https://doi.org/10.31925/farmacia.2026.3.20 **ORIGINAL ARTICLE**

MARKET DYNAMICS, TREATMENT COSTS AND EVIDENCE-BASED POSITIONING OF ANTIPLATELET AGENTS IN ROMANIA: A NATIONAL SELL-OUT ANALYSIS (2022 - 2025)

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Abstract

This study evaluated the Romanian market for antiplatelet agents and linked real-world consumption patterns to treatment costs and clinical evidence. A national aggregated sell-out dataset covering August 2022–July 2025 was analyzed for antiplatelet agents classified as B01AC. Products were grouped by active substance, brand, manufacturer, originator/generic status and prescription status. Costs per treatment scheme were estimated from the Romanian National Catalogue of Maximum Prices of Medicinal Products and realized retail prices. During August 2024 - July 2025, B01AC medicines accounted for 19.43 million packages and 378.27 million RON in manufacturer-level value, increasing by 4.57% and 7.19%, respectively, versus the previous 12 months. Acetylsalicylic acid dominated volume and value, while clopidogrel and ticagrelor defined the main prescription segment. The first three brands represented 75.15% of value and the brand-level Herfindahl-Hirschman Index was 2767. Direct monthly cost ranged from approximately 22 RON for acetylsalicylic acid to 358 RON for dual therapy with ticagrelor 90 mg. These findings show a concentrated, cost-sensitive market requiring patient-level pharmacy data to evaluate persistence, switching and guideline alignment. Ticagrelor represented only 1.09% of packages but 12.36% of manufacturer-level value, and the estimated annual cost of acetylsalicylic acid plus ticagrelor was approximately 4.2-fold that of acetylsalicylic acid plus clopidogrel.

Rezumat

Studiul a evaluat piața românească a antiagregantelor plachetare și a corelat modelele de consum real cu costurile schemelor terapeutice și cu dovezile clinice disponibile. A fost analizat un set agregat național de tip sell-out pentru perioada august 2022–iulie 2025, incluzând medicamentele antiagregante încadrate în B01AC. Produsele au fost grupate după substanță activă, brand, producător, statut originator/generic și statut de prescripție. Costurile pe schemă au fost estimate din CANAMED și din prețurile retail realizate. În august 2024 - iulie 2025, segmentul B01AC a însumat 19,43 milioane pachete și 378,27 milioane RON valoare la nivel de producător, cu creșteri de 4,57% și, respectiv, 7,19% față de ultimele 12 luni anterioare. Acidul acetilsalicilic a dominat volumul și valoarea, iar clopidogrelul și ticagrelorul au definit segmentul principal de prescripție. Primele trei branduri au cumulat 75,15% din valoare, iar indicele Herfindahl-Hirschman a fost 2767. Costul lunar direct a variat de la aproximativ 22 RON pentru acid acetilsalicilic la 358 RON pentru terapia dual cu ticagrelor 90 mg. Ticagrelorul a reprezentat numai 1,09% din pachete, dar 12,36% din valoarea la nivel de producător, iar costul anual estimat al asocierii acid acetilsalicilic plus ticagrelor a fost de aproximativ 4,2 ori mai mare decât al asocierii acid acetilsalicilic plus clopidogrel.

Keywords: antiplatelet agents, acetylsalicylic acid, clopidogrel, ticagrelor, pharmacoepidemiology

