



# **Public Assessment Report**

## **National Procedure**

**Ticagrelor 60 mg film-coated tablets**

**Ticagrelor 90 mg film-coated tablets**

**ticagrelor**

**PL 36390/0449, PL 36390/0446**

**Cipla (EU) Limited**

## LAY SUMMARY

### Ticagrelor 60 & 90 mg film-coated tablets ticagrelor

This is a summary of the Public Assessment Report (PAR) for Ticagrelor 60 & 90 mg film-coated tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Ticagrelor tablets in this lay summary for ease of reading.

For practical information about using Ticagrelor tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

#### **What are Ticagrelor tablets and what are they used for?**

These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Brilique 60 & 90 mg film-coated tablets (PLGB 17901/0310-0311).

Ticagrelor tablets in combination with acetylsalicylic acid (another antiplatelet agent) is to be used in adults only.

These medicines are given to patients because they have had:

*Ticagrelor 60 mg film-coated tablets*

- a heart attack, over a year ago.

*Ticagrelor 90 mg film-coated tablets*

- a heart attack, over a year ago.
- unstable angina (angina or chest pain that is not well controlled).

It reduces the chances of the patient having another heart attack, stroke or dying from a disease related to the heart or blood vessels.

#### **How do Ticagrelor tablets work?**

Ticagrelor tablets contains an active substance called ticagrelor. This belongs to a group of medicines called antiplatelet medicines.

Ticagrelor tablets affects cells called ‘platelets’ (also called thrombocytes). These very small blood cells help stop bleeding by clumping together to plug tiny holes in blood vessels that are cut or damaged.

However, platelets can also form clots inside diseased blood vessels in the heart and brain. This can be very dangerous because:

- the clot can cut off the blood supply completely; this can cause a heart attack (myocardial infarction) or stroke, or
- the clot can partly block the blood vessels to the heart; this reduces the blood flow to the heart and can cause chest pain which comes and goes (called ‘unstable angina’).

Ticagrelor tablets helps stop the clumping of platelets. This reduces the chance of a blood clot forming that can reduce blood flow.

**How are Ticagrelor tablets used?**

The pharmaceutical form of these medicines is a film-coated tablet and the route of administration is oral (by mouth).

**Ticagrelor 60 mg film-coated tablets**

The usual dose is one tablet of 60 mg twice a day. The patient should continue taking Ticagrelor tablets as long as their doctor tells them.

Take this medicine around the same time every day (for example, one tablet in the morning and one in the evening).

**Ticagrelor 90 mg film-coated tablets**

The starting dose is two tablets at the same time (loading dose of 180 mg). This dose will usually be given to the patient in the hospital.

After this starting dose, the usual dose is one tablet of 90 mg twice a day for up to 12 months unless the patient's doctor tells them differently.

Take this medicine around the same time every day (for example, one tablet in the morning and one in the evening).

**Taking Ticagrelor tablets with other medicines for blood clotting**

The patient's doctor will usually also tell them to take acetylsalicylic acid. This is a substance present in many medicines used to prevent blood clotting. The patient's doctor will tell them how much to take (usually between 75- 150 mg daily).

**How to take Ticagrelor tablets**

- The patient can take the tablet with or without food.
- The patient can check when they last took a tablet of Ticagrelor tablets by looking on the blister. There is a sun (for the morning) and a moon (for the evening). This will tell the patient whether they have taken the dose.

**If the patient has trouble swallowing the tablet**

If the patient has trouble swallowing the tablet they can crush it and mix with water as follows:

- Crush the tablet to a fine powder.
- Pour the powder into half a glass of water.
- Stir and drink immediately.
- To make sure there is no medicine left, rinse the empty glass with another half a glass of water and drink it.

If the patient is in the hospital they may be given this tablet mixed with some water and given through a tube via the nose (nasogastric tube).

For further information on how Ticagrelor tablets are used, refer to the PILs and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

### **What benefits of Ticagrelor tablets have been shown in studies?**

Because Ticagrelor tablets are generic medicines, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

### **What are the possible side effects of Ticagrelor tablets?**

For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at <https://yellowcard.mhra.gov.uk> or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Ticagrelor tablets are generic medicines and are bioequivalent to the reference medicines, their benefits and possible side effects are considered to be the same as the reference medicines.

