Prescription Review Rules of Anticoagulant Drugs

Pharmaceutical Administration Committee of Chongqing Hospital Association

Abstract: The purpose of this study is to further standardize the clinical application of anticoagulant drugs and provide reference for improving the efficiency of prescription review in medical institutions. The initiative was led by the Pharmaceutical Management Professional Committee of the Chongqing Hospital Association, with the Second Affiliated Hospital of Chongqing Medical University taking the lead. Collaboration involved experts from various provinces nationwide. Based on drug instructions, basic prescription review rules, warning levels, and corresponding intervention measures were established for 12 commonly used anticoagulant drugs. For clinical applications not covered in the basic rules, consensus was reached by consulting 42 experts from 22 hospitals in 8 provinces nationwide, considering existing guidelines and expert consensus.

Results and Conclusions: The basic rules for prescription review were established for 12 anticoagulant drugs, including unfractionated heparin, enoxaparin sodium, nadroparin calcium, dalteparin sodium, fondaparinux sodium, bivalirudin, argatroban, warfarin, dabigatran etexilate, rivaroxaban, apixaban, and edoxaban. Warning levels and corresponding intervention measures beyond the basic rules were outlined. For clinical applications not covered in the basic rules, 17 prescription review recommendations were formed through two rounds of expert consultation. As clinical research progresses, this consensus will be further updated and adjusted. Additionally, since the consensus does not cover all clinical uses of anticoagulant drugs, prescription reviewers must conduct individualized assessments based on the specific circumstances of the patients.

Keywords: Anticoagulant drugs; Prescription appropriateness; Prescription review rules; Clinical application; Expert consensus.

As the aging population in China intensifies, the proportion of patients taking anticoagulant drugs for the prevention and treatment of thrombotic diseases continues to increase[1–2]. Anticoagulant drugs prevent thrombus formation by inhibiting blood coagulation and are clinically used primarily in the prevention and treatment of thromboembolic diseases, such as atrial fibrillation (AF), acute myocardial infarction, post-operative mechanical heart valve replacement, deep vein thrombosis (DVT), pulmonary embolism (PE), disseminated intravascular coagulation (DIC), etc. Anticoagulant drugs can be categorized by their mechanisms of action into: (1) Vitamin K antagonists (VKA), such as warfarin; (2) Indirect coagulation factor inhibitors, including unfractionated heparin (UFH), low molecular weight heparin (LMWH), fondaparinux sodium, etc.; (3) Direct thrombin inhibitors, such as dabigatran etexilate, bivalirudin, argatroban, etc.; (4) Direct factor Xa inhibitors, including rivaroxaban, apixaban, edoxaban, etc. These drugs are widely used in clinical practice across various disciplines such as cardiovascular, respiratory, oncology, obstetrics and gynecology, immunology and others.

In recent years, with the increasing variety of anticoagulant drugs, expanding clinical applications, and rising usage, off-label use in clinical practice has become more prevalent, significantly increasing the medication risks and economic burden for patients. Several thrombotic disease prevention and treatment guidelines have been issued globally, to some extent, standardizing the clinical use of anticoagulant drugs and providing important references for rational drug use in clinical settings. However, issues such as lack of professional knowledge among prescription reviewers and inconsistent prescription review rules persist in medical institutions. Therefore, in May 2022, the Pharmaceutical Management Professional Committee of the Chongqing Hospital Association initiated the "Anticoagulant Drug Prescription Review Rule Development Project." Led by the Second Affiliated Hospital of Chongqing Medical University and in collaboration with clinical experts, pharmacy experts, evidence-based medicine experts, and others from

various medical institutions, a consensus was reached through discussions focusing on key review topics such as indications, dosages, special populations, and drug interactions of anticoagulant drugs.

This consensus includes two main components: (1) The basic prescription review rules for anticoagulant drugs, including unfractionated heparin (UFH), low molecular weight heparin (LMWH) (such as enoxaparin sodium, nadroparin calcium and dalteparin sodium), fondaparinux sodium, rivaroxaban, apixaban, warfarin, dabigatran etexilate, rivaroxaban, apixaban, edoxaban, etc., established based on drug instructions. It also includes Warning levels beyond the basic rules for prescription review and corresponding intervention measures. (2) Recommendations for prescription review formed based on evidence from evidence-based medicine for clinical applications not covered by the basic prescription review rules, totaling 17 recommendations. This consensus, based on a comprehensive review of relevant domestic and international guidelines, latest research findings, and clinical practice experiences, takes the perspective of medical institution prescription (order) review work for the first time. It comprehensively summarizes prescription recommendations for various common anticoagulant drugs in terms of indications, dosages, special populations, and specific pathological conditions. The goal is to enhance the operability of manual and/or computerized prescription review in medical institutions. This is crucial for improving the efficiency of anticoagulant drug prescription review, ensuring the safety and effectiveness of patient medication.

1. Prescription Review Rules of Anticoagulant Drugs, Warning levels for Drug Use Exceeding Prescription Review Rules, and Intervention Measures

This section includes three parts of basic prescription review rules, Warning levels of rules exceeded, and intervention measures. The anticoagulant drugs for which basic prescription review rules are established include unfractionated heparin (UFH), low molecular weight heparin (LMWH) (such as enoxaparin sodium, nadroparin calcium and dalteparin sodium), fondaparinux sodium, rivaroxaban, apixaban, warfarin, dabigatran etexilate, rivaroxaban, apixaban, edoxaban, etc. The content of prescription review rules includes indications, dosages, medication for special populations and specific pathological conditions, contraindications, drug interactions, etc. For clinical applications beyond the basic prescription review rules for anticoagulant drugs, this consensus defines four Warning levels of prohibited, not recommended, use in caution and need close attention. Specific intervention measures are recommended for prescriptions (orders) for each of these four Warning levels (Table 1). Detailed information on the basic rules for prescription review and the Warning levels of rules exceeded for each anticoagulant drug is shown in Tables 2~13.

Table 1 Warning Levels and Intervention Measures for Drug Use Exceeding Prescription Review Rules

Warning Level	Definition	Intervention Measures
Prohibited	The drug use is prohibited, which can cause serious consequences and even endanger life if used.	Forced failure in the prescription review system, and the doctor cannot write prescriptions.
Not recommended	Including drug use exceeding the instructions (indications, dosage, course of treatment, etc.)[a], drug use violating the regulations of the state on rational drug use control, drug use with no relevant research evidence for special people, and drug use that can cause serious consequences in combined use. There can be a greater risk if used.	Failure in the prescription review system, and the prescription shall be submitted to pharmacists for review. Doctors may give up or force prescriptions for those failing to pass the pharmacist's review. Prescriptions imposed by doctors must be communicated afterwards or included in the evaluation of rational drug use.
Use with caution	Use with caution. Use it if necessary, and close attention should be paid to any adverse reactions. Once the adverse reactions occur, the drug use should be discontinued immediately to avoid serious consequences. If there is no adverse reaction, the use of medicine can be continued.	Approval after review in the prescription review system, but a pop-up message is required to remind doctors of the possible risks.
Need close attention	It can be used, but there may be risks in need of close attention.	Automatic approval in the prescription review system, but pharmacists should pay close attention to its use.

a: If the drug use exceeding the instructions have been filed in medical authorities, the warning level will be adjusted to "use in caution"

Table 2 Prescription Review Rules of Heparin Sodium Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention and treatment of thrombosis or embolic diseases (myocardial infarction, thrombophlebitis, PE, etc.); (2) DIC caused by various reasons; (3) Anticoagulant treatment in hemodialysis, cardiopulmonary bypass, catheterization, microvascular surgery and some blood samples or instruments.	Not recommended
Dosage	Adults	(1) Deep subcutaneous injection: 5,000~10,000 IU for the first time, and then 8,000~10,000 IU every 8 hours or 15,000~20,000 IU every 12 hours; The total amount is 30,000~40,000 IU every 24 hours; (2) Intravenous injection: 5,000~10,000 IU for the first time, then 100 IU/kg per time, once every 4 hours, diluted with 0.9% sodium chloride injection before use; (3) Intravenous drip: 20,000~40,000 IU daily, added to 1,000 mL of 0.9% sodium chloride injection for continuous drip. Intravenous injection of 5,000 IU can be used as the initial dose before drip; (4) Preventive treatment: Mostly used after abdominal surgery in patients with high-risk thrombosis to prevent deep venous thrombosis. 5,000 IU is given subcutaneously 2 hours before surgery, but epidural anesthesia should be avoided. 5,000 IU is given every 8~12 hours after surgery, for about 7 days.	Not recommended
	Children	(1) Intravenous injection: 50 IU/kg for the first time, and then 50~100 IU every 4 hours; (2) Intravenous drip: 50 IU/kg for the first time, then 20,000 IU/m^2 per day according to the body surface area, and then slowly drip with 0.9% sodium chloride injection.	Use with caution
	Route of medication	Subcutaneous injection, intravenous injection, and intravenous drip	Prohibited
	Solvent	0.9% sodium chloride injection	Prohibited
Special Population	The elderly	Reduce use and strengthen monitoring.	Use with caution
	Children	Dose adjusted according to drug instructions.	Use with caution
	Pregnant women	Use with caution according to the recommended dose for adults.	Use with caution
	Breast feeding women	Use with caution according to the recommended dose for adults.	Use with caution
Special Pathological State	Abnormal renal function	No need for dose adjustment.	Need close attention
	Abnormal liver function	Prohibited for patients with severe liver dysfunction.	Prohibited
Taboo		Prohibited for patients allergic to heparin, or with spontaneous bleeding tendency, blood coagulation retardation (such as hemophilia, purpura and thrombocytopenia), ulcer, trauma, postpartum hemorrhage and severe liver dysfunction.	Prohibited
Drug Interaction		(1) Combined use of heparin with other anticoagulants, antiplatelet drugs, thrombolytic drugs, nonsteroidal anti-inflammatory drugs (NSAIDs) and systemic hormones may increase the risk of bleeding; (2) Combined use of heparin with some antimicrobial agents may increase the risk of bleeding.	Use with caution