Introduction

Antiplatelet therapy is central to the prevention and treatment of arterial thrombotic events, particularly acute coronary syndromes, percutaneous coronary intervention and secondary prevention after non-cardioembolic ischemic stroke or transient ischemic attack. Current European and American guidance positions acetylsalicylic acid, P2Y12 inhibitors and dual antiplatelet therapy according to indication, ischemic risk, bleeding risk and treatment phase (1, 2).
The clinical evidence base for antiplatelet therapy is extensive. Clopidogrel showed modest superiority over aspirin in the CAPRIE population, the addition of clopidogrel to aspirin reduced ischemic events in non-ST elevation acute coronary syndromes, and more potent P2Y12 inhibitors changed the management of acute coronary syndromes at the cost of differentiated bleeding and tolerability profiles (3-6). In cerebrovascular disease, short-term dual antiplatelet therapy after minor ischemic stroke or high-risk transient ischemic attack reduced early recurrent ischemic events, but the duration and drug combination remain strongly dependent on bleeding risk (7-9).
Despite the maturity of the clinical evidence, real-world use is shaped by medicine availability, reimbursement, generic penetration, out-of-pocket cost,

prescriber preference, patient adherence and pharmacy-level substitution. For a pharmacist-led doctoral research program, market and dispensing data are therefore not merely commercial indicators; they provide a pragmatic pharmacoepidemiological entry point for understanding how evidence-based therapies are actually used. Romanian hospital experience and European utilization studies further show that antiplatelet selection in practice is shaped by clinical context, access and the structure of the available data source (10, 11).

The aim of this study was to describe the structure and dynamics of the Romanian market for antiplatelet agents, estimate direct drug costs for relevant treatment schemes and interpret these findings in relation to the current evidence base on efficacy, safety and treatment individualization.

Materials and Methods

Study design

This was a descriptive pharmacoepidemiological and market analysis based on a retrospective analysis of an aggregated national sell-out dataset comprising 36 monthly observations from August 2022 to July 2025. The analytical unit was the stock keeping unit, aggregated by month. No patient-level or prescription-level data were available; therefore, the study describes market structure and treatment costs but cannot infer individual patient adherence, prescriber behaviour or indication-specific use. Because no formal EQUATOR guideline applies to aggregated market data, the reporting followed general pharmacoepidemiological principles adapted from the RECORD-PE extension for observational studies using routinely collected health data. The main analytical window was the 12-month period August 2024–July 2025, compared with August 2023–July 2024 as the prior-year reference. A rolling 12-month (moving annual total, MAT) design was chosen rather than calendar years to smooth short-term fluctuations, to avoid boundary effects at January and December, and to align the latest available window with the data extraction date of July 2025. Ethics approval was not applicable because the study used aggregated, non-identifiable commercial data that did not involve human participants.

Data source and provenance

The dataset was an aggregated national sell-out panel provided by IQVIA through its Romanian retail pharmacy audit. The panel covers approximately 95% of community pharmacy turnover nationally and is projected to 100% coverage using a proprietary expansion model. Sell-out denotes dispensing from pharmacy to patient (or patient representative), as opposed to sell-in (wholesale to pharmacy) or stock movement. The data capture is restricted to community pharmacies; hospital pharmacy dispensing is not included. The analytical unit was the stock keeping unit defined by active substance, brand, strength, pharmaceutical form and pack size, aggregated by calendar month.

Definition of the target population (drugs)

The target group consisted of medicines classified as platelet aggregation inhibitors excluding heparin, corresponding to Anatomical Therapeutic Chemical code B01AC in the World Health Organization ATC/DDD system (12), using the 2026 ATC/DDD Index. All active substances listed under B01AC were retained in the dataset: acetylsalicylic acid, cilostazol, clopidogrel, dipyridamole, iloprost, selexipag, ticagrelor, ticlopidine and triflusal. No active substance was excluded a priori, but iloprost and selexipag are prostacyclin-pathway agents indicated for pulmonary arterial hypertension and are not antiplatelet drugs in the thrombosis-prevention sense; they were retained for ATC completeness but are flagged when interpreting clinical relevance. Fixed-dose combinations containing a B01AC substance were included when they fell under B01AC in the ATC hierarchy. All strengths, pharmaceutical forms and pack sizes were retained; no SKU-level filtering by dose or pack size was applied because the analysis described overall market structure rather than a specific indication. For the broader antithrombotic context, comparator classes B01A (antithrombotic agents, total) and B01AF (direct factor Xa inhibitors) were also defined using their ATC codes.

