



MHRA PUBLIC ASSESSMENT REPORT

Warfarin: changes to product safety information

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EXECUTIVE SUMMARY

(Please note that this summary is intended to be accessible to all members of the public, including health professionals)

Background

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating the effectiveness and safety of medicines and medical devices in the UK. We continually review the safety of all medicines in the UK, and inform healthcare professionals and the public of the latest safety updates. In our Public Assessment Reports, we discuss the evidence for a particular drug safety issue, and any changes made to product information for the drug on the basis of this evidence, which will help safeguard public health. This MHRA Public Assessment Report discusses some recent changes to the product information for the medicine warfarin.

Warfarin is an important anticoagulant^a medicine which has been in clinical use for over 50 years. It is widely used to treat stroke^b patients, patients who develop deep vein thrombosis^c, and to prevent embolism^d in patients at risk.

As with any medicine, the use of warfarin may lead to adverse reactions^e in some individuals, which are described in the product information – the Summary of Product Characteristics (SPC) and patient information leaflet^f. The MHRA and an advisory group called the [Pharmacovigilance Expert Advisory Group](#) (PEAG) have reviewed this section of the SPC, along with other sections covering warnings to the prescriber, drug interactions, use in pregnancy and breast-feeding, and the treatment of warfarin overdose. (PEAG is comprised of health professionals in several specialist medical areas, who advise the [Commission on Human Medicines](#)^g in their task). The MHRA decided that the safety sections of the product information for warfarin required review because case reports of adverse reactions with this medicine continue to be received through our [Yellow Card](#)^h scheme, and the SPCs needed to be updated.

Results and conclusions

The safety sections of the SPC were reviewed in 2009 in accordance with reports of adverse reactions with warfarin stored in [the MHRA's case report database](#), the medical literature, and current practice guidelines including guidelines from the British Society of Haematology. Although no new safety issues were identified during the review, the SPC was amended to give clearer and up-to-date advice to health professionals.

Outcome

^a Prevents or treats blood clots

^b Weakness on one side of the body or loss of speech or vision, caused by an interruption of blood flow to the brain

^c A blood clot, usually in the veins of the leg

^d Blockages of the circulation system, usually caused by a blood clot

^e Side-effects

^f See the [Electronic Medicines Compendium \(product information\) website](#). Further information on the safer use of anticoagulant therapy is available from the National Patient Safety Agency at: <http://www.nrls.npsa.nhs.uk/resources/?entryid45=59814>

^g An independent committee comprised of health professionals and scientists that gives advice to government Ministers on the safety, effectiveness and quality of medicines

^h Suspected adverse drug reactions to any medicine in the UK can be reported to the MHRA through our [Yellow Card Scheme](#) (www.yellowcard.gov.uk)

A revised core SPC has been agreed which aims to better reflect the information received through the Yellow Card scheme, the current literature and current guidelines for warfarin use in clinical practice. This core SPC will also be used as the basis for a core patient information leaflet on warfarin, to help ensure patients get consistent and appropriate information about this important medicine.

1. INTRODUCTION

(See glossary for terms used in this document)

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating the effectiveness and safety of medicines and medical devices in the UK. We continually review the safety of all medicines in the UK, and inform healthcare professionals and the public of the latest safety updates. In our Public Assessment Reports, we discuss the evidence for a particular drug safety issue, and any changes made to product information for the drug on the basis of this evidence, which will help safeguard public health. This MHRA Public Assessment Report discusses the background for recent changes to the Summary of Product Characteristics (SPC) for warfarin.

Warfarin is a well-established anticoagulant which has been widely-used in the UK since the 1950s. Anticoagulants prevent the abnormal formation of blood clots and are commonly used to treat stroke patients, and patients who develop deep vein thrombosis or are at risk of embolism. Despite its use in clinical practice for over 50 years, the MHRA still receives a substantial number of case reports on adverse reactions with warfarin through the [Yellow Card](#)^a scheme. Therefore the Agency, helped by the [Pharmacovigilance Expert Advisory Group](#) (PEAG; a group of health professionals who advise the [Commission on Human Medicines](#)^b in their task), reviewed the current product information for warfarin, in parallel with Yellow Card data, the latest published literature and practice guidance, including the current [guidelines from the British Society of Haematology](#). All safety sections of the SPC were reviewed, including contraindications, warnings and precautions for use, interactions, pregnancy and lactation, adverse effects and overdose. Note that the scope of the review did not cover other aspects of the SPC, including the therapeutic indications or dose regime of warfarin.