### **Why were Ticagrelor tablets approved?**

It was concluded that, Ticagrelor tablets has been shown to be bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

### **What measures are being taken to ensure the safe and effective use of Ticagrelor tablets?**

As for all newly-authorized medicines, a Risk Management Plan (RMP) has been developed for Ticagrelor tablets. The RMP details the important risks of Ticagrelor tablets, how these risks can be minimised, any uncertainties about Ticagrelor tablets (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Ticagrelor tablets:

<b>Summary of safety concerns</b>	
<b>Important identified risks</b>	• None
<b>Important potential risks</b>	• None
<b>Missing information</b>	• Long term use in patients with prior ischaemic stroke

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Ticagrelor tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

**Other information about Ticagrelor tablets**

Marketing Authorisations for Ticagrelor tablets were granted in the United Kingdom (UK) on 26 August 2025.

The full PAR for Ticagrelor tablets follows this summary.

This summary was last updated in October 2025.

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## I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Ticagrelor 60 & 90 mg film-coated tablets (PL 36390/0449, PL 36390/0446) could be approved.

The products are approved for the following indications:

Ticagrelor, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with

- acute coronary syndromes (ACS) or
- a history of myocardial infarction (MI) and a high risk of developing an atherothrombotic event

Ticagrelor tablet contains ticagrelor, a member of the chemical class cyclopentyltriazolo-pyrimidines (CPTP), which is an oral, direct acting, selective and reversibly binding P2Y<sub>12</sub> receptor antagonist that prevents ADP-mediated P2Y<sub>12</sub> dependent platelet activation and aggregation. Ticagrelor does not prevent ADP binding but when bound to the P2Y<sub>12</sub> receptor prevents ADP-induced signal transduction. Since platelets participate in the initiation and/or evolution of thrombotic complications of atherosclerotic disease, inhibition of platelet function has been shown to reduce the risk of CV events such as death, MI or stroke.

Ticagrelor also increases local endogenous adenosine levels by inhibiting the equilibrative nucleoside transporter-1 (ENT-1).

Ticagrelor has been documented to augment the following adenosine-induced effects in healthy subjects and in patients with ACS: vasodilation (measured by coronary blood flow increases in healthy volunteers and ACS patients; headache), inhibition of platelet function (in human whole blood *in vitro*) and dyspnoea. However, a link between the observed increases in adenosine and clinical outcomes (e.g. morbidity-mortality) has not been clearly elucidated.

These applications were approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of suitable originator medicinal products, Brilique 60 & 90 mg film-coated tablets (PLGB 17901/0310-0311) that has been licensed for suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products.

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products. The bioequivalence study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing Authorisations for Ticagrelor tablets were granted in the United Kingdom (UK) on 26 August 2025.

## II QUALITY ASPECTS

### II.1 Introduction

The active substance is ticagrelor. Each film-coated tablet contains 60 or 90 mg of ticagrelor respectively.

The other ingredients are:

Tablet core: calcium hydrogen phosphate dihydrate, croscarmellose sodium hydroxypropylcellulose (E463), magnesium stearate (E470b) and mannitol (E421).

60 mg Tablet film-coating: ferrosferric oxide (E172), hypromellose (E464), iron oxide red (E172), macrogol 400 (E1521) and titanium dioxide (E171).

90 mg Tablet film-coating: hypromellose (E464), iron oxide yellow (E172), macrogol 400 (E1521), talc (E553b) and titanium dioxide (E171).

The finished products are packaged as follows:

#### 60 mg Tablet

- PVC-PVDC/Al transparent blister (with sun/moon symbols) of 10 tablets; cartons of 60 tablets (6 blisters) and 180 tablets (18 blisters).
- PVC-PVDC/Al transparent calendar blister (with sun/moon symbols) of 14 tablets; cartons of 14 tablets (1 blister), 56 tablets (4 blisters) and 168 tablets (12 blisters).

#### 90 mg Tablet

- PVC-PVDC/Al transparent blister (with sun/moon symbols) of 10 tablets; cartons of 60 tablets (6 blisters) and 180 tablets (18 blisters).
- PVC-PVDC/Al transparent calendar blister (with sun/moon symbols) of 14 tablets; cartons of 14 tablets (1 blister), 56 tablets (4 blisters) and 168 tablets (12 blisters).
- PVC-PVDC/Al perforated unit dose transparent blister of 10 tablets; cartons of 100x1 tablets (10 blisters).

Not all pack sizes may be marketed.

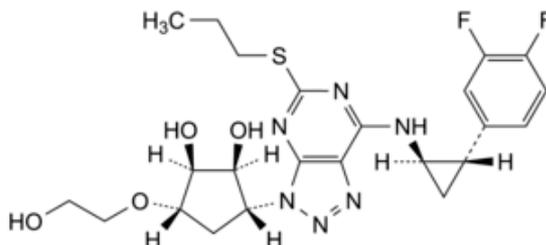
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

### II.2 ACTIVE SUBSTANCE

**rINN:** ticagrelor

**Chemical Name:** (1*S*,2*S*,3*R*,5*S*)-3-[7-[[[(1*R*,2*S*)-2-(3,4 Difluorophenyl)cyclopropyl]amino]-5-(propylsulfanyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2hydroxyethoxy) cyclopentane-1,2-diol.

**Molecular Formula:** C<sub>23</sub>H<sub>28</sub>F<sub>2</sub>N<sub>6</sub>O<sub>4</sub>S



Chemical Structure:

Molecular Weight: 522.6  
Appearance: White or almost white to pale pink powder.  
Solubility: Practically insoluble in water, freely soluble in methanol, soluble in anhydrous ethanol, practically insoluble in heptane.

Ticagrelor is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

The information related to the active substance was provided in an ASMF. The Active substance is the subject of a Ph.Eur. monograph.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting suitable retest period when stored in the proposed packaging.

## **II.3 DRUG PRODUCTS**

### **Pharmaceutical development**

A satisfactory account of the pharmaceutical development was provided.

Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

### **Manufacture of the products**

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

### **Finished Product Specifications**

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

### **Stability**

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 3 years, with no special storage conditions, is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

## **II.4 Discussion on chemical, pharmaceutical and biological aspects**

The grant of marketing authorisations was recommended.

## **III NON-CLINICAL ASPECTS**

### **III.1 Introduction**

As the pharmacodynamic, pharmacokinetic and toxicological properties of ticagrelor are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

### **III.2 Pharmacology**

No new pharmacology data were provided, and none were required for these applications.

### **III.3 Pharmacokinetics**

No new pharmacokinetic data were provided, and none were required for these applications.

### **III.4 Toxicology**

No new toxicology data were provided, and none were required for these applications.

### **III.5 Ecotoxicity/Environmental Risk Assessment**

Suitable justification was provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of already authorised products, an increase in environmental exposure is not anticipated following approval of the marketing authorisations for the proposed products.

### **III.6 Discussion on the non-clinical aspects**

The grant of marketing authorisations was recommended.

## IV CLINICAL ASPECTS

### IV.1 Introduction

The clinical pharmacology, efficacy and safety of ticagrelor are well-known. With the exception of data from a single bioequivalence study undertaken, no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this study is, thus, satisfactory.

### IV.2 Pharmacokinetics

In support of the application, the applicant submitted the following:

#### Study 1:

This study was an open label, balanced, randomised, single-dose, two-treatment, two-sequence, two-period, crossover, oral bioequivalence study comparing Ticagrelor 90 mg film-coated tablets (test product) with Brilique 90 mg film-coated tablets (reference product) in healthy, adult, human subjects under fasting conditions.

A single dose of either the test or reference product was administered after an overnight fast of at least 10 hours, in each study period. Blood samples were taken pre-dose and up to 48 hours post dose, with a washout period of 7 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Pharmacokinetic parameter	Geometric Mean Ratio Test/Ref	Confidence Intervals	CV% <sup>1</sup>
AUC <sub>(0-t)</sub> <sup>2</sup>	105.25	100.92% - 109.75%	8.66
C <sub>max</sub>	111.81	105.39% - 118.62%	12.23

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

As the additional (60 mg) strength of the product met the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence study on the product strength can be extrapolated to the other strengths.

### IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted for these applications and none were required.

### IV.4 Clinical efficacy

No new efficacy data were submitted with these applications and none were required.

### IV.5 Clinical safety

The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

**IV.6 Risk Management Plan (RMP)**

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

**IV.7 Discussion on the clinical aspects**

The grant of marketing authorisations was recommended for these applications.

**V USER CONSULTATION**

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

**VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION**

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with ticagrelor is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PILs for these products are available on the MHRA website.

**TABLE OF CONTENT OF THE PAR UPDATE**

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

<b>Application type</b>	<b>Scope</b>	<b>Product information affected</b>	<b>Date of grant</b>	<b>Outcome</b>	<b>Assessment report attached Y/N</b>