Variables and definitions

For each SKU-month observation, the dataset provided the following quantitative fields: number of packages dispensed; standard units (SU), defined by the data vendor as the smallest common dose unit (e.g., one tablet or one capsule); manufacturer-level value (MNF), representing the invoiced value at ex-factory level excluding VAT; wholesale value (WHS), representing the value at wholesaler level excluding VAT; and retail value (RET), representing the pharmacy-level sales value to the patient or payer, including VAT where applicable. Categorical descriptors included active substance, brand name, manufacturer or corporation name, product status and prescription status. Product status distinguished originator (innovator brand), branded generic and unbranded generic; in the analysis, originator and branded-generic products were grouped as branded products. Prescription status classified each SKU as prescription-only (Rx) or over-the-counter (OTC) based on the Romanian Medicines Agency classification at the time of dispensing. All monetary values are nominal Romanian leu (RON) and were not inflation-adjusted because the analysis period was relatively short (36 months) and year-on-year comparisons were computed within the same calendar period.

Market-structure analysis

Market shares were computed by active substance and by brand as percentages of total packages and of total manufacturer-level value within the B01AC class. Year-on-year variation was calculated for packages and value between the two 12-month windows. Market concentration was summarised using the Herfindahl-Hirschman Index (HHI), computed as the sum of squared value shares across the complete set of brands present in the market (not only the top brands), expressed on a 0–10,000 scale. The HHI was computed at brand level rather than manufacturer/corporation level to reflect the competitive structure as experienced by prescribers and patients. Concentration thresholds followed the conventional categorisation: HHI below 1,500 indicates an unconcentrated market, 1,500–2,500 moderate concentration, and above 2,500 high concentration. The share basis for HHI was manufacturer-level value.

Price and growth-decomposition methods

Monthly average retail price per package was calculated as RET divided by packages for each month. Because this average is a mix-composite reflecting the product-mix sold in a given month rather than a constant-basket price index, it was interpreted as a proxy for price level rather than a true price index; no Laspeyres or Paasche adjustment was applied. Exploratory price-volume association was evaluated on monthly log differences to reduce spurious correlation from common trends. Pearson and Spearman correlation coefficients were calculated between change in log average retail price per package and change in log package volume. An exploratory ordinary least squares model with heteroscedasticity and autocorrelation robust standard errors (Newey-West) estimated the slope of this association. Growth decomposition of the retail-value increase between the two 12-month windows was performed using a Laspeyres-type volume-price decomposition: the volume component was calculated by applying the prior-period average retail price per package to the change in package volume, and the residual was attributed to price or product-mix effects. Statistical significance was interpreted at $p < 0.05$ (two-sided tests).

Cost-estimation methods (treatment schemes)

Direct drug costs were estimated per day, 21 days, 30 days, 90 days and 365 days for selected monotherapy and dual antiplatelet therapy schemes. For prescription antiplatelet agents, maximum retail prices were extracted from the Romanian National Catalogue of Maximum Prices of Medicinal Products (CANAMED), published by the Ministry of Health (13), using the median price among available products for the generic substance when multiple generic strengths or pack sizes existed. Because low-dose acetylsalicylic acid products in the dataset were predominantly over-the-counter, their cost was estimated from realized sell-out retail prices (RET divided by packages) rather than from CANAMED. The calculations used usual maintenance regimens as defined by current guidelines: acetylsalicylic acid 75–100 mg once daily, clopidogrel 75 mg once daily, ticagrelor 90 mg twice daily (acute-phase maintenance), ticagrelor 60 mg twice daily (post-myocardial infarction long-term maintenance, *per* PEGASUS-TIMI 54), and cilostazol 100 mg twice daily. Costs are direct drug costs and do not include medical visits, diagnostic tests, adverse-event management, or reimbursement/copayment effects.