The MHRA received 2233 suspected adverse reaction reports with warfarin use between 29 June 1963–16 June 2008, of which 297 were fatal. The majority of adverse reactions reported with warfarin were a result of over anticoagulation and bleeding, and the majority of fatal cases reported were associated with haemorrhage (208 fatal reports). Therefore, the safety information was reviewed with a particular focus on haemorrhage. No new safety issues were identified during the review.

As a large number of other medicines can affect the way warfarin works, the interactions section of the SPC was significantly revised to help healthcare professionals identify potential interactions more easily. The overdose section was updated to incorporate new information from [Toxbase](#)^c.

After the review, the following core SPC was agreed which best reflects the information received through the Yellow Card scheme, the current medical literature, and current guidelines on the use of warfarin in clinical practice. This core SPC will also be used as the basis for a core patient information leaflet on warfarin, to help ensure patients get consistent and appropriate information on this important medicine.

^a Suspected adverse drug reactions to any medicine in the UK can be reported to the MHRA through our [Yellow Card Scheme](#) (www.yellowcard.gov.uk)

^b An independent committee comprised of health professionals and scientists that gives advice to government Ministers on the safety, effectiveness and quality of medicines

^c Online database of the National Poisons Information Service (<http://www.toxbase.org/>)

2. UPDATED SAFETY SECTIONS FOR SPC

Section 4.3 Contraindications

- Known hypersensitivity to warfarin or to any of the excipients
- Haemorrhagic stroke (see section 4.4 for further details)
- Clinically significant bleeding
- Within 72 hours of major surgery with risk of severe bleeding (for information on other surgery, see section 4.4)
- Within 48 hours postpartum
- Pregnancy (first and third trimesters, see section 4.6)
- Drugs where interactions may lead to a significantly increased risk of bleeding (see section 4.5)

Section 4.4 Special warnings and precautions for use

Most adverse events reported with warfarin are a result of over anticoagulation therefore it is important that the need for therapy is reviewed on a regular basis and therapy discontinued when no longer required.

Patients should be given a patient-held information booklet ('warfarin card') and informed of symptoms for which they should seek medical attention.

Commencement of therapy

Monitoring

When warfarin is started using a standard dosing regimen the INR should be determined daily or on alternate days in the early days of treatment. Once the INR has stabilised in the target range the INR can be determined at longer intervals. INR should be monitored more frequently in patients at an increased risk of over coagulation e.g. patients with severe hypertension, liver or renal disease. Patients for whom adherence may be difficult should be monitored more frequently.

Thrombophilia

Patients with protein C deficiency are at risk of developing skin necrosis when starting warfarin treatment. In patients with protein C deficiency, therapy should be introduced without a loading dose of warfarin even if heparin is given. Patients with protein S deficiency may also be at risk and it is advisable to introduce warfarin therapy slowly in these circumstances.

Risk of haemorrhage

The most frequently reported adverse effect of all oral anticoagulants is haemorrhage. Warfarin should be given with caution to patients where there is a risk of serious haemorrhage (e.g. concomitant NSAID use, recent ischaemic stroke, bacterial endocarditis, previous gastrointestinal bleeding).

Risk factors for bleeding include high intensity of anticoagulation (INR >4.0), age ≥65, highly variable INRs, history of gastrointestinal bleeding, uncontrolled hypertension, cerebrovascular disease, serious heart disease, risk of falling, anaemia, malignancy, trauma, renal insufficiency, concomitant drugs (see section 4.5). All patients treated with warfarin should have INR monitored regularly. Those at high risk of bleeding may benefit from more frequent INR monitoring, careful dose

adjustment to desired INR, and a shorter duration of therapy. Patients should be instructed on measures to minimise risk of bleeding and to report immediately to physicians signs and symptoms of bleeding.