Table 3 Prescription Review Rules of Enoxaparin Sodium Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention of venous thromboembolism (VTE); (2) Treatment of DVT with or without PE; (3) Treatment of unstable angina pectoris and non-Q wave myocardial infarction, in combined use with aspirin; (4) Prevention of thrombosis in extracorporeal circulation of hemodialysis; (5) Treatment of acute ST-segment elevation myocardial infarction, in combined use with thrombolytic agent or percutaneous coronary intervention (PCI).	Not recommended
Dosage	Adults	(1) Prevention of VTE: ①When surgical patients are at moderate risk of thrombosis, a subcutaneous injection of 2,000 IU (0.2 mL, based on anti-Xa activity, the same below) or 4,000 IU (0.4 mL) is recommended once a day, and the first administration should be given 2 hours before operation. When there is a high risk of thrombosis, a subcutaneous injection of 4,000 IU (0.4 mL) is recommended once a day, and the administration should be given 12 hours before operation, and last for 7~10 days, which can be extended until the risk of embolism is eliminated and the patient does not need to stay in bed; ②For internal medicine patients, a subcutaneous injection of 4,000 IU (0.4 mL) is recommended once a day for 6~14 days. (2) Treatment of DVT, with or without PE: a subcutaneous injection of 150 IU/kg once a day or 100 IU/kg twice a day is recommended. (3) Treatment of unstable angina pectoris and non-Q-wave myocardial infarction: a subcutaneous injection of 100 IU/kg, twice a day is recommended. The general course of treatment is 2~8 days in combined use with aspirin. (4) Prevention of thrombosis in extracorporeal circulation of hemodialysis: An arterial line injection of 100 IU/kg is recommended at the beginning of hemodialysis. For patients with high bleeding tendency, the dosage should be reduced to 50 IU/kg for bilateral vascular access or 75 IU/kg for unilateral thrombus access. When fibrin ring appears, a dose of 50~100 IU/kg should be given again.	Not recommended

		(5) Treatment of acute ST-segment elevation myocardial infarction: In combined use with thrombolytic agents or undergoing PCI at the same time, a subcutaneous injection of 100 IU/kg is given within 15 minutes after the initial intravenous injection of 3,100 IU/kg (≥75 IU/kg can be given subcutaneously for patients over 75 years old), and then given subcutaneously every 12 hours, and the recommended course of treatment is 8 days or until discharge (≤8 days). For patients undergoing coronary angioplasty, if the last subcutaneous injection is more than 8 hours before balloon dilatation, an intravenous injection of 30 IU/kg should be given.	
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Route of medication	Subcutaneous injection and intravascular injection	Prohibited
	Solvent	0.9% sodium chloride injection and 5% glucose injection	Prohibited
Special Population	The elderly	Use according to the recommended dose of adults or reduce it, and strengthen monitoring.	Use with caution
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Pregnant women	Use according to the recommended dose of adults, and strengthen monitoring.	Need close attention
	Breast feeding women	Use according to the recommended dose of adults, and strengthen monitoring.	Need close attention
	Patients with special weight	Low-weight patients (<40 kg) and obese patients [>100 kg or body mass index (BMI)>30 kg/m^2] should use according to the recommended dose of adults and the monitoring should be strengthened.	Use with caution
Special Pathological State	Abnormal renal function	(1) Patients with mild [creatinine clearance (CrCl) of 50~80 ml/min] and moderate (CrCl of 30~< 50 ml/min) renal damage are recommended to use it with caution without dose adjustment under close monitoring. (2) For patients with severe renal damage (CrCl of 15~<30 ml/min), the recommended preventive dose is 2,000 IU, once a day, injected subcutaneously; The recommended therapeutic dose is 100 IU/kg, once a day, injected subcutaneously, and use with caution under close monitoring.	Use with caution
	Abnormal liver function	Use with caution	Use with caution
Taboo		(1) Prohibited under the following circumstances: ①Patients allergic to enoxaparin sodium, heparin or its derivatives, including other LMWH; ②Patients with hemorrhage or bleeding related to severe coagulation disorder (except DIC unrelated to heparin therapy); ③Patients with a history of immune-mediated thrombocytopenia (HIT) or circulating antibodies in the past 100 days; ④Patients with obvious clinical active bleeding and diseases with high risk of bleeding, including recent hemorrhagic stroke, gastrointestinal ulcer, malignant tumor with high risk of bleeding, recent brain/spine/eye surgery, known or suspected esophageal varices, arteriovenous malformation, hemangioma or major vascular abnormalities in spinal canal or brain, or organ injury with bleeding tendency; ⑤Patients with spinal or epidural anesthesia or local anesthesia performed within 24 hours before using enoxaparin sodium.	Prohibited
		(2) Not recommended under the following circumstances: ①Patients with acute massive ischemic stroke with or without disturbance of consciousness; If the stroke is caused by embolism, enoxaparin should not be injected within 72 hours after the event; ②Patients with end-stage renal disease (CrCl<15 ml/min); ③Patients with uncontrollable arterial hypertension; ④Patients with acute infective endocarditis (except some embolic heart diseases).	Not recommended
Drug Interaction		(1) Not recommended for combined use with NSAIDs, thrombolytics and anticoagulants, except when there are strict indications; (2) Use with caution in combined use with antiplatelet drugs, dextran 40 and systemic glucocorticoid.	Use with caution

Table 4 Prescription Review Rules of Nadroparin Calcium Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention of VTE in patients with moderate or high risk of venous thrombosis in surgery; (2) Treatment of DVT; (3) Treatment of unstable angina pectoris and non-Q-wave myocardial infarction with aspirin; (4) Prevention of blood clots during cardiopulmonary bypass during hemodialysis.	Not recommended
Dosage	Adults	(1) Prevention of VTE: ①For operations with moderate risk of thromboembolism, a dose of 2,850 IU (0.3 mL) per time, once a day, and the first injection is 2 hours before operation; ②For operations with high risk of thromboembolism (such as hip and knee joint operations), the dosage is adjusted according to the body weight, and the daily injection dosage is 38 IU/kg; It can be used 12 hours before operation and 12 hours after operation, and daily (0.2~0.4 ml) on the third day after operation; From day 4, the adjusted dose is 57 IU/kg (0.3~0.6 ml) once a day, generally not exceeding 10 days. (2) Treatment of DVT: a dose of 85 IU/kg per time (or 0.1 ml per 10 kg), twice a day, injected subcutaneously, generally no more than 10 days. (3) Treatment of unstable angina pectoris and non-Q-wave myocardial infarction: a dose of 86 IU/kg per time, twice a day, injected subcutaneously, in combined use with aspirin. The course of treatment is generally about 6 days. (4) Hemodialysis: When dialysis starts, a dose of about 65 IU/kg (0.3~0.6 mL) is injected through the arterial end once, and the dosage can be adjusted according to the body weight and	Not recommended

		bleeding risk.	
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Route of medication	Subcutaneous injection and intravascular injection	Prohibited
	Solvent	Do not mix with other preparations.	Prohibited
Special Population	The elderly	Use according to the recommended dose of adults or reduce it, and strengthen monitoring.	Use with caution
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Pregnant women	See Table16.	Need close attention
	Breast feeding women	See Table16.	Need close attention
	Patients with special weight	For low-weight patients (<40 kg) and obese patients (>100 kg), use according to the recommended dose of adults, and strengthen monitoring.	Use with caution
Special Pathological State	Abnormal renal function	(1) Prevention of VTE: For patients with moderate renal damage (CrCl 30~50 ml/min) and severe renal damage (CrCl 30~50 mL/min), the dosage should be reduced by 25%~33% according to the specific situation;	Use with caution
		(2) Treatment of thromboembolic diseases, unstable angina pectoris and non-Q wave myocardial infarction: ①For patients with moderate renal damage (CrCl 30~50 ml/min), the dosage should be reduced by 25%~33% according to the specific situation;	Use with caution
		②Prohibited in patients with severe renal damage (CrCl<30 ml/min).	Prohibited
	Abnormal liver function	Use with caution	Use with caution
Taboo		(1) Prohibited for the following patients: ①Patients allergic to nadroparin or any excipient in its injection; ②Patients with a history of thrombocytopenia caused by nadroparin; ③Patients with active bleeding or increased risk of bleeding related to abnormal hemostasis (except DIC not caused by heparin); ④Patients with organic injuries (such as active peptic ulcer) that may cause bleeding; ⑤Patients suffering hemorrhagic cerebrovascular accident; ⑥Patients with acute infective endocarditis.	Prohibited
		(2) Generally not suitable for the following patients: ①Patients with severe renal dysfunction; ②Patients suffering hemorrhagic cerebrovascular accident; ③Patients with uncontrolled hypertension.	Not recommended
Drug Interaction		(1) Combined use with acetylsalicylic acid (used in antipyretic and analgesic doses), NSAIDs, dextran 40 and ticlopidine may increase the risk of bleeding; (2) Use with caution in combined use with systemic glucocorticoids; (3) Use with caution in combined use with antiplatelet drugs.	Use with caution