Evidence mapping

The clinical evidence section was structured as a selective evidence map rather than a full systematic review. Landmark randomised trials and recent guideline or consensus documents were selected by the authors through expert identification to contextualise the market data. Selection criteria focused on: (a) large phase-3 randomised controlled trials that influenced guideline recommendations for antiplatelet therapy in coronary artery disease, cerebrovascular disease or peripheral artery disease; (b) meta-analyses or individual patient data analyses published in 2023–2025; and (c) contemporary European or international guideline or consensus documents (2021–2024) addressing antiplatelet selection, duration, pharmacogenetic testing or platelet function testing. Trials were identified from PubMed and guideline databases using the search terms “antiplatelet therapy”, “dual antiplatelet therapy”, “aspirin”, “clopidogrel”, “ticagrelor”, “prasugrel”, “acute coronary syndrome”, “stroke”, “percutaneous coronary intervention”, and “platelet function test”, with date limits 1996–2025. Two authors independently reviewed trial eligibility and extracted efficacy endpoints, bleeding outcomes, tolerability data and the role of platelet function or pharmacogenetic testing. Disagreements were resolved by consensus.

Statistical analysis (consolidated)

All analyses were performed using Python 3.12 (pandas, scipy, statsmodels). Descriptive statistics were used to report volumes, values, year-on-year variation, market shares and treatment costs. All statistical tests were two-sided. Analyses were performed on aggregated data; no patient-level inference was attempted.

Results and Discussion

Market size and dynamics

In the latest 12-month window, B01AC medicines generated 19.43 million packages and 581.84 million SU. Manufacturer-level value was 378.27 million RON, wholesale value was 430.29 million RON and retail value was 557.97 million RON. The market increased by 4.57% in packages and 7.19% in

MNF value compared with the previous 12-month window (Table I).

The monthly series suggested moderate growth with visible short-term fluctuations. Package volume remained between approximately 1.3 and 1.8 million packages per month, while retail value increased from 38.73 million RON in August 2022 to 44.17 million RON in July 2025 (Figures 1 and 2).

Table I

Key market indicators for B01AC medicines in Romania, 12-month comparison

Indicator	202308 - 202407	202408 - 202507	YoY change (%)
Units (packages)	18 584 641	19 434 273	4,57
Standard Units (SU)	556 912 518	581 842 565	4,48
Valoare MNF (mil. RON)	352,89	378,27	7,19
Valoare WHS (mil. RON)	400,07	430,29	7,55
Valoare RET (mil. RON)	516,36	557,97	8,06

Legend: B01AC = platelet aggregation inhibitors excluding heparin; MNF = manufacturer-level value; WHS = wholesale value; RET = retail value; SU = standard units; YoY = year-on-year. Monetary values are expressed as million RON, as available in the source data.

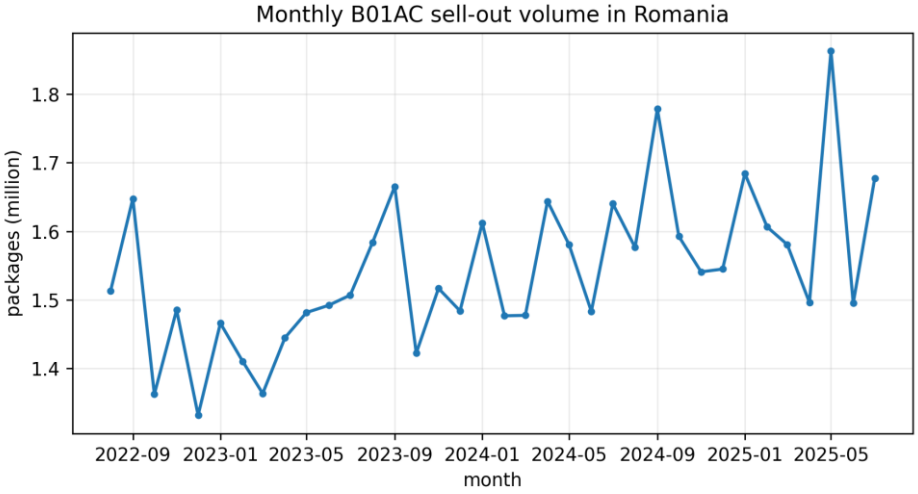

Figure 1.