Checking the INR and reducing or omitting doses depending on INR level is essential, following consultation with anticoagulation services if necessary. If the INR is found to be too high, reduce dose or stop warfarin treatment; sometimes it will be necessary to reverse anticoagulation. INR should be checked within 2–3 days to ensure that it is falling.

Any concomitant anti-platelet drugs should be used with caution due to an increased risk of bleeding.

Haemorrhage

Haemorrhage can indicate an overdose of warfarin has been taken. For advice on treatment of haemorrhage see section 4.9.

Unexpected bleeding at therapeutic levels should always be investigated and INR monitored.

Ischaemic stroke

Anticoagulation following an ischaemic stroke increases the risk of secondary haemorrhage into the infarcted brain. In patients with atrial fibrillation long term treatment with warfarin is beneficial, but the risk of early recurrent embolism is low and therefore a break in treatment after ischaemic stroke is justified. Warfarin treatment should be re-started 2–14 days following ischaemic stroke, depending on the size of the infarct and blood pressure. In patients with large embolic strokes, or uncontrolled hypertension, warfarin treatment should be stopped for 14 days.

Surgery

For surgery where there is no risk of severe bleeding, surgery can be performed with an INR of <2.5.

For surgery where there is a risk of severe bleeding, warfarin should be stopped 3 days prior to surgery.

Where it is necessary to continue anticoagulation e.g. risk of life-threatening thromboembolism, the INR should be reduced to <2.5 and heparin therapy should be started.

If surgery is required and warfarin cannot be stopped 3 days beforehand, anticoagulation should be reversed with low-dose vitamin K.

The timing for re-instating warfarin therapy depends on the risk of post-operative haemorrhage. In most instances warfarin treatment can be re-started as soon as the patient has an oral intake.

Dental Surgery

Warfarin need not be stopped before routine dental surgery, eg, tooth extraction.

Active peptic ulceration

Due to a high risk of bleeding, patients with active peptic ulcers should be treated with caution. Such patients should be reviewed regularly and informed of how to recognise bleeding and what to do in the event of bleeding occurring.

Interactions

Many drugs and foods interact with warfarin and affect the prothrombin time (see section 4.5). Any change to medication, including self-medication with OTC products, warrants increased monitoring of the INR. Patients should be instructed to inform their doctor before they start to take any additional medications including over the counter medicines, herbal remedies or vitamin preparations.

Thyroid disorders

The rate of warfarin metabolism depends on thyroid status. Therefore patients with hyper- or hypo-thyroidism should be closely monitored on starting warfarin therapy.

Additional circumstances where changes in dose may be required

The following also may exaggerate the effect of warfarin tablets, and necessitate a reduction of dosage:

- Loss of weight
- Acute illness
- Cessation of smoking

The following may reduce the effect of warfarin tablets, and require the dosage to be increased:

- Weight gain
- Diarrhoea
- Vomiting

Other warnings

Acquired or inherited warfarin resistance should be suspected if larger than usual daily doses of warfarin are required to achieve the desired anticoagulant effect.

Genetic information

Genetic variability particularly in relation to CYP2C9 and VKORC1 can significantly affect dose requirements for warfarin. If a family association with these polymorphisms is known extra care is warranted.

Section 4.5 Interaction with other medicinal products and other forms of interaction

Warfarin has a narrow therapeutic range and care is required with all concomitant therapy. The individual product information for any new concomitant therapy should be consulted for specific guidance on warfarin dose adjustment and therapeutic monitoring. If no information is provided the possibility of an interaction should be considered. Increased monitoring should be considered when commencing any new therapy if there is any doubt as to the extent of interaction.

Pharmacodynamic interactions

Drugs which are contraindicated

Concomitant use of drugs used in the treatment or prophylaxis of thrombosis, or other drugs with adverse effects on haemostasis may increase the pharmacological effect of warfarin, increasing the risk of bleeding.

Fibrinolytic drugs such as streptokinase and alteplase are contraindicated in patients receiving warfarin.

Drugs which should be avoided if possible

The following examples should be avoided, or administered with caution with increased clinical and laboratory monitoring:

- Clopidogrel
- NSAIDs (including aspirin and cox-2 specific NSAIDs)
- Sulfinpyrazone
- Thrombin inhibitors such as bivalirudin, dabigatran
- Dipyridamole
- Unfractionated heparins and heparin derivatives, low molecular weight heparins
- Fondaparinux, rivaroxaban
- Glycoprotein IIb/IIIa receptor antagonists such as eptifibatide, tirofiban and abciximab
- Prostacyclin
- SSRI and SNRI antidepressants
- Other drugs which inhibit haemostasis, clotting or platelet action

Low-dose aspirin with warfarin may have a role in some patients but the risk of gastrointestinal bleeding is increased. Warfarin may initially be given with a heparin in the initial treatment of thrombosis, until the INR is in the correct range.

Metabolic interactions

Warfarin is a mixture of enantiomers which are metabolised by different CYP450 cytochromes. R-warfarin is metabolised primarily by CYP1A2 and CYP3A4. S-warfarin is metabolised primarily by CYP2C9. The efficacy of warfarin is affected primarily when the metabolism of S-warfarin is altered.

Drugs that compete as substrates for these cytochromes or inhibit their activity may increase warfarin plasma concentrations and INR, potentially increasing the risk of bleeding. When these drugs are co-administered, warfarin dosage may need to be reduced and the level of monitoring increased.

Conversely, drugs which induce these metabolic pathways may decrease warfarin plasma concentrations and INR, potentially leading to reduced efficacy. When these drugs are co-administered, warfarin dosage may need to be increased and the level of monitoring increased.

There is a small subset of drugs for which interactions are known; however their clinical effect on the INR is variable. In these cases increased monitoring on starting and stopping therapy is advised.

Care should also be taken when stopping or reducing the dose of a metabolic inhibitor or inducer, once patients are stable on this combination (offset effect). Listed below are drugs which are known to interact with warfarin in a clinically significant way.

Examples of drugs which potentiate the effect of warfarin
allopurinol, capecitabine, erlotinib, disulfiram, azole antifungals (ketoconazole, fluconazole etc)
omeprazole, paracetamol (prolonged regular use), propafenone, amiodarone, tamoxifen, methylphenidate
zafirlukast, fibrates, statins (not pravastatin; predominantly associated with fluvastatin)
erythromycin, sulfamethoxazole, metronidazole
Examples of drugs which antagonise the effect of warfarin
Barbiturates, primidone, carbamazepine, griseofulvin, oral contraceptives, rifampicin, azathioprine, phenytoin
Examples of drugs with variable effect
Corticosteroids, nevirapine, ritonavir

Other drug interactions

Broad spectrum antibiotics may potentiate the effect of warfarin by reducing the gut flora which produce vitamin K. Similarly, orlistat may reduce absorption of vitamin K. Cholestyramine and sucralfate potentially decrease absorption of warfarin. Increased INR has been reported in patients taking glucosamine and warfarin. This combination is not recommended.

Interactions with herbal products

Herbal preparations containing St John's Wort (*Hypericum perforatum*) must not be used whilst taking warfarin due to a proven risk of decreased plasma concentrations and reduced clinical effects of warfarin.

Many other herbal products have a theoretical effect on warfarin; however most of these interactions are not proven. Patients should generally avoid taking any herbal medicines or food supplements whilst taking warfarin, and should be told to advise their doctor if they are taking any, as more frequent monitoring is advisable.

Alcohol

Acute ingestion of a large amount of alcohol may inhibit the metabolism of warfarin and increase INR. Conversely, chronic heavy alcohol intake may induce the metabolism of warfarin. Moderate alcohol intake can be permitted.

Interactions with food and food supplements

Individual case reports suggest a possible interaction between warfarin and cranberry juice, in most cases leading to an increase in INR or bleeding event. Patients should be advised to avoid cranberry products. Increased supervision and INR monitoring should be considered for any patient taking warfarin and regular cranberry juice.

Limited evidence suggests that grapefruit juice may cause a modest rise in INR in some patients taking warfarin.

Certain foods such as liver, broccoli, Brussels sprouts and green leafy vegetables contain large amounts of vitamin K. Sudden changes in diet can potentially affect control of anticoagulation. Patients should be informed of the need to seek medical

advice before undertaking any major changes in diet.

Many other food supplements have a theoretical effect on warfarin; however most of these interactions are not proven. Patients should generally avoid taking any food supplements whilst taking warfarin, and should be told to advise their doctor if they are taking any, as more frequent monitoring is advisable.

Laboratory tests

Heparins and danaparoid may prolong the prothrombin time, therefore a sufficient time interval should be allowed after administration before performing the test.

Section 4.6 Pregnancy and lactation

Pregnancy

Based on human experience warfarin causes congenital malformations and foetal death when administered during pregnancy.

Warfarin is contraindicated in pregnancy in the first and third trimester. Women of child-bearing age who are taking warfarin tablets should use effective contraception during treatment.

Lactation

Warfarin is excreted in breast milk in small amounts. However, at therapeutic doses of warfarin no effects on the breast-feeding child are anticipated. Warfarin can be used during breast-feeding.

Section 4.8 Undesirable effects

MedDRA system organ class^a	Adverse reaction
Infections and infestations	Fever
Immune system disorders	Hypersensitivity
Nervous system disorders	Cerebral haemorrhage; cerebral subdural haematoma
Vascular disorders	Haemorrhage
Respiratory, thoracic and mediastinal disorders	Haemothorax, epistaxis

^a MedDRA is a dictionary of medical terminology used by the MHRA to enter data into the Yellow Card database. The dictionary is organized by system organ class

Gastrointestinal disorders	Gastrointestinal haemorrhage; rectal haemorrhage; haematemesis; pancreatitis; diarrhoea; nausea; vomiting; melaena
Hepatobiliary disorders	Jaundice; hepatic dysfunction
Skin and subcutaneous disorders	Rash; alopecia; purpura; 'purple toes' syndrome; erythematous swollen skin patches leading to ecchymosis, infarction and skin necrosis
Renal and urinary disorders	Haematuria
Investigations	Unexplained drop in haematocrit; haemoglobin decreased

Section 4.9 Overdose

The benefit of gastric decontamination is uncertain. If the patient presents within 1 hour of ingestion of more than 0.25 mg/kg or more than the patient's therapeutic dose, consider activated charcoal (50 g for adults; 1 g/kg for children)

In cases of life-threatening haemorrhage

Stop warfarin treatment, give prothrombin complex concentrate (factors II, VII, IX, and X) 30–50 units/kg *or* (if no concentrate available) fresh frozen plasma 15 mL/kg. Discuss with local haematologist or National Poisons Information Service, or both.

Non-life threatening haemorrhage

Where anticoagulation can be suspended, give slow intravenous injection of phytomenadione (vitamin K₁) 10–20 mg for adults (250 micrograms/kg for a child)

Where rapid re-anticoagulation is desirable (eg, valve replacements) give prothrombin complex concentrate (factors II, VII, IX, and X) 30–50 units/kg *or* (if no concentrate available) fresh frozen plasma 15 mL/kg.

Monitor INR to determine when to restart normal therapy. Monitor INR for at least 48 hours post overdose.

For patients on long-term warfarin therapy without major haemorrhage

- INR >8.0, no bleeding or minor bleeding—stop warfarin, and give phytomenadione (vitamin K₁) 0.5–1 mg for adults, 0.015–0.030 mg/kg (15–30 micrograms/kg) for children by slow intravenous injection or 5 mg by mouth (for partial reversal of anticoagulation give smaller oral doses of phytomenadione eg, 0.5–2.5 mg using the intravenous preparation orally); repeat dose of phytomenadione if INR still too high after 24 hours. Large doses of phytomenadione may completely reverse the effects of warfarin and make re-establishment of anticoagulation difficult.
- INR 6.0–8.0, no bleeding or minor bleeding—stop warfarin, restart when INR <5.0
- INR <6.0 but more than 0.5 units above target value—reduce dose or stop warfarin, restart when INR <5.0

For patients NOT on long-term anticoagulants without major haemorrhage
Measure the INR (prothrombin time) at presentation and sequentially every 24–48 hours after ingestion depending on the initial dose and initial INR.

- If the INR remains normal for 24–48 hours and there is no evidence of bleeding, there should be no further monitoring necessary.
- Give vitamin K₁ (phytomenadione) if:
 - a) there is no active bleeding and the patient has ingested more than 0.25 mg/kg;
 - OR
 - b) the prothrombin time is already significantly prolonged (INR >4.0).

The adult dose of vitamin K₁ is 10–20 mg orally (250 micrograms/kg body weight for a child). Delay oral vitamin K₁ at least 4 hours after any activated charcoal has been given. Repeat INR at 24 hours and consider further vitamin K₁.

3. GLOSSARY

Activated charcoal

Porous charcoal that is used to treat poisonings and overdoses

Alopecia

Hair loss

Alteplase

Medicine used to dissolve blood clots, particularly in the arteries of the heart

Anaemia

A condition caused by a reduced quantity of **haemoglobin** in the blood; symptoms include excessive tiredness, breathlessness and poor resistance to infection

Antagonist

A drug with opposite actions to another drug or natural body chemical, which it inhibits

Antibiotics

Used to treat infections caused by bacteria or fungi

Anti-platelet

A class of drug that reduce **platelet** collection in the blood, therefore reducing clot formation

Atrial

Related to the upper chambers of the heart

Bile

A fluid produced by the gall bladder (part of the digestive system) in the body, which helps to digest fats

Cerebrovascular

Related to the blood vessels of the brain

Cessation

Ending or stopping (treatment)

Cholestyramine

A drug that helps a body chemical called bile to be excreted and is used relieve conditions such as itching in jaundice and diarrhoea

Chronic

Lasting over a long time, or frequently recurring

Clinically significant

A result or effect that is large enough to be of practical importance to patients and healthcare providers

Clopidogrel

An **anti-platelet** drug given to prevent strokes or heart attacks

Concomitant

Two or more medicines given in the same period

Congenital

A medical condition that is present at birth

Contraindication

Any factor that makes it unwise to give a particular medicine to a patient

Cox-2 specific NSAIDs

An **NSAID** that specifically blocks the actions of the enzyme cyclo-oxygenase 2 (Cox-2), providing pain relief from inflammation

CYP P450

A family of proteins which break down many substances in the body

CYP2C9

A protein in the **CYP P450** family

Cytochrome

A substance in cells consisting of a protein linked to haem (another substance containing iron)

Danaparoid

An anticoagulant medicine

Dipyridamole

A drug that widens the blood vessels of the heart and reduces **platelet** collection in the blood, given to prevent thrombosis around artificial heart valves

Dosing regimen

The formal schedule by which drugs are administered, including the amount given per time unit

Ecchymosis

Bruise

Efficacy

The effectiveness of a drug measured under laboratory conditions or in clinical trials

Embolism

A blockage in an artery which obstructs blood flow

Enantiomers

One of two forms of a molecule that are mirror-images of each other

Endocarditis (bacterial)

Inflammation of the lining of the heart cavity

Erythematous

Abnormal redness of the skin caused by the widening of blood vessels called capillaries

Excipients

An inactive substance that is combined with an active drug so that it is in a form that is suitable for a patient to take; ie, capsules or tablets

Fibrillation

Chaotic electrical and mechanical activity of a heart chamber, that results in abnormal contractions

Fibrinolytic

A class of drugs that break down the protein fibrin, the main constituent of blood clots

Foetal

Of a foetus (an unborn child)

Fondaparinux

An anticoagulant medicine

Glucosamine

A derivative of glucose that is a component of **heparin**

Glycoprotein

A compound consisting of a protein combined with a carbohydrate

Gut flora

A reservoir of bacteria naturally present in human digestive tracts

Haematemesis

The act of vomiting blood

Haematocrit

Relates to the number of red blood cells in blood

Haematology

The study of blood and blood disorders

Haematuria

Passing blood in urine

Haemoglobin

Substance contained in red blood cells that binds to oxygen and transports it around the body

Haemorrhage

Internal or external bleeding from a burst blood vessel

Haemostasis

Stopping bleeding from damaged blood vessels

Haemothorax

Blood found in the chest cavity that is usually a result of an injury

Heparin

An anticoagulant drug

Hepatic

Related to the liver

Hepatobiliary

Related to the liver and gallbladder, bile ducts or bile

Hypersensitivity

Abnormal allergic responses

Hypertension

High blood pressure

Hyperthyroidism

Overactivity of the **thyroid** gland

Hypothyroidism

Below normal activity of the **thyroid** gland

Infarcted

Death of part or a whole organ in the body, caused by an obstruction of bloodflow to that organ (usually by a blood clot)

INR

International normalized ratio: the ratio of a patient's **prothrombin** time to a standard 'normal' prothrombin time, which is used to assess the time taken for a blood clot to form

Interaction (drug)

Where the effects of a medicine are affected by other substances in the body (food or other medicines)

Intravenous

Into, or within a vein

Ischaemic

An inadequate flow of blood to a part of the body, caused by blockage of the blood vessels supplying it

Jaundice

Yellow colouring of the skin or whites of the eyes, caused by excessive **bile** pigments in the blood

Lactation

Production of milk by breasts, normally at the end of pregnancy

Malformations

Abnormal physical structure

Malignancy

A tumour or cancer that invades, spreads and destroys tissue in the body

MedDRA

Medical Dictionary for Regulatory Activities: a dictionary of medical terms used by authorities regulating medicines (eg, the MHRA)

Mediastinal

Contained in the chest cavity

Melaena

Black faeces caused by the presence of partly-digested blood

Metabolised

The act of the body breaking down substances

Necrosis (skin)

The death of tissue or organs in a body, caused by disease, injury or interference with the blood supply to the affected part

NSAID

Non-steroidal anti-inflammatory drug: a class of drug used for the relief of pain, particularly associated with inflammation

Oral

Related to the mouth

Orlistat

A drug used to treat (clinical) obesity, which acts by reducing fat absorption in the digestive system

OTC

Over-the-counter: drugs that can be purchased directly from a pharmacist without a prescription from a health professional

Overdose

An accidental or intentional use of a drug or medicine in an amount that is higher than recommended

Pancreatitis

A condition characterised by inflammation of the pancreas

Peptic ulcer

A hole in the lining of the digestive system produced by abnormally high concentrations of stomach acid

Pharmacodynamic

The interaction of drugs with cells in the body

Pharmacological

Related to the science of drugs and their effect on the body

Phytomenadione

A form of vitamin K used to treat overdose with **anticoagulants**

Plasma

The fluid part of blood that contains the blood cells

Platelets

Blood cells that play a role in stopping bleeding

Postpartum

The period of a few days immediately after birth

Potentiate

Increase the effect of a drug

Prophylaxis

Prevention of disease

Prostacyclin

A drug in the prostaglandin class that widens blood vessels and inhibits platelet clumping (therefore preventing blood clots)

Protein C

A protein dependent on vitamin K that inhibits blood clot formation

Protein S

A protein dependent on vitamin K that inhibits blood clot formation

Prothrombin

A substance required for the normal clotting of blood

Purpura

A skin rash resulting from bleeding into the skin from small blood vessels called capillaries

Rectal

Related to the rectum, the end part of the digestive system

Renal

Related to the kidney

Rivaroxaban

An oral anticoagulant drug

SNRI

Selective serotonin and noradrenaline reuptake inhibitor: a class of antidepressant drugs

SSRI

Selective serotonin reuptake inhibitor: a class of antidepressant drugs

St John's wort

A herbal medicine used to treat mild depression

Streptokinase

An enzyme that is capable of breaking down blood clots, which is used to treat deep vein thrombosis

Subcutaneous

Beneath the skin

Subdural

Located below the dura mater (the outer membrane covering the brain)

Substrates

The substance that an enzyme acts upon

Sucralfate

A drug used to treat **peptic ulcers**

Sulfinpyrazone

A drug used to treat **chronic** gout (an inflammatory condition of the joints)

Therapeutic range

The range of concentrations at which a drug is effective

Thoracic

Related to the chest

Thromboembolism

A condition where a blood clot formed in one part of the blood circulation system travels to another part

Thrombosis

A blood clot in the circulation

Thyroid

An area located in the neck that produces chemicals that regulate metabolism (breakdown of substances in the body)

Trauma

A physical wound or injury

Trimester

One of the three 3-month periods that a pregnancy can be divided

Unfractionated

Not divided or broken up into separate parts

Vascular Related to blood vessels

Vitamin K

A substance required for blood clotting