Table 5 Prescription Review Rules of Dalmatine Sodium Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Treatment of acute DVT; (2) Prevention of coagulation in extracorporeal circulation system during hemodialysis and hemofiltration in patients with acute renal failure or chronic renal insufficiency; (3) Treatment of unstable coronary artery diseases, such as unstable angina pectoris and non-Q-wave myocardial infarction; (4) Prevention of thrombosis related to operation.	Not recommended
Dosage	Adults	(1) Treatment of acute DVT: 200 IU/kg per time, once a day, injected subcutaneously. The total daily amount is ≤1,8000 IU; Or 100 IU/kg per time, twice a day, injected subcutaneously; Or continuous intravenous infusion with an initial dose of 100 IU/kg, and it can be repeated after 12 hours. (2) Prevention of blood coagulation during hemodialysis and hemofiltration: Chronic renal failure, when the time of hemodialysis and hemofiltration is ≤4 hours, 5,000 IU can be given by rapid intravenous injection; When the time of hemodialysis and hemofiltration is >4 hours, 30~40 IU/kg can be rapidly injected intravenously, followed by intravenous infusion at the rate of 10~15 IU/kg per hour. Patients with acute renal failure can be rapidly injected with 5~10 IU/kg intravenously, followed by intravenous infusion at the rate of 4~5 IU/kg per hour. (3) Treatment of unstable coronary artery diseases, such as unstable angina pectoris and non-Q-wave myocardial infarction: 120 IU/kg per time, twice a day, injected subcutaneously, with the maximum dose of 10,000 IU every 12 hours, for at least 6 days, and the treatment can be extended if necessary, with the total course of treatment not exceeding 45 days. A fixed dose for follow-up treatment: 5,000 IU for female patients weighing <80 kg and male patients <70 kg; 7,500 IU for female patients ≥80kg and male patients ≥70 kg; Injected subcutaneously, twice a day. (4) Prevention of thrombosis related to operation: ①For patients with moderate risk of thrombosis, 2,500 IU is injected subcutaneously 1~2 hours before operation, and 2,500 IU is given once a day every morning after operation until they can move, which usually takes 5~7 days or more; Patients with persistent activity limitation are given 5,000 IU, once a day, injected subcutaneously, usually for 12~14 days or longer;	Not recommended

		②Patients with high risk of thrombosis are given subcutaneous injection of 5,000 IU at night before operation and 5,000 IU at night after operation, once a day, until the patient can move, which usually takes 5~7 days or more; Or 2,500 IU injected subcutaneously 1~2 hours before operation, 2,500 IU subcutaneously 8~12 hours after operation, and then 5,000 IU subcutaneously once a day every morning.	
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Route of medication	Subcutaneous injection and intravascular injection	Prohibited
	Solvent	0.9% sodium chloride injection and 5% glucose injection	Prohibited
Special Population	The elderly	Use according to the recommended dose of adults or reduce it, and strengthen monitoring.	Use with caution
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Pregnant women	See Table16.	Need close attention
	Breast feeding women	See Table16.	Need close attention
Special Pathological State	Abnormal renal function	Patients with severe renal damage may need to reduce the dosage and strengthen monitoring.	Use with caution
	Abnormal liver function	Use with caution in patients with severe liver dysfunction.	Use with caution
Taboo		(1) Patients allergic to dalteparin sodium, any auxiliary materials, other LMWH and/or heparin or pork products; (2) Patients confirmed or suspected to have a history of heparin-induced immune-mediated thrombocytopenia (type II); (3) Patients with acute gastroduodenal ulcer; (4) Patients with cerebral hemorrhage or other active bleeding; (5) Patients with severe coagulation diseases; (6) Patients suffering from septic endocarditis; (7) Patients with injuries to the central nervous system, eyes and ears and operations; (8) Prohibited to perform spinal or epidural anesthesia or spinal puncture when receiving large doses of dalteparin (such as treating acute DVT, PE and unstable coronary artery disease).	Prohibited
Drug Interaction		(1) Combined use with drugs that can increase the risk of bleeding (anticoagulants, antiplatelet drugs, thrombolytic drugs, NSAIDs, etc.) increases the risk of bleeding; (2) In combined use with drugs that may interact with heparin, interaction is not excluded.	Use with caution

Table 6 Prescription Review Rules of Fondaparinux Sodium Injection

Indicator of Review	**Type of Review**	**Content of Review**	**Warning Level for Drug Use Beyond Rules**
Indication[a]		(1) Prevention of VTE in patients undergoing major orthopedic surgery of lower limbs (hip fracture, major knee surgery hip replacement, etc.); (2) Treatment of patients with unstable angina pectoris/non-ST-segment elevation myocardial infarction without indication for emergency (<120 min) PCI; (3) Treatment of patients with ST-segment elevation myocardial infarction who used thrombolysis or did not initially receive other forms of reperfusion therapy.	Not recommended
Dosage	Adults	(1) Patients undergoing major orthopedic surgery: The recommended dose is 2.5 mg per time, once a day, injected subcutaneously after operation. The first dose should be 6 hours after operation, and the drug can only be given after confirming hemostasis. The administration should last for at least 5~9 days after operation, usually until the patient can get up and walk around. The course of treatment for patients with hip fracture surgery can be increased by 24 days. (2) Treatment of unstable angina pectoris/non-ST-segment elevation myocardial infarction: The recommended dose is 2.5 mg per time, once a day, injected subcutaneously. The longest duration of treatment is 8 days or until the patient leaves the hospital (<8 days). After PCI, the time of administration again is not earlier than 2 hours after sheath removal. (3) Treatment of ST-segment elevation myocardial infarction: The recommended dose is 2.5 mg per time, once a day. The first dose should be given intravenously, followed by subcutaneous injection. The longest duration of treatment is 8 days or until the patient leaves the hospital (<8 days). After PCI, the time of administration again is not earlier than 3 hours after sheath withdrawal. Patients undergoing coronary artery bypass grafting should not be given drugs within 24 hours before operation, and they can be given drugs again 48 hours after operation.	Not recommended
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Route of medication	Subcutaneous injection and intravenous injection	Prohibited
	Solvent	0.9% sodium chloride injection	Prohibited
Special Population	The elderly	Use according to the recommended dose of adults, and strengthen monitoring.	Use with caution
	Children	See prescription review recommendation 13 in Table 15.	Use with caution
	Pregnant women	See Table16.	Use with caution
	Breast feeding women	See Table16.	Need close attention
	Patients with special weight	For patients weighing <50 kg, use according to the recommended dose for adults, and strengthen monitoring.	Use with caution
Special Pathological State	Abnormal renal function	(1) Prevention of VTE: For patients with CrCl of 20~50 ml/min, the dosage should be adjusted to 1.5 mg once a day;	Use with caution
		(2) Prohibited in patients with CrCl<20 ml/min.	Prohibited
	Abnormal liver function	Use with caution in patients with severe liver damage.	Use with caution
Taboo		(1) Patients allergic to fondaparinux sodium or any excipient component in this medicine; (2) Patients with active bleeding with clinical significance; (3) Patients with acute bacterial endocarditis.	Prohibited

Drug Interaction		Combined use with drugs that can increase the risk of bleeding (anticoagulants, antiplatelet drugs, NSAIDs, etc.) increases the risk of bleeding.	Use with caution

a: The indications in the drug instructions and related guidelines of fondaparinux sodium approved by FDA in the US also include (1) prevention of deep vein thrombosis after abdominal surgery, and the usage and dosage are the same as those in preventing VTE[3-4]; (2) Treatment of DVT and PE: Patients weighing <50 kg are given 5mg per time, once a day, injected subcutaneously; Those weighing 50~100 kg are given 7.5mg per time, once a day, injected subcutaneously; Those weighing >100 kg are given 10mg per time, once a day, injected subcutaneously. The course of treatment is 5~9 days, followed by oral anticoagulants[3,5]. However, this consensus recommends that it be used after being approved by medical authorities for "drug use exceeding the instructions" in view of the above indications.

Table 7 Prescription Review Rules of Bivarudine for Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Anticoagulant therapy for patients with unstable angina undergoing percutaneous transluminal coronary angioplasty (PTCA); (2) Anticoagulant therapy for patients undergoing PCI, including anticoagulation therapy for patients with HIT or heparin-induced thrombocytopenia and thrombosis syndrome (HITTS) or patients with the above risks.	Not recommended
Dosage	Adults	(1) Patients without HIT/HITTS: Before PCI/PTCA, a dose of 0.75 mg/kg is given intravenously, and immediately after that, a dose of 1.75 mg/kg is given intravenously until the end of the operation. 5 minutes after intravenous injection, the acti-vated clotting time (ACT) should be monitored, and if necessary, a dose of 0.3 mg/kg can be injected intravenously again. After 4 hours of administration, if necessary, the infusion continues at the rate of 0.2 mg/kg per hour, and the longest administration time is 20 hours. (2) Patients with HIT/HITTS: a dose of 0.75 mg/kg is given intravenously first, and a dose of 1.75mg/kg is given continuously during PCI.	Not recommended
	Children	Unknown	Not recommended
	Route of medication	Intravenous injection and intravenous infusion	Prohibited
	Solvent	5% glucose injection and 0.9% sodium chloride injection	Prohibited
Special Population	The elderly	Use according to the recommended dose of adults, and strengthen monitoring.	Use with caution
	Children	Unknown	Not recommended
	Pregnant women	Unknown	Not recommended
	Breast feeding women	Unknown	Not recommended
Special Pathological State	Abnormal renal function	No need to reduce the dosage of intravenous injection, but the dosage of intravenous infusion should be reduced: (1) 1.75 mg/kg per hour for patients with CrCl 30~59 mL/min; (2) 1 mg/kg per hour for patients with CrCl<30 mL/min; (3) 0.25 mg/kg per hour for hemodialysis patients.	Use with caution
	Abnormal liver function	No need for dose adjustment.	Need close attention
Taboo		(1) Patients with active bleeding; (2) Patients allergic to bivarudine and its auxiliary materials or hirudin.	Prohibited
Drug Interaction		Combined use of anticoagulants, antiplatelet drugs or thrombolytic drugs increases the risk of bleeding.	Use with caution

Table 8 Prescription Review Rules of Agatraban Injection

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Improvement of neurological symptoms (motor paralysis) and daily activities (walking, standing up, sitting eating) of patients with acute ischemic cerebral infarction within 48 hours after onset; (2) Improvement of limb ulcer, resting pain and cold sensation in patients with chronic arterial occlusive disease (thromboangiitis obliterans and arteriosclerosis obliterans).	Not recommended
Dosage	Adults	(1) Improvement of neurological symptoms and daily activities of patients with acute ischemic cerebral infarction within 48 hours of onset: 60 mg once a day for 2 days, and continuous intravenous drip for 24 hours; After 5 days, 10 mg per time, twice a day, 3 hours per time. It can be appropriately increased or decreased according to age and symptoms; (2) Improvement of the ulcer, rest pain and cold sensation of limbs in patients with chronic arterial occlusive disease: 10 mg per time, twice a day, and intravenous drip for 2~3 hours per time. It can be appropriately increased or decreased according to age and symptoms. The course of treatment is within 4 weeks.	Not recommended
	Children	Unknown	Not recommended
	Route of medication	Intravenous infusion	Prohibited
	Solvent	0.9% sodium chloride injection, 5% glucose injection and sodium lactate ringer injection	Prohibited
Special Population	The elderly	Reduce dosage and strengthen monitoring.	Use with caution
	Children	Unknown	Not recommended
	Pregnant women	See Table 16.	Use with caution
	Breast feeding women	See Table 16.	Not recommended
Special Pathological State	Abnormal renal function	No need for dose adjustment.	Need close attention
	Abnormal liver function	Use with caution in patients with severe liver dysfunction.	Use with caution
Taboo		(1) Hemorrhagic patients; (2) Patients with cerebral embolism or possible cerebral embolism;	Prohibited

		(3) Patients with cardiogenic cerebral infarction with serious disturbance of consciousness; (4) Patients allergic to the components of this medicine.	
Drug Interaction		Combined use with anticoagulants, antiplatelet drugs, thrombolytic drugs and defibrase drugs increases the risk of bleeding.	Use with caution

Table 9 Prescription Review Rules of Warfarin Sodium Tablets

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention and treatment of DVT and PE; (2) Prevention and treatment of thromboembolic complications after AF and/or heart valve replacement; (3) Reduction of the risk of death, recurrence and thromboembolism events (such as stroke or systemic embolism) after myocardial infarction.	Not recommended
Dosage	Adults	Dose adjusted according to the international normalized ratio (INR).	Not recommended
	Children	Dose adjusted according to INR.	Not recommended
Special Population	The elderly	Dose adjusted according to INR.	Use with caution
	Children	Dose adjusted according to INR.	Not recommended
	Pregnant women	(1) Use with caution in pregnant women with mechanical heart valves with high risk of thromboembolism;	Use with caution
		(2) Prohibited for pregnant women in other cases.	Prohibited
	Breast feeding women	Dose adjusted according to INR.	Need close attention
Special Pathological State	Abnormal renal function	Dose adjusted according to INR.	Need close attention
	Abnormal liver function	Dose adjusted according to INR.	Need close attention
Taboo		(1) Patients with bleeding tendency or blood dyscrasias; (2) Patients who have recently or are expected to undergo traumatic operations on the central nervous system, eyes or large open wounds; (3) Patients with bleeding tendency related to the following diseases: active ulcer or obvious bleeding of gastrointestinal tract, urogenital tract or respiratory tract, central nervous system bleeding, cerebral aneurysm, aortic dissection aneurysm, pericarditis, pericardial effusion, and infectious endocarditis; (4) Patients with premature abortion, eclampsia and preeclampsia; (5) Unsupervised patients with poor potential compliance; (6) Patients using spinal puncture and other diagnostic measures or treatments that may lead to uncontrollable bleeding; (7) Patients allergic to warfarin or any other components of this medicine; (8) Patients who have undergone block anesthesia or lumbar anesthesia in the main area; (9) Patients with malignant hypertension.	Prohibited
Drug Interaction		(1) Warfarin's metabolism is related to cytochrome P450 (CYP) isoenzymes CYP2C9, 1A2 and 3A4, which may be influenced by its inducers or inhibitors; (2) Use with caution in combined use of warfarin and other drugs that can increase the risk of bleeding (such as antiplatelet drugs and NSAIDs); (3) Warfarin may be affected in combined use with some antibacterial drugs; (4) Warfarin may be affected in combined use with some traditional Chinese medicines.	Use with caution

Table 10 Prescription Review Rules of Dabigatran Etexilate Capsules

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention of stroke and systemic embolism in adult non-valvularatrial fibrillation (NVAF) with one or more of the following risk factors: ①Previous stroke, transient ischemic attack or systemic embolism; ②Left ventricular ejection fraction <40%; ③Heart failure with symptoms, the heart function rating of New York Heart Association is ≥2; ④Patients ≥75 years old; ⑤Patients ≥65 years old with diabetes, coronary heart disease or hypertension. (2) Treatment of acute DVT and/or PE and preventing related deaths. (3) Prevention of DVT and/or PE recurrence and related deaths.	Not recommended
Dosage	Adults	150 mg per time, twice a day. The treatment of DVT and PE should be started after at least 5 days of parenteral anticoagulation.	Not recommended
	Children	See prescription review recommendation 13 in Table 15.	Not recommended
Special Population	The elderly	For patients ≥80 years old, the adjusted dose is 110 mg per time, twice a day; For patients >75 years old, the dose can be adjusted to 110 mg per time, twice a day.	Use with caution
	Children	See prescription review recommendation 13 in Table 15.	Not recommended
	Pregnant women	Unknown	Not recommended
	Breast feeding women	Unknown	Not recommended
	Patients with special weight	Use according to the recommended dose of adults for patients weighing <50 kg, and strengthen monitoring.	Use with caution
Special	Abnormal renal function	(1) For patients with CrCl of 30~50 ml/min and high risk of bleeding, a dose of 110 mg,	Use with caution

Pathological State		twice a day is recommended;	
		(2) Not recommended for patients with CrCl <30 ml/min.	Not recommended
	Abnormal liver function	(1) Use with caution in patients with hepatic insufficiency;	Use with caution
		(2) When used to prevent NVAF-related stroke and systemic embolism, there is no treatment experience for patients whose liver transaminase is higher than 2 times the upper limits of normal (ULN).	Not recommended
	Others	Patients with gastritis, esophagitis or gastroesophageal reflux can be given a does of 150 mg, twice a day, or a dose of 110 mg, twice a day.	Need close attention
Taboo		(1) Patients allergic to active components or any auxiliary materials of this medicine; (2) Patients with clinically significant active bleeding; (3) Lesions or conditions with significant risk of massive hemorrhage, such as current or recent digestive tract ulcer, malignant vegetation with high risk of hemorrhage, recent brain or spinal cord injury, recent brain, spinal cord or eye surgery, recent intracranial hemorrhage, known or suspected esophageal varices, arteriovenous malformations, vascular aneurysms or vascular abnormalities in the main spine or brain; (4) Except for special circumstances such as switching anticoagulation therapy or giving UFH at a dose required to maintain the patency of central vein or arterial catheter, the combined therapy of any other anticoagulants is prohibited; (5) Patients with liver function damage or liver disease that is expected to affect the survival time; (6) Patients who need anticoagulant therapy for artificial heart valve replacement.	Prohibited
Drug Interaction		(1) Combined use of anticoagulant and antiplatelet drugs can increase the risk of bleeding. If combined, a dose of 110 mg, twice a day is recommended.	Use with caution
		(2) Dabigatran etexilate is the substrate of P-glycoprotein (P-gp): ①Strong P-gp inhibitors can increase the blood concentration of dabigatran etexilate, so its combined use with cyclosporine, systemic ketoconazole, itraconazole and dronedarone is prohibited.	Prohibited
		②Combined use with tacrolimus is not recommended.	Not recommended
		③Use with caution in combined use with other strong P-gp inhibitors, such as amiodarone, quinidine, verapamil and tigrello. In combined use of dabigatran etexilate and verapamil, a dose of 110 mg, twice a day is recommended.	Use with caution
		④Combined use with P-gp inducers, such as rifampicin, hypericum perforatum, carbamazepine or phenytoin may reduce the drug concentration, so its combined use with the above drugs should be avoided.	Not recommended
		⑤Protease inhibitors, such as ritonavir, can affect P-gp, so its combined use is not recommended.	Not recommended
		(3) Combined use of selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) can increase the risk of bleeding.	Use with caution

Table 11 Prescription Review Rules of Rivaroxaban Tablets

Indicator of Review	**Type of Review**	**Content of Review**	**Warning Level for Drug Use Beyond Rules**
Indication		(1) Prevention of venous thrombosis in adult patients undergoing elective hip or knee replacement surgery; (2) Treatment of DVT and PE in adult patients and reducing the risk of recurrence of DVT and/or PE; (3) For adult patients with NVAF who have one or more risk factors (such as congestive heart failure, hypertension, age ≥75 years old, diabetes, stroke or transient ischemic attack) to reduce the risk of stroke and systemic embolism; (4) Combined use with aspirin for patients with chronic coronary artery disease (CAD) or peripheral arterial disease (PAD) with high risk of ischemic events to reduce the risk of major cardiovascular events (cardiovascular death, myocardial infarction and stroke); (5) Treatment of VTE and prevention of the recurrence in children and adolescents under the age of 18 and weighing more than >30 kg after initial non-oral anticoagulation treatment for at least 5 days.	Not recommended
Dosage	Adults	(1) Prevention of venous thrombosis in adult patients undergoing elective hip or knee replacement: 10 mg per time, once a day. If the wound has stopped bleeding, the first medication should be taken 6~10 hours after the operation. For patients undergoing major hip surgery, the recommended course of treatment is 35 days; The recommended course of treatment for patients undergoing major knee surgery is 12 days; (2) Treatment of DVT and PE: 15 mg per time for the first 3 weeks, twice a day; 20 mg per time, once a day. The treatment course should be determined based on risk factors; (3) Reduction of the risk of recurrence of DVT and PE: After the completion of standard anticoagulant therapy, 10 mg once a day is recommended. For patients with high risk of recurrence, 20 mg once a day should be considered; (4) For adult patients with NVAF to reduce the risk of stroke and systemic embolism: 20 mg once a day; (5) For patients with CAD or PAD: 2.5 mg per time, twice a day, and 75~100 mg aspirin should be taken at the same time.	Not recommended
	Children	Dose adjusted according to body weight.	Not recommended
Special Population	The elderly	Patients >75 years old with NVAF should take it as appropriate, with a dose of 15 mg once a day. Dose adjusted according to body weight	Use with caution

	Children	Unknown	Not recommended
	Pregnant women	Unknown	Not recommended
	Breast feeding women	Unknown	Not recommended
	Patients with special weight	Low-weight patients with NAVF should use it as appropriate, with a dose of 15 mg once a day.	Use with caution
Special Pathological State	Abnormal renal function	(1) Prevention of venous thrombosis in adult patients undergoing elective hip or knee replacement surgery: Patients with CrCl <30 ml/min should avoid using it.	Not recommended
		(2) Treatment of DVT and PE in adult patients and reducing the risk of recurrence of DVT and/or PE: ①After 3 weeks' treatment, the dosage can be adjusted to 15 mg once a day for patients with CrCl of 30~49 ml/min;	Use with caution
		②Patients with CrCl <30 ml/min should avoid using it.	Not recommended
		(3) Reduction of the risk of stroke and systemic embolism in adult patients with NVAF: ①For patients with CrCl of 15~49 ml/min, 15 mg is recommended once a day;	Use with caution
		②Patients with CrCl <15 ml/min should avoid using it.	Not recommended
	Abnormal liver function	Prohibited in patients with liver disease who have the risk of abnormal coagulation and clinically related bleeding, including patients with liver cirrhosis who have reached Child Pugh B and C.	Prohibited
Taboo		(1) Patients allergic to rivaroxaban or any auxiliary materials of this medicine; (2) Patients with clinically significant active bleeding; (3) Lesions with significant risk of massive hemorrhage or the following situations: currently or recently suffering from gastrointestinal ulcer, malignant tumor with high risk of hemorrhage, recent brain or spinal injury, recent brain/spinal/ophthalmic surgery, recent intracranial hemorrhage, known or suspected esophageal varices, arteriovenous malformation, vascular aneurysm or major vascular malformation in spine or brain; (4) Except for special circumstances such as switching anticoagulant therapy or giving the dosage of UFH needed to maintain the patency of central vein or arterial catheter, it is prohibited to be used together with any other anticoagulant.	Prohibited
Drug Interaction		(1) Rivaroxaban is metabolized by CYP3A4 and is the substrate of P-gp, so: ①Pyrrole antifungal drugs (such as ketoconazole, itraconazole, voriconazole and posaconazole) or human immunodeficiency virus (HIV) protease inhibitors (such as ritonavir), which are strong inhibitors of CYP3A4 and P-gp, increase the risk of bleeding in combined use with rivaroxaban, so their combined use is not recommended;	Not recommended
		②Inhibitors of other pharmaceutical enzymes or proteins (such as clarithromycin, erythromycin and fluconazole.) may affect the pharmacokinetics of rivaroxaban in vivo, but it has no clinical significance;	Need close attention
		③The clinical data of dronedarone is limited, so its combined use with rivaroxaban should be avoided;	Not recommended
		④Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's wort, which are strong inducers of CYP3A4, can reduce the blood concentration of rivaroxaban, so it should be used with caution with monitoring strengthened.	Use with caution
		(2) In combined use with NSAIDs, antiplatelet drugs or SSRIs/SNRIs, the risk of bleeding increases.	Use with caution

Table 12 Prescription Review Rules of Apixaban Tablets

Indicator of Review	**Type of Review**	**Content of Review**	**Warning Level for Drug Use Beyond Rules**
Indication[a]		Prevention of VTE in adult patients undergoing elective hip or knee replacement.	Not recommended
Dosage	Adults	A dose of 2.5mg per time, twice a day. The first dose should be taken 12~24h after operation. The recommended course of treatment after hip replacement is 32~38 days; The recommended course of treatment after knee replacement is 10~14 days.	Not recommended
	Children	Use according to the recommended dose of adults, and strengthen monitoring.	Not recommended
Special Population	The elderly	Unknown	Need close attention
	Children	Unknown	Not recommended
	Pregnant women	Unknown	Not recommended
	Breast feeding women	Unknown	Not recommended
Special Pathological State	Abnormal renal function	(1) Use with caution in patients with severe renal damage (CrCl 15~30 ml/min);	Use with caution
		(2) Not recommended for patients with CrCl<15ml/min.	Not recommended
	Abnormal liver function	(1) Use with caution in patients with moderate liver damage, patients whose liver transaminase [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] is >2 ULN or whose total bilirubin is ≥1.5 ULN;	Use with caution
		(2) Not recommended for patients with severe liver damage.	Not recommended
Taboo		(1) Patients allergic to active components or any auxiliary materials of this medicine; (2) Patients with clinically active bleeding; (3) Patients with liver disease with abnormal coagulation and clinically relevant bleeding risk.	Prohibited
Drug Interaction		(1) Apixaban is mainly metabolized by CYP3A4/5, and it is also a P-gp substrate, so: ①Strong CYP3A4 and P-gp inhibitors can increase the absorption of apixaban, such as pyrrole antifungal drugs (ketoconazole, itraconazole, voriconazole and posaconazole) and HIV protease inhibitors (such as ritonavir), which can increase the area under the concentration-time curve (AUC) of apixaban by 2 times; ②Strong CYP3A4 and P-gp inducers can reduce the absorption of apixaban, such as	Use with caution

		rifampicin, phenytoin, phenobarbital or St. John's wort, which can reduce the average exposure of apixaban by about 50%. (2) In combined use with antiplatelet drugs, SSRIs/SNRIs or NSAIDs, the risk of bleeding increases. (3) Apixaban has a weak effect on liver drug enzymes, and generally does not affect the metabolism of other drugs.	

a: The indications in the drug instructions and related guidelines of apixaban tablets approved by FDA in the US also include (1) reduction of the risk of stroke and systemic embolism in patients with NVAF, which can be given 5 mg per time, twice a day[6-9]; (2) Treatment of DVT and PE, which can be given 10mg per time, twice a day 7 days before treatment, and 5 mg per time, twice a day 7 days after treatment[10-11]; (3) Reduction of the risk of recurrence of DVT and PE, which can be given 2.5 mg per time, twice a day with the first dose given at least 6 months after the initiation of treating DVT and PE[10-12]. However, this consensus recommends that it be used after being approved by medical authorities for "drugs exceeding the instructions" in view of the above indications.

Table 13 Prescription Review Rules of Edoxaban Tablets

Indicator of Review	Type of Review	Content of Review	Warning Level for Drug Use Beyond Rules
Indication		(1) Prevention of stroke and systemic embolism in adult patients with NVAF accompanied by one or more risk factors (such as congestive heart failure, hypertension, age≥75 years, diabetes, previous stroke or transient ischemic attack); (2) Treatment of adult DVT and PE and prevention of the recurrence of adult DVT and PE.	Not recommended
Dosage	Adults	(1) Prevention of stroke and systemic embolism: 60 mg per time, once a day for long-term use; (2) Treatment of DVT and PE and prevention of the recurrence: 60 mg per time, once a day, starting administration at least 5 days after initial non-oral anticoagulant therapy, and determining the course of treatment according to risk factors.	Not recommended
	Children	Use according to the recommended dose of adults, and strengthen monitoring.	Not recommended
Special Population	The elderly	Unknown	Need close attention
	Children	Unknown	Not recommended
	Pregnant women	Unknown	Not recommended
	Breast feeding women	Unknown	Not recommended
	Patients with special weight	Dose adjusted to 30 mg per time, once a day for patients weighing ≤60 kg.	Use with caution
Special Pathological State	Abnormal renal function	(1) For patients with moderate or severe renal damage (CrCl 15~50 ml/min), the dosage is adjusted to 30mg once a day;	Use with caution
		(2) Not recommended for patients with end-stage renal disease (CrCl <15 ml/min) or hemohemodialysis patients.	Not recommended
	Abnormal liver function	(1) No need for dose adjustment in patients with mild or moderate liver damage; Use with caution in patients with liver transaminase (ALT/AST) elevation >2 ULN or total bilirubin elevation ≥1.5 ULN;	Use with caution
		(2) Not recommended for patients with severe liver damage.	Not recommended
Taboo		(1) Patients who are allergic to active components or other auxiliary materials of this medicine; (2) Patients with clinically significant active bleeding; (3) Patients with liver disease accompanied by coagulation disorder and clinically relevant bleeding risk; (4) Lesions with significant bleeding risk or the following conditions, such as recent gastrointestinal ulcer, malignant tumor with high bleeding risk, recent brain or spinal injury, recent brain/spine/eye surgery, recent intracranial hemorrhage, known or suspected esophageal varices, arteriovenous malformation, vascular aneurysm or major spinal or cerebral vascular malformation; (5) Patients with uncontrollable severe hypertension; (6) Combined use with any other anticoagulants is prohibited, except for special circumstances such as switching anticoagulation therapy or giving UFH at a dose required to maintain the patency of central vein or arterial catheter.	Prohibited
Drug Interaction	Effects of other drugs on edoxaban	(1) Edoxaban is absorbed in the upper digestive tract, so drugs that accelerate gastric emptying and intestinal peristalsis may reduce the absorption of edoxaban . (2) Edoxaban is the substrate of P-gp, so: ①P-gp inhibitors can increase the absorption of edoxaban, so the blood concentration of edoxaban will increase when cyclosporine, dronedarone, erythromycin, ketoconazole, quinidine, verapamil and amiodarone are used together with edoxaban; In combined used with cyclosporine, dronedarone, erythromycin and ketoconazole, the dose of edoxaban should be adjusted to 30mg once a day; ②P-gp inducers can reduce the absorption of edoxaban, and its combined use with rifampicin can reduce the AUC and shorten the half-life ($t_{1/2}$) of edoxaban. The combined use with other P-gp inducers (such as phenytoin sodium, carbamazepine, phenobarbital or hypericum perforatum) can lead to the decrease of the blood concentration of edoxaban, so they should be used with caution. (3) In combined use with antiplatelet drugs, NSAIDs, SSRIs/SNRIs, the risk of bleeding increases.	Use with caution
	Effect of edoxaban on other drugs	(1) Edoxaban can increase the peak concentration (c_{max}) of digoxin, but has no effect on AUC; (2) Edoxaban can decrease c_{max} and AUC of verapamil.	Need close attention

2. Prescription Review Recommendations of Anticoagulant Drugs

In the drafting of consensus, the project team addressed clinical applications of anticoagulant drugs not covered by the aforementioned basic prescription review rules. Based on the existing guidelines and expert consensus and evidence-based medical evidence, the team conducted two rounds of consultations and opinion modifications by holding project initiation meetings, seminars and expert workshops, and conducting online surveys via phone calls and WeChat questionnaires. The consultations involved 42 clinical experts, pharmacy experts, and evidence-based medicine experts from 18 comprehensive tertiary Grade A hospitals and 4 specialized tertiary Grade A hospitals across 8 provinces and municipalities in China, including Beijing, Shanghai, and Jiangsu province. Eventually, prescription review recommendations were formulated for the clinical applications of 17 anticoagulant drugs. The evidence quality and recommendation strength were graded using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system, in which the evidence quality was divided into four grades: high, moderate, low, and very low, denoted as A, B, C and D respectively (Table 14). The recommendation strength, determined by a comprehensive assessment of the evidence quality, the balance of benefits and harms, patients' values and preferences, and resource consumption, was categorized into strong and weak recommendations, represented by 1 and 2 respectively. Detailed information on the 17 prescription review recommendations is available in Table 15, and the specific drug recommendations for special populations can be found in Tables 16~19.

Table 14 Criteria for Grading the Evidence Quality of Recommendations

Grade	Evidence Quality	Specific Description
A	High	Highly credible: The observed value is close to the true value.
B	Moderate	Moderately credible to the observed value: The observed value may be close to the true value, but it may also be very different.
C	Low	Limited credibility for the observed value: The observed value may be quite different from the true value.
D	Very low	Little certainty about the observed value: The observed value is likely to be very different from the true value.

Table 15 Prescription Review Recommendations of Anticoagulants in Some Clinical Applications

No.	Clinical Application	Recommendations	Recommendation Strength/Evidence Quality
1	Used for thrombosis in special parts[13]	(1) Selection, usage and dosage of anticoagulant drugs for portal vein thrombosis: UFH, LMWH and fondaparinux sodium can be selected for initial treatment, and warfarin and direct oral anticoagulants (DOACs) can be selected for long-term treatment, with the same usage and dosage as those used for VTE treatment, and the principle of individualized administration should be followed[14-23];	2/C
		(2) Selection, usage and dosage of anticoagulant drugs for mesenteric venous thrombosis: UFH, LMWH and fondaparinux sodium can be selected for initial treatment, and warfarin and DOACs can be selected for long-term treatment, with the same usage and dosage as the above drugs used for VTE treatment, and the principle of individualized administration should be followed[16, 21, 24-30];	2/C
		(3) Selection, usage and dosage of anticoagulant drugs for acute cranial vein (sinus) thrombosis: UFH and LMWH can be selected for acute phase treatment, and the usage and dosage are the same as those of the above drugs for VTE treatment, and the principle of individualized administration should be followed[31-35];	1/C
		(4) Selection, usage and dosage of long-term anticoagulant drugs for cranial vein (sinus) thrombosis: Warfarin and DOACs can be selected for long-term treatment, and the usage and dosage are the same as those of the above drugs for VTE treatment, and the principle of individualized administration should be followed[36-40].	2/C
2	Used after femoral iliac vein stent implantation	Selection, usage and dosage of anticoagulant drugs: UFH, LMWH, fondaparinux sodium, DOACs and warfarin, the usage and dosage are the same as those of the above drugs in VTE treatment[41-42].	Recommended by guidelines, and the evidence quality grading is not applicable.
3	Used after left atrial appendage occlusion and catheter ablation	(1) Selection, usage and dosage of anticoagulant drugs after left atrial appendage occlusion: warfarin and DOACs, the usage and dosage are the same as those of the above drugs used for AF stroke prevention[43-46];	Recommended by guidelines, and the evidence quality grading is not applicable.
		(2) Selection, usage and dosage of anticoagulant drugs after catheter ablation: UFH, LMWH, fondaparinux, warfarin, DOACs, and the usage and dosage are the same as those of the above drugs for AF stroke prevention[47-49].	1/B
4	Used for left ventricular thrombosis	Selection, usage and dosage of anticoagulant drugs: UFH, LMWH, fondaparinux, warfarin, DOACs, the usage and dosage are the same as those of the above drugs used in AF stroke prevention[50-52].	2/C
5	Used for valvular atrial fibrillation[53-55]	Indications: atrial fibrillation after mechanical valve replacement and moderate or severe mitral stenosis;	1/A
		Selection, usage and dosage of anticoagulant drugs: warfarin (Dose adjusted according to INR individualization, long-term anticoagulation)	1/A

6	Used after heart valve surgery[7, 56-58]	(1) Selection, usage and dosage of anticoagulants after mechanical valve replacement: See No.5 in this table for "valvular atrial fibrillation".	1/A
		(2) Selection, usage and dosage of anticoagulants after biological valve replacement: ①Warfarin, the dosage is adjusted according to INR individualization;	1/A
		②DOACs can be used in patients with AF, and the dosage is the same as that of DOACs used in AF stroke prevention.	Recommended by guidelines, and the evidence quality grading is not applicable.
		(3) Selection, usage and dosage of anticoagulants after valvuloplasty: ①Warfarin, the dosage is adjusted according to INR individualization;	1/A
		②DOACs, which can be used in patients with AF after 3 months of operation, have the same dosage as DOACs used in AF stroke prevention.	Recommended by guidelines, and the evidence quality grading is not applicable.
7	Used for acute peripheral arterial thrombosis[59-60]	(1) Selection, usage and dosage of anticoagulant drugs for patients with acute arterial embolism or thrombosis: UFH and LMWH, and the principle of individualized administration should be followed in usage and dosage;	Recommended by guidelines, and the evidence quality grading is not applicable.
		(2) Selection, usage and dosage of long-term anticoagulants for acute peripheral arterial thrombosis caused by AF are the same as those used for stroke prevention in AF patients, and long-term anticoagulation is required.	1/A
8	Used for immune diseases	(1) Indications: patients with antiphospholipid syndrome (APS) complicated with thrombosis[61-64].	1/A
		Selection, usage and dosage of anticoagulant drugs: ①UFH, LMWH and warfarin, with the same usage and dosage as those used in VTE treatment;	1/A
		②DOACs should be used with caution in APS patients, especially those with a history of arterial thrombosis;	1/A
		③Rivaroxaban is not recommended for patients with three kinds of phospholipid antibody positive arteriovenous thrombosis events;	1/A
		④When VKA or LMWH is not applicable, fondaparinux sodium can be selected, and the usage and dosage are the same as those of fondaparinux sodium in VTE treatment.	2/C
		(2) Indications: Nephrotic syndrome complicated with thrombosis[65-67].	1/A
		Selection, usage and dosage of anticoagulant drugs: ①UFH, LMWH and warfarin, with the same usage and dosage as those used in VTE treatment;	1/A
		②DOACs, the usage and dosage are the same as those of the above drugs in VTE treatment.	2/C
9	Used for patients with thrombophilia[68]	(1) UFH, LMWH and fondaparinux sodium are not recommended for patients with antithrombin deficiency;	1/C
		(2) Warfarin cannot be use for patients with protein C and protein S deficiency as the initial anticoagulant therapy, which may lead to the aggravation of thrombus tendency and skin necrosis.	1/A
10	Used for thrombocytopenia complicated with thrombosis.	(1) When the platelet count is $>50\times10^9\,L^{-1}$, anticoagulants can be used in full dose; When the platelet count is 25×10^9~$50\times10^9\,L^{-1}$, half or enough anticoagulants combined with platelet transfusion can be considered for prevention; When the platelet count is $<25\times10^9\,L^{-1}$, anticoagulants should be avoided[2,7,68-69].	Recommended by guidelines, and the evidence quality grading is not applicable.
		(2) Selection of anticoagulant drugs for HIT patients[70-72]: argatroban, bivalirudin, fondaparinux sodium, DOACs.	Recommended by guidelines, and the evidence quality grading is not applicable.
11	Used for patients with hepatic and renal insufficiency[2, 7]	(1) Liver dysfunction: ①Selection, usage and dosage of parenteral anticoagulants: UFH, with dose adjusted according to activated partial thromboplastin time (APTT); LMWH should be used with caution and the dosage should follow the principle of individualization; Fondaparinux sodium, bivalirudin and argatroban should be used with caution. ②Warfarin should be used with caution. ③The selection, usage and dosage of DOACs are shown in Table 17.	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.
		(2) Renal insufficiency[73]: ①See Table 18 for the selection, usage and dosage of parenteral anticoagulants; ②Warfarin dosage should be adjusted according to INR; ③The selection, usage and dosage of DOACs are shown in Table 19.	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.
12	Used for reproductive adjuvant therapy	(1) LMWH can be used in patients with recurrent abortion complicated with prethrombotic state (PTS) and APS[74-76];	1/A
		(2) In patients with recurrent abortion complicated with systemic lupus erythematosus (SLE), LMWH can be used for patients with negative antiphospholipid antibody (aPL) but complicated with nephrotic syndrome or positive aPL[74,77];	1/B
		(3) LMWH can be used when PTS and APS are combined in patients with repeated implantation failure[78];	2/C
		(4) LMWH can be used for patients with moderate and severe ovarian hyperstimulation syndrome (OHSS) during assisted reproductive technology[78];	1/A
		(5) Under the above circumstances, fondaparinux sodium can also be selected, and the usage and dosage should follow the principle of individualization[3,79].	2/C
13	Used for thrombotic	(1) Selection of anticoagulant drugs: UFH, LMWH, warfarin, rivaroxaban[a] and dabigatran etexilate[b]; Usage and dosage: UFH, LMWH, rivaroxaban and dabigatran etexilate are adjusted according to body weight, and warfarin is adjusted according to INR.	1/A

	diseases in children[80-81]	(2) Selection, usage and dosage of anticoagulant drugs: fondaparinux sodium can be used for the treatment of VTE in children, with a dose of 0.1mg/kg once a day[82-83].	2/C
14	Used for the prevention and treatment of thrombotic diseases in tumor patients[84-89]	(1) Selection of anticoagulant drugs in prevention of thrombotic diseases: ①Medical inpatients: LMWH, UFH and fondaparinux sodium; ②Surgical inpatients: LMWH, fondaparinux sodium, UFH and DOACs (rivaroxaban, apixaban); ③Discharged or outpatient patients: DOACs (rivaroxaban, apixaban), LMWH and fondaparinux sodium. Usage and dosage: the same as the above drugs used for VTE prevention.	Recommended by guidelines, and the evidence quality grading is not applicable.
		(2) Selection, usage and dosage of anticoagulants in the treatment of thrombotic diseases: the same as the use of anticoagulants in VTE patients.	Recommended by guidelines, and the evidence quality grading is not applicable.
15	Used for catheter-related thrombosis	Selection, usage and dosage of anticoagulants in the event of catheter-related thrombosis: the same as the use of anticoagulants in VTE patients [90-91]	Recommended by guidelines, and the evidence quality grading is not applicable.
16	Used for thrombotic diseases in low weight/obesity patients.	For patients with low body weight (<40 kg)/obesity (>100 kg or BMI >30 kg/m^2), UFH, LMWH, fondaparinux sodium, warfarin and DOACs can be selected, but the monitoring should be strengthened[7,92].	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.
17	Combined use of anticoagulant drugs, antiplatelet drugs and thrombolytic drugs	(1)Between anticoagulant drugs: ①Warfarin and heparin drugs can be used together when bridging[93]; ②DOACs can be used together when they are converted into warfarin.	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.
		(2) No contraindication for the combined use of anticoagulants and antiplatelet drugs[94-95];	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.
		(3) Anticoagulant drugs and antithrombotic drugs: ①For patients with ST-segment elevation myocardial infarction, anticoagulant and thrombolytic drugs can be used together[96]; ②For patients with acute VTE, anticoagulant and thrombolytic drugs can be used together[5,97].	Recommended by drug instructions/guidelines, and the evidence quality grading is not applicable.

a: The instructions for rivaroxaban indicate that anticoagulant therapy in children is only approved for (1) treatment of VTE in children and prevention of the recurrence; (2) Prevention of thrombosis after Fontan operation in children with congenital heart disease (FDA drug instructions). b: Dabigatran etexilate has been approved by FDA and European Medicines Agency (EMA) for the treatment and the prevention of the recurrence in children.

Table 16 Selection of Anticoagulants for Special Population

Category	Drug Name	Pregnant Women[53, 98-102]	Breast Feeding Women[53, 98-102]	Children	The Elderly
Parenteral Anticoagulants	UFH	Usable	Usable	Usable	Usable
	LMWH	Usable	Usable	Usable	Usable
	Fondaparinux sodium	Use with caution	Usable	Usable	Usable
	Bivarudine	Unknown	Unknown	Unknown	Usable
	Agatraban	Use when the pros outweigh the cons	Not recommended	Unknown	Usable
Oral Anticoagulants	Warfarin	Use with caution	Usable	Usable	Usable
	Dabigatran etexilate	Not recommended	Not recommended	Usable	Usable
	Rivaroxaban	Not recommended	Not recommended	Usable	Usable
	Apixaban	Not recommended	Not recommended	Not recommended	Usable
	Edoxaban	Not recommended	Not recommended	Not recommended	Usable

Note: This section refers to domestic and foreign drug instructions, FDA pregnancy grading and the latest clinical diagnosis and treatment guidelines.

Table 17 Dose Adjustment of Oral Anticoagulants in Patients with Abnormal Liver Function

Drug Name	Liver Function Grading		
	Child-Pugh A (5~6)	Child-Pugh B (7~9)	Child-Pugh C (≥10)
Warfarin	Dose adjusted based on INR target value	Dose adjusted based on INR target value	Dose adjusted based on INR target value
Rivaroxaban	Normal dose	Prohibited	Prohibited
Apixaban	Normal dose	Use with caution	Prohibited
Edoxaban	Normal dose	Use with caution	Prohibited
Dabigatran Etexilate	Normal dose	Use with caution	Prohibited

Table 18 Dose Adjustment of Parenteral Anticoagulants in Patients with Renal Dysfunction

Drug Name	Disease	CrCl 50~<90 mL/min	CrCl 30~<50 mL/min	CrCl<30 mL/min
UFH		Adjusted according to APTT, anti-Xa activity and body weight.	Adjusted according to APTT, anti-Xa activity and body weight.	Adjusted according to APTT, anti-Xa activity and body weight.
Enoxaparin Sodium	VTE prevention	No adjustment required	No adjustment required	2000 IU, once a day[a]
	VTE treatment	No adjustment required	No adjustment required	100 IU/kg, once a day[a]
Nadroparin Calcium	VTE prevention	No adjustment required	Dose reduction by 25% to 33%	Dose reduction by 25% to 33%
	VTE treatment	No adjustment required	Dose reduction by 25% to 33%	Not recommended

Dalmatine Sodium	VTE prevention VTE treatment	No adjustment required No adjustment required	No adjustment required No adjustment required	Monitoring strengthened Use with caution
Fondaparinux Sodium	VTE prevention	No adjustment required	1.5 mg, once a day[b]	Not recommended[c]

a: Not recommended for patients with CrCl <15 ml/min; b: For patients using fondaparinux sodium, the dosage is suggested to be adjusted to 1.5 mg once a day when CrCl is 20~<50 ml/min; c: Fondaparinux sodium is not recommended for patients with CrCl<20 ml/min.

Table 19 Dose Adjustment of Oral Anticoagulants in Patients with Renal Dysfunction[a]

Drug Name	Disease	CrCl 50~<90 mL/min	CrCl 30~<50 mL/min	CrCl 15~<30 mL/min	CrCl<15mL/min	Hemodialysis
Warfarin		Dose adjusted according to INR target value.	Dose adjusted according to INR target value.	Dose adjusted according to INR target value.	Dose adjusted according to INR target value.	Dose adjusted according to INR target value.
Rivaroxaban	AF VTE prevention VTE treatment	No adjustment required No adjustment required No adjustment required	15 mg, once a day No adjustment required 15 mg, once a day	15 mg, once a day Not recommended Not recommended	Not recommended Not recommended Not recommended	10 mg, once a day[73]b 10 mg, once a day[73]b 10 mg, once a day[73]
Apixaban	VTE prevention	No adjustment required	No adjustment required	Use with caution	Not recommended	2.5 mg, twice a day[73]
Edoxaban	AF VTE treatment	No adjustment required No adjustment required	30 mg, once a day 30 mg, once a day	30mg, once a day 30mg, once a day	Not recommended Not recommended	Not recommended Not recommended
Dabigatran Etexilate	AF VTE treatment	No adjustment required No adjustment required	110 mg, twice a day 110 mg, twice a day	Not recommended Not recommended	Not recommended Not recommended	Not recommended Not recommended

a: This part refers to the domestic and foreign drug instructions and the latest clinical diagnosis and treatment guidelines; b: Hemohemodialysis.

3. Conclusion

This consensus, developed from the perspective of the prescription (doctor's advice) review of anticoagulants in medical institutions, summarizes the recommendations of commonly used anticoagulants across various aspects, including those based on drug instructions and beyond instructions. The aim is to provide valuable reference for the establishment of prescription review rules for anticoagulants in medical institutions and the subsequent development of rules for other drugs. However, there are still limitations in this consensus: this consensus is based on the existing knowledge and experience, and there may be some limitations. With the progress of clinical research, the content may need further updates and adjustments. In addition, clinical situations vary widely, and this consensus does not cover all relevant clinical scenarios. Therefore, when applying this consensus, prescription reviewers still need to conduct individualized assessments according to the specific conditions of patients, combining their own professional knowledge and practical experience for judgment and application.

Reference Drug Instruction Version

Heparin Sodium Injection (manufacturer: SPH No.1 Biochemical & Pharmaceutical Co., Ltd.), modified on Dec 1, 2020.
Enoxaparin Sodium Injection (trade name: Clexane), modified on Nov 5, 2020.
Nadroparin Calcium Injection (trade name: Fraxiparine), modified on Jan 28, 2021.
Dalmatine Sodium Injection (trade name: Fragmin), modified on June 17, 2023.
Fondaparinux Sodium Injection (trade name: Arixtra), modified on Jan 28, 2021.
Bivarudine for Injection (trade name: Taganin), modified on Aug 7, 2018.

Agatraban Injection (trade name: Novastan), modified on Mar 5, 2020.
Warfarin Sodium Tablets (trade name: Qipuhua), modified on Dec 23, 2021.
Dabigatran Axetil Capsules (trade name: Pradaxa), modified on Nov 24, 2021.
Rivaroxaban Tablets (trade name: Xarelto), modified on March 25, 2021.
Apixaban Tablets (trade name: Eliquis), modified on Oct 14, 2022.
Aidoshaban Toluene Sulfonate Tablets (trade name: Lixiana), modified on Aug 26, 2022.

Consensus Expert Group (in alphabetical order)

BIAN Yuan, Sichuan Academy of Medical Sciences Sichuan Provincial People's Hospital
CHEN Hong, First Affiliated Hospital of Chongqing Medical University
CHEN Wanyi, Cancer Hospital Affiliated to Chongqing University
DU Liping, Peking Union Medical College Hospital, China Academy of Medical Sciences

FANG Wei, Three Gorges Hospital affiliated to Chongqing University
GU Zhichun, Renji Hospital affiliated to Shanghai Jiaotong University School of Medicine
JIA Yuntao, Children's Hospital Affiliated to Chongqing Medical University
LI Juan, Tongji Hospital Affiliated to Tongji Medical College, Huazhong University of Science and Technology
LI Qin, First People's Hospital Affiliated to Shanghai Jiaotong University School of Medicine
LING Zhiyu, Second Affiliated Hospital of Chongqing Medical University
LIU Yao, PLA Army Special Medical Center
QIAN Yan, Second Affiliated Hospital of Chongqing Medical University
QIU Feng, First Affiliated Hospital of Chongqing Medical University
SHEN Zhengze, Yongchuan Hospital Affiliated to Chongqing Medical University
SUN Jianming, Second Affiliated Hospital of Chongqing Medical University
TAO Jianhong, Sichuan Academy of Medical Sciences Sichuan Provincial People's Hospital
WANG Qian, First Affiliated Hospital of Army Military Medical University
XIA Peiyuan, First Affiliated Hospital of Army Military Medical University
XU Hang, Gulou Hospital Affiliated to Nanjing University School of Medicine
YI Qun, Sichuan Cancer Hospital
YIN Yuehui, Second Affiliated Hospital of Chongqing Medical University
ZHANG Jin, First People's Hospital of Yunnan Province
ZHANG Jinhua, Fujian Maternal and Child Health Hospital
ZHANG Lingli, West China Second Hospital of Sichuan University
ZHANG Zhe, Second Affiliated Hospital of Army Military Medical University
ZHAO Chunjing, Second Affiliated Hospital of Chongqing Medical University
ZHAO Li, China-Japan Friendship Hospital

Consensus Writing Group (in alphabetical order)
DU Qingqing, Second Affiliated Hospital of Chongqing Medical University
Feng Shimei, Yongchuan Hospital Affiliated to Chongqing Medical University
LI Xinyu, First Affiliated Hospital of Chongqing Medical University
LIAO Lin, Chongqing People's Hospital
MA Yunqi, Shapingba Hospital Affiliated to Chongqing University
QIU Sha, Second Affiliated Hospital of Chongqing Medical University
TANG Zongwei, Cancer Hospital Affiliated to Chongqing University

WANG Na, Second Affiliated Hospital of Chongqing Medical University
XU Caibing, Three Gorges Hospital Affiliated to Chongqing University
YANG Xue, PLA Army Special Medical Center
YU Qiusha, West China Second Hospital of Sichuan University
ZHAN Shipeng, First Affiliated Hospital of Army Military Medical University
ZHENG Dan, Women and Children Hospital Affiliated to Chongqing Medical University
ZHOU Bo, Children's Hospital Affiliated to Chongqing Medical University
ZOU Lang, Second Affiliated Hospital of Army Military Medical University

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