Evolution of monthly B01AC sell-out volume in Romania, August 2022–July 2025. Values are expressed as million packages

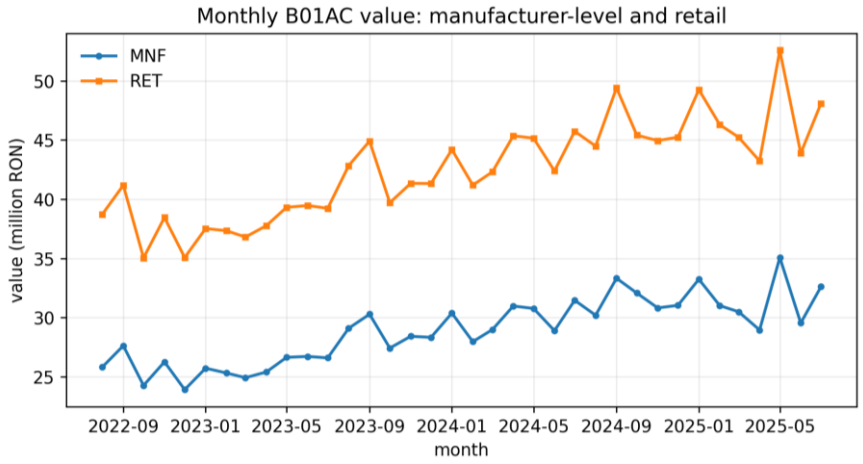

Figure 2.

Evolution of monthly B01AC value in Romania, August 2022–July 2025. MNF = manufacturer-level value; RET = retail value. Values are expressed as million RON

In the broader antithrombotic market, B01AC represented 72.70% of B01A packages but only 22.84% of B01A manufacturer-level value during August 2024 - July 2025. This difference reflects the relatively low unit cost of acetylsalicylic acid and generic clopidogrel compared with direct oral anticoagulants, particularly B01AF products, which accounted for 55.34% of B01A value but only 13.03% of packages.

Active substance and brand structure

The Romanian B01AC market was dominated by acetylsalicylic acid, followed by clopidogrel and

ticagrelor. These three active substances accounted for more than 94% of manufacturer-level value, while acetylsalicylic acid alone represented 81.17% of packages and 58.91% of value (Table II and Figure 3). The contrast was most pronounced for ticagrelor: 1.09% of packages generated 12.36% of manufacturer-level value, corresponding to a value-share-to-package-share ratio of approximately 11.3. Its package volume increased by 1.7%, whereas value decreased by 3.4%, suggesting a change in average value per package and/or product mix rather than a decline in dispensed volume. The high concentration of the market may support supply efficiency, but it also increases vulnerability to disruptions, especially in low-margin generic segments, where shortages or temporary unavailability can alter both market shares and dispensing behavior (14). In a market such as Romania, this is particularly relevant for long-established cardiovascular medicines, where even modest supply disturbances may be amplified by price regulation and substitution constraints.

Table II

Composition and codification of metronidazole gel formulations

Active substance	MNF value (mil. RON)	Value share (%)	Packages	Package share (%)	YoY packages (%)	YoY value (%)
acetylsalicylic acid	222.83	58.91	15 774 544	81.17	5.7	12.8
clopidogrel	87.90	23.24	3 068 777	15.79	0.6	1.2
ticagrelor	46.77	12.36	212 675	1.09	1.7	-3.4
cilostazol	18.19	4.81	280 084	1.44	9.8	9.1
triflusal	2.35	0.62	89 517	0.46	-6.6	-6.2
ticlopidine	0.17	0.04	5 911	0.03	-50.1	-50.0
iloprost	0.04	0.01	53	0.00	-17.2	-16.9
dipyridamole	0.03	0.01	2 712	0.01	-93.3	-92.9
selexipag	0.00	0.00	0	0.00	-100.0	-100.0

Legend: MNF = manufacturer-level value; YoY = year-on-year. Active substances are written in lowercase according to journal style.

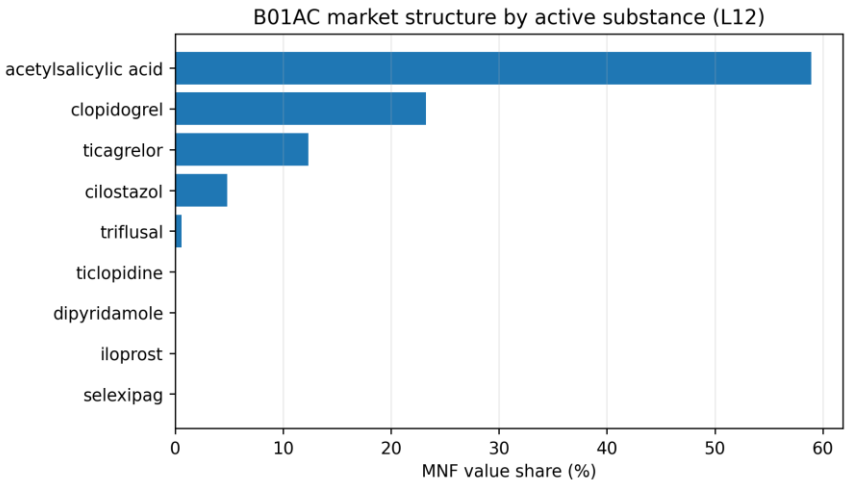

Figure 3.

Manufacturer-level value share by active substance in the B01AC market, August 2024–July 2025

The brand landscape was highly concentrated. The first three brands, Aspenter, Plavix and Brilique, represented 75.15% of B01AC manufacturer-level value. The brand-level HHI was 2767, computed across the complete set of brands in the market (not only the top three), compatible with a concentrated market structure. At segment level, branded generics represented 72.34% of value and 91.97% of packages, while over-the-counter products represented 58.91% of value and 81.18% of packages; these shares coincide numerically with those of acetylsalicylic acid as an active substance because the OTC segment is composed almost entirely of aspirin products, but they are conceptually distinct classifications (active substance *vs*. prescription status). These findings indicate that market behavior is driven by a high-volume, lower-cost acetylsalicylic acid segment and by a smaller prescription segment where clopidogrel and ticagrelor have greater economic weight.

Price-volume signal and market growth decomposition

Using monthly log differences, changes in average retail price per package were negatively associated with changes in package volume. The Pearson correlation was $r = -0.73$ ($p < 0.001$) and the Spearman correlation was $r = -0.73$ ($p < 0.001$). In the exploratory log-difference model, the price-volume

coefficient was -3.01 (95% confidence interval -4.22 to -1.80, $p < 0.001$), suggesting that shifts in the average retail price or product mix coincided with lower monthly volume growth (Figure 4). This should not be interpreted as causal elasticity because the data are aggregated and not adjusted for diagnosis, prescriber behavior, reimbursement, stock availability or seasonality.

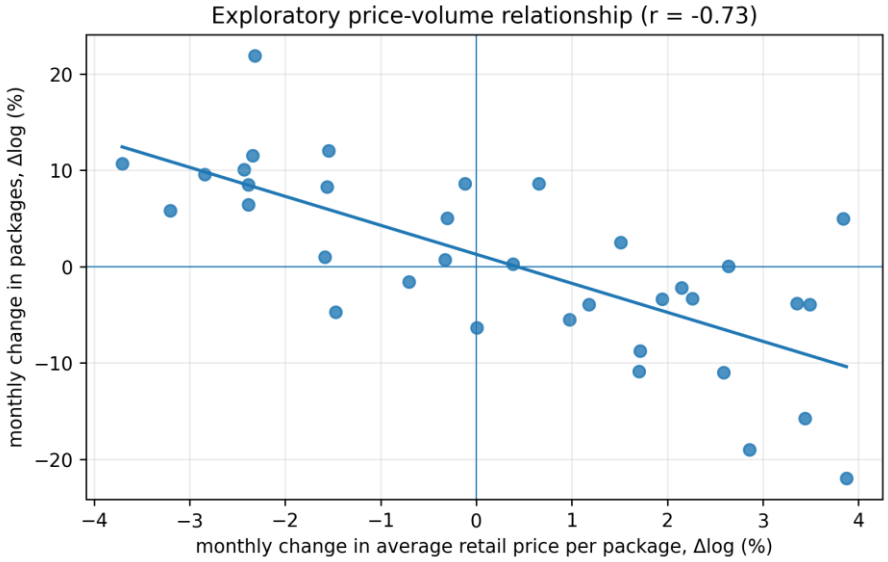

Figure 4.
Exploratory relationship between monthly changes in average retail price per package and monthly changes in B01AC package volume. Changes are expressed as Δlog percentages

Retail value increased by 41.6 million RON between the two 12-month windows, from 516.4 million RON to 558.0 million RON. Approximately 23.6 million RON was attributable to volume growth and 18.0 million RON to price or product mix. Therefore, market growth was not purely volume-driven; average price and composition effects contributed substantially.

On this decomposition, volume accounted for approximately 56.7% and price or product mix for 43.3% of the observed retail-value increase.

The inverse price-volume association observed in the exploratory model is fundamentally shaped by the Romanian pharmacoeconomic and regulatory environment. The national reference pricing system strictly anchors maximum allowable reimbursement limits to the lowest-priced generic equivalent available in the Romanian National Catalogue of Maximum Prices of Medicinal Products (CANAMED). Furthermore, the application of the national clawback tax—a fiscal mechanism shifting the financial risk of public healthcare overspending onto pharmaceutical manufacturers—disproportionately impacts high-volume, low-cost generic medicines priced below 100 RON. As demonstrated in recent market analyses, this uniform fiscal pressure renders essential cardiovascular treatments highly vulnerable to recurrent supply discontinuities and market withdrawals (18). Consequently, the broad generic penetration seen in the clopidogrel and acetylsalicylic acid segments inherently drives down maximum allowable prices but frequently triggers volumetric fluctuations, as community pharmacies and patients are forced to navigate copayment changes and localized supply chain disruptions.

Treatment costs and therapeutic schemes

The cost analysis showed large differences between low-dose acetylsalicylic acid, clopidogrel and ticagrelor-based schemes. The estimated 30-day direct drug cost was 21.95 RON for acetylsalicylic acid, 63.29 RON for median-cost clopidogrel, 335.69 RON for ticagrelor 90 mg twice daily and 357.64 RON for dual antiplatelet therapy with acetylsalicylic acid plus ticagrelor 90 mg twice daily (Table III and Figure 5). On an annual basis, ticagrelor 90 mg monotherapy was approximately 5.3-fold more expensive than median-cost clopidogrel, while acetylsalicylic acid plus ticagrelor dual therapy was approximately 4.2-fold more expensive than acetylsalicylic acid plus clopidogrel dual therapy.

The marked difference in direct treatment costs across regimens is clinically relevant because medication cost is a recognized driver of cost-related nonadherence in cardiovascular disease, and financial barriers can reduce adherence and persistence in real-world practice (15, 16). In Romania, delayed access to reimbursed innovative medicines and reimbursement bottlenecks may further amplify affordability constraints and shape dispensing behavior (17, 18).

Table III

Estimated direct drug costs for selected antiplatelet treatment schemes

Treatment scheme	Cost/day (RON)	Cost/30 days (RON)	Cost/90 days (RON)	Cost/365 days (RON)
acetylsalicylic acid 75–100 mg OD	0.73	21.95	65.86	267.10
clopidogrel 75 mg OD, median CANAMED	2.11	63.29	189.87	770.03
ticagrelor 90 mg BID	11.19	335.69	1 007.07	4 084.22
ticagrelor 60 mg BID	9.30	278.98	836.94	3 394.24
DAPT: acetylsalicylic acid + clopidogrel, median	2.84	85.24	255.73	1 037.13
DAPT: acetylsalicylic acid + ticagrelor 90 mg BID	11.92	357.64	1 072.93	4 351.32
cilostazol 100 mg BID, median CANAMED	3.84	115.07	345.21	1 400.02

Legend: BID = twice daily; CANAMED = Romanian National Catalogue of Maximum Prices of Medicinal Products; DAPT = dual antiplatelet therapy; OD = once daily. Costs are direct drug costs and do not include medical visits, tests, adverse-event management or reimbursement/copay effects.

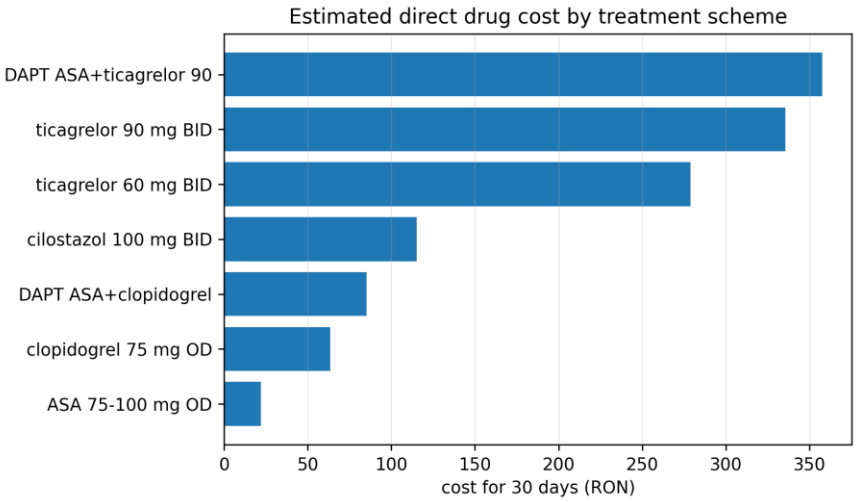

Figure 5.

Estimated direct drug cost for 30 days by selected antiplatelet treatment scheme. DAPT = dual antiplatelet therapy; OD = once daily; BID = twice daily

The clinical interpretation of these cost differences is not that low-cost schemes are automatically preferable. Rather, price and affordability may influence long-term persistence, de-escalation and dispensing behavior. In acute coronary syndrome, ticagrelor or prasugrel may be clinically preferred in selected patients, whereas clopidogrel remains relevant when bleeding risk, tolerability, availability, genotype, comorbidity or affordability constrain the use of more potent agents (1, 10, 11).

The clinical interpretation of these marked cost differences transcends simple budget impact; out-of-pocket prices heavily influence long-term therapeutic persistence and dispensing behavior. When the financial burden of copayment is transferred directly to the patient, the direct drug cost becomes a primary determinant of treatment continuity. Recent pharmacoepidemiological research evaluating cardiovascular treatment adherence in Romanian patients using the Medication Adherence Report Scale (MARS) demonstrated that adherence to prescribed therapies is significantly influenced by financial accessibility, monthly income, and the distance to the pharmacy providing the optimal out-of-pocket price (19). Consequently, while potent P2Y12 inhibitors such as ticagrelor are clinically preferred in the acute phase of coronary syndromes, clopidogrel remains highly relevant when bleeding risk, tolerability constraints, or out-of-pocket affordability limit the long-term use of more expensive agents. These utilization patterