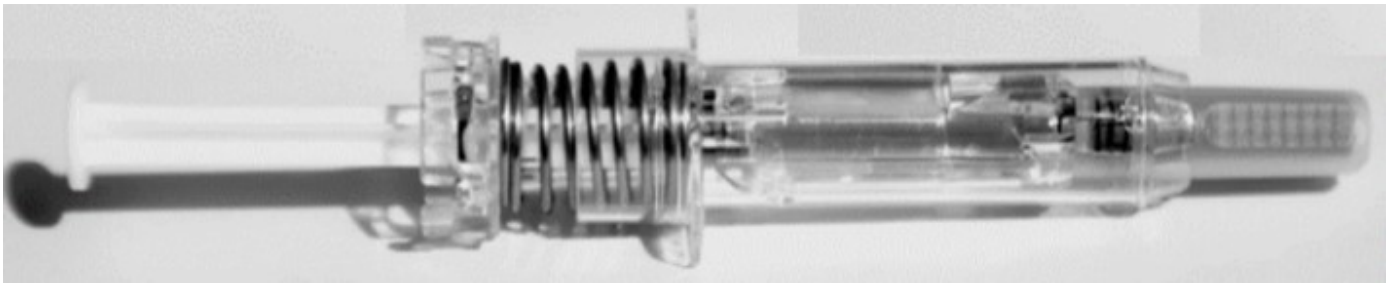
This Instructions for Use has been approved by the U.S. Food and Drug Administration
Revised: 02/2025
Manufactured by Jiangsu Hengrui Pharmaceuticals Co., Ltd.
Lianyungang, Jiangsu 222047, China for
Sandoz Inc., Princeton, NJ 08540
09UF10

INSTRUCTIONS FOR USE
Fondaparinux (fon-da-PEH-rih-nux) sodium injection
for subcutaneous use

This Instructions for Use contains information on how to inject fondaparinux sodium injection. Before you use fondaparinux sodium injection, read and follow the step-by-step instructions. Talk to your or your child's doctor or pharmacist if you have any questions.

Important Information You Need to Know Before Injecting Fondaparinux Sodium Injection

• Fondaparinux sodium injection is available in different types of syringes. Confirm the syringe looks like the figure (Syring looks 1) below before you continue:



• Your healthcare provider should show you how to prepare and inject fondaparinux sodium injection. **Do not**inject yourself or someone else until you have been shown how to inject fondaparinux sodium injection.

• Each fondaparinux sodium injection syringe is 1 dose of fondaparinux sodium injection. **The syringe is for a one-time use only.**

• Use fondaparinux sodium injection exactly as prescribed by your doctor.

How should I store fondaparinux sodium injection syringes?

• Store fondaparinux sodium injection at room temperature between 68°F to 77°F (20°C to 25°C).

• Keep fondaparinux sodium injection syringes and all medicines out of the reach of children.

Do not use fondaparinux sodium injection if:

• the solution appears discolored (the solution should normally appear clear)

• you see any particles in the solution

• the syringe is damaged

• it is out of date (expired)

How should I give an injection of fondaparinux sodium injection?
Fondaparinux sodium injection is injected into a skinfold of the lower stomach-area (abdomen) as directed by your or your child's doctor. **Do not**inject fondaparinux sodium injection into muscle. **The following instructions are specific to the Hypak ™SCF ™injection system and may differ from the directions for other injection systems.**

Instructions for self-administration
The different parts of fondaparinux sodium injection safety syringe are:
1. Rigid needle shield

2. Plunger
3. Finger-grip
4. Security sleeve

Figure Syringe BEFORE USE

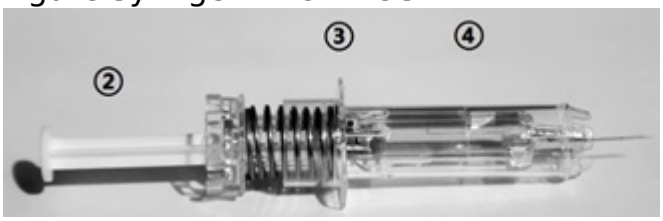


Figure Syringe AFTER USE

1. Wash your hands well with soap and water, rinse and towel dry.
2. Sit or lie down in a comfortable position. Choose a spot on the lower stomach area (abdomen), at least 2 inches below your belly button (**Figure A**). Change (alternate) between using the left and right side of the lower abdomen for each injection. If you have any questions talk to your nurse or doctor.

Figure A.

3. Clean the injection area with an alcohol swab.
4. Remove the needle shield, by pulling it in a straight line away from the body of the syringe (**Figure B**). Discard (throw away) the needle shield.

Figure B.

- **Do not touch the needle or let it come in contact with any surface before the injection.**A small air bubble in the syringe is normal.
- To be sure that you do not lose any medicine from the syringe, do not try to remove air bubbles from the syringe before giving the injection.

5. Gently pinch the skin that has been cleaned to make a fold. Hold the fold between the thumb and the forefinger of one hand during the entire injection (**Figure C**).

Figure C.

6. Hold the syringe firmly in your other hand using the finger grip. Insert the full length of the needle directly up and down (at an angle of 90°) into the skin fold (**Figure D**).

Figure D.

7. Inject all of the medicine in the syringe by pressing down on the plunger as far as it goes. This will ensure you have injected all the contents of the syringe (**Figure E**).

Figure E.

8. Remove the syringe from the injection site keeping your finger on the plunger. Orient the needle away from you and others, and activate the safety shield by firmly pushing the plunger. The protective sleeve will automatically cover the needle and you will hear a “click” when safety shield is activated (**Figure F**and **Figure G**). Throw away the used fondaparinux sodium injection syringe. See “Disposing of used fondaparinux sodium injection needles and syringes” below.

Figure F.

Figure G.

9. Throw away (dispose of) used and unused fondaparinux sodium injection syringes:

- Put your used fondaparinux sodium injection needles and syringes in an FDA-cleared sharps disposal container right away after use. **Do not**throw away (dispose of) loose needles and syringes in your household trash.

- If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

1. made of a heavy-duty plastic,
2. can be closed with a tight-fitting, puncture- resistant lid, without sharps being able to come out,
3. upright and stable during use,
4. leak- resistant, and

- properly labeled to warn of hazardous waste inside the container.When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

This Instructions for Use has been approved by the U.S. Food and Drug Administration

Revised: 02/2025

Manufactured by Jiangsu Hengrui Pharmaceuticals Co., Ltd.

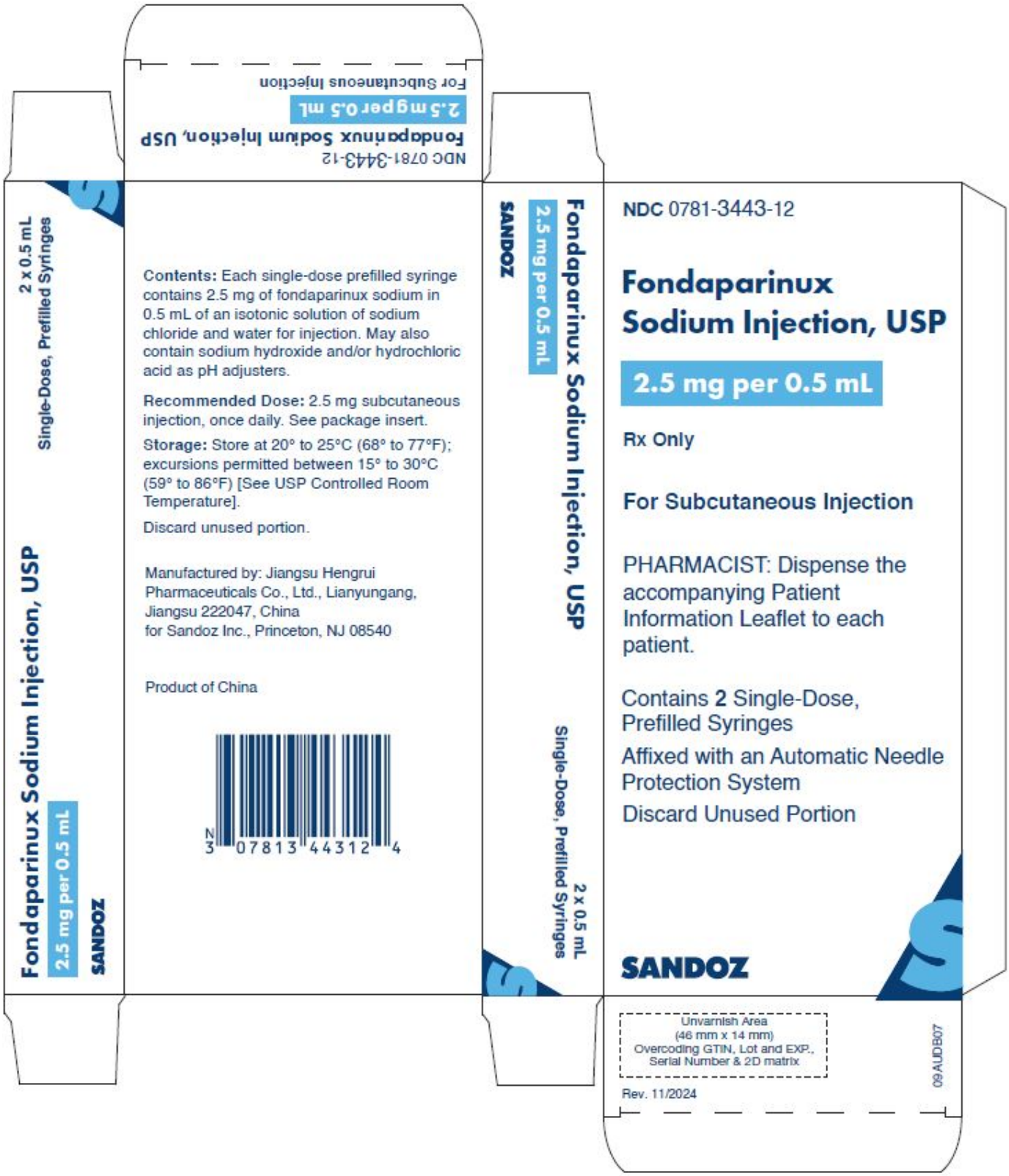
Lianyungang, Jiangsu 222047, China for

Sandoz Inc., Princeton, NJ 08540

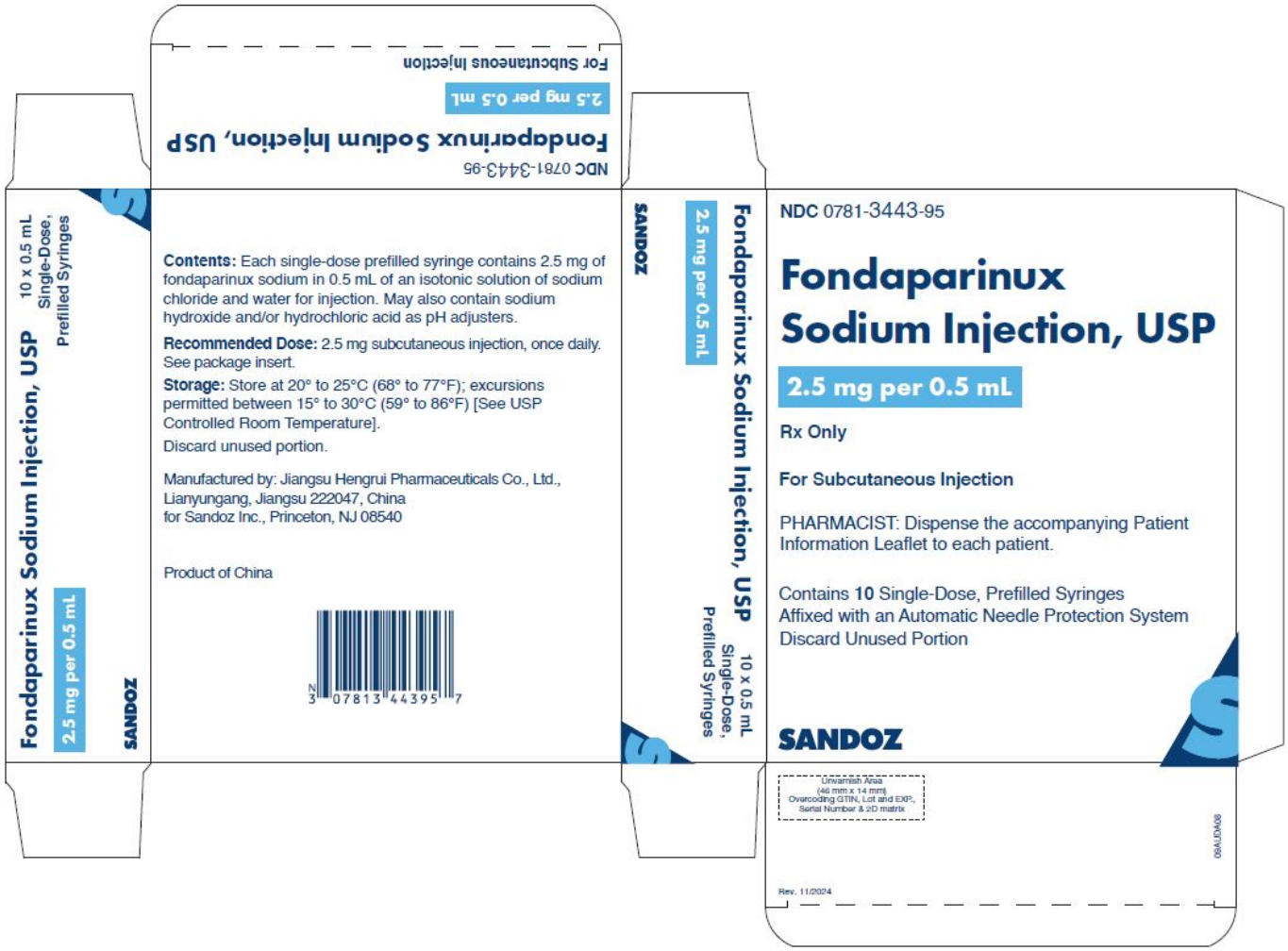
09UF10

2.5 mg/0.5 mL

2-pack carton label **NDC 0781-3443-12**

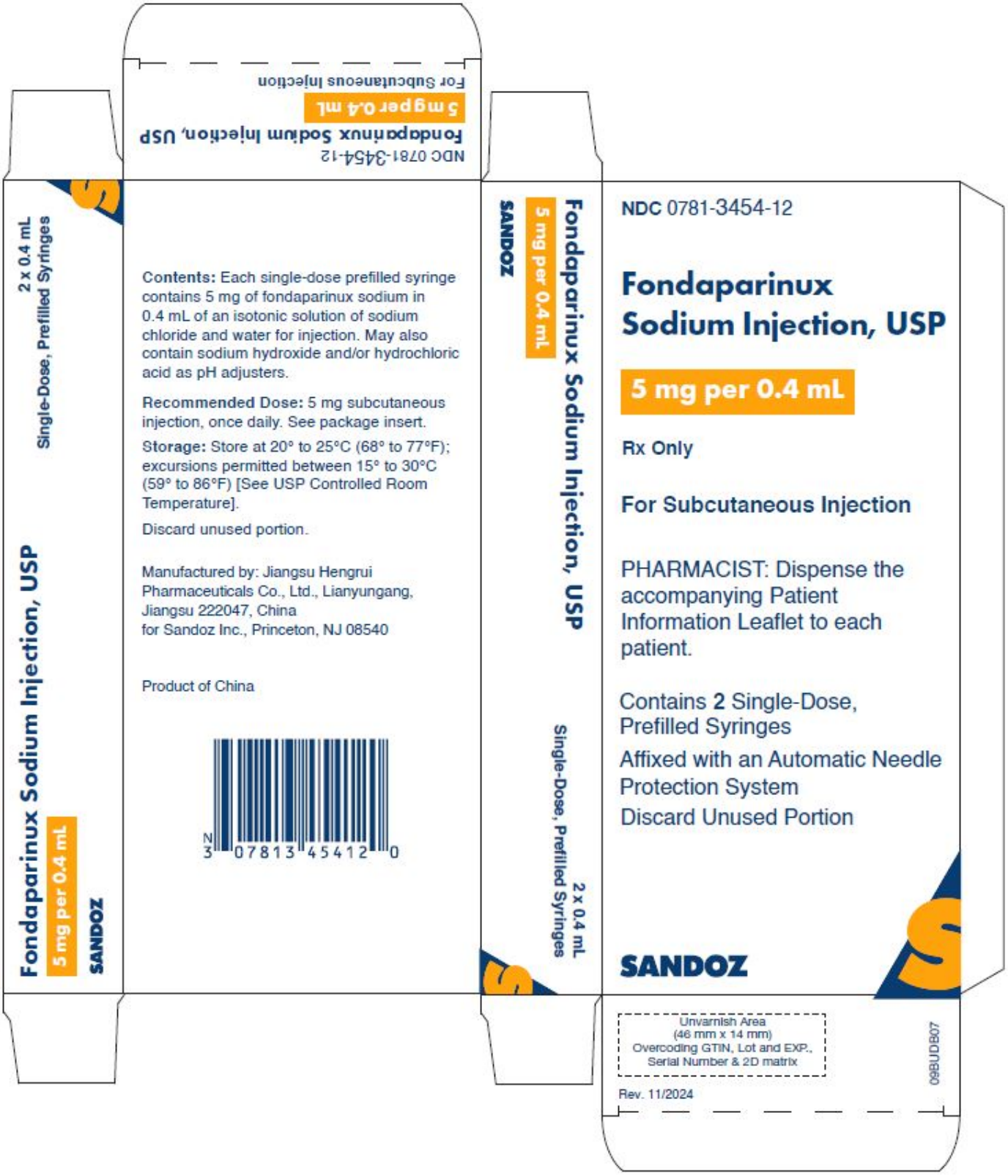


10-pack carton label **NDC 0781-3443-95**



5 mg/0.4 mL

2-pack carton label **NDC 0781-3454-12**



10-pack carton label **NDC 0781-3454-95**

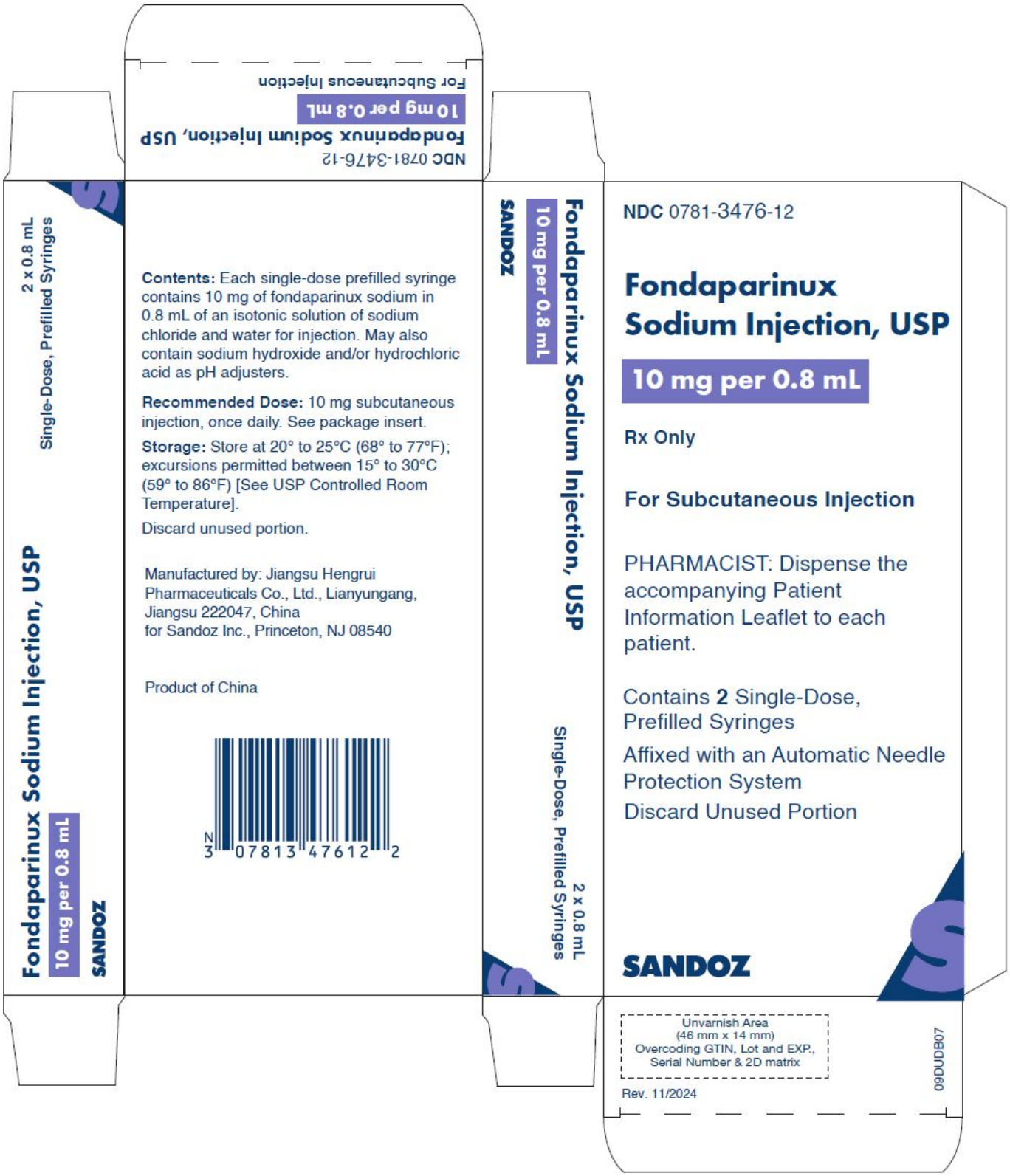
7.5 mg/0.6 mL

2-pack carton label **NDC 0781-3465-12**

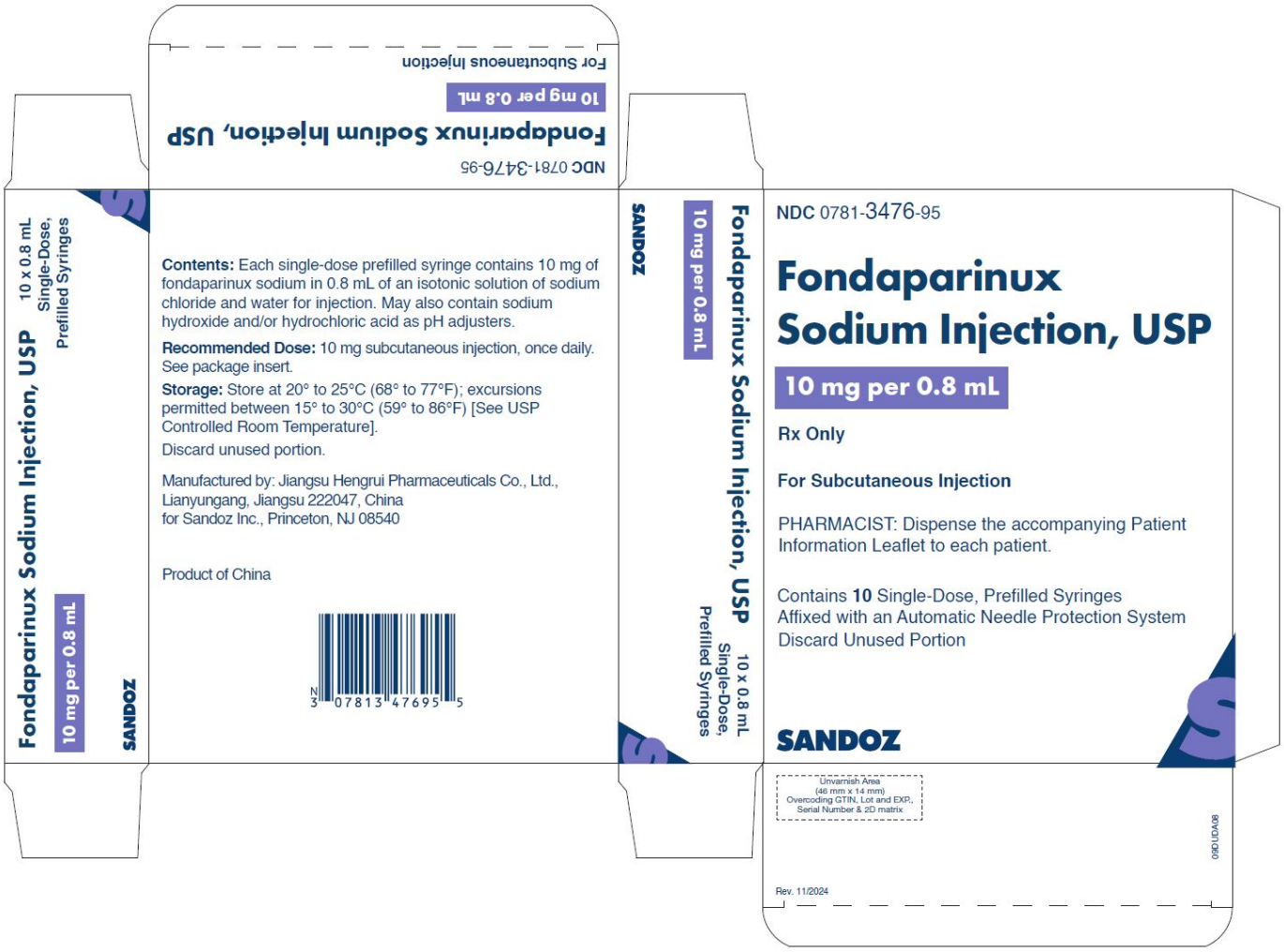
10-pack carton label **NDC 0781-3465-95**

10 mg/0.8 mL

2-pack carton label **NDC 0781-3476-12**



10-pack carton label **NDC 0781-3476-95**



FONDAPARINUX SODIUM

fondaparinux sodium injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-3443
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
FONDAPARINUX SODIUM (UNII: X0Q6N9USOZ) (FONDAPARINUX - UNII:J177FOW5JL)	FONDAPARINUX SODIUM	2.5 mg in 0.5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-3443-12	2 in 1 CARTON	06/18/2019	
1	NDC:0781-3443-94	0.5 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0781-3443-95	10 in 1 CARTON	06/18/2019	
2	NDC:0781-3443-94	0.5 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206812	06/18/2019	

FONDAPARINUX SODIUM

fondaparinux sodium injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-3454
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
FONDAPARINUX SODIUM (UNII: X0Q6N9USOZ) (FONDAPARINUX - UNII:J177FOW5JL)	FONDAPARINUX SODIUM	5 mg in 0.4 mL

Inactive Ingredients	
Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-3454-12	2 in 1 CARTON	06/18/2019	
1	NDC:0781-3454-94	0.4 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0781-3454-95	10 in 1 CARTON	06/18/2019	

2	NDC:0781-3454-94	0.4 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206812	06/18/2019	

FONDAPARINUX SODIUM

fondaparinux sodium injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-3465
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FONDAPARINUX SODIUM (UNII: X0Q6N9USOZ) (FONDAPARINUX - UNII:J177FOW5JL)	FONDAPARINUX SODIUM	7.5 mg in 0.6 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-3465-12	2 in 1 CARTON	06/18/2019	
1	NDC:0781-3465-94	0.6 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0781-3465-95	10 in 1 CARTON	06/18/2019	
2	NDC:0781-3465-94	0.6 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206812	06/18/2019	

FONDAPARINUX SODIUM

fondaparinux sodium injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-3476
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FONDAPARINUX SODIUM (UNII: X0Q6N9USOZ) (FONDAPARINUX - UNII:J177FOW5JL)	FONDAPARINUX SODIUM	10 mg in 0.8 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-3476-12	2 in 1 CARTON	06/18/2019	
1	NDC:0781-3476-94	0.8 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:0781-3476-95	10 in 1 CARTON	06/18/2019	
2	NDC:0781-3476-94	0.8 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206812	06/18/2019	

Labeler - Sandoz Inc. (005387188)

Registrant - Jiangsu Hengrui Pharmaceuticals Co., Ltd. (654147255)

Establishment

Name	Address	ID/FEI	Business Operations
Jiangsu Hengrui			analysis(0781-3443, 0781-3454, 0781-3465, 0781-3476) , pack(0781-3443,

Pharmaceuticals Co., Ltd. (Dongjin Road Site)		421324417	0781-3454, 0781-3465, 0781-3476) , sterilize(0781-3443, 0781-3454, 0781-3465, 0781-3476) , label(0781-3443, 0781-3454, 0781-3465, 0781-3476) , manufacture(0781-3443, 0781-3454, 0781-3465, 0781-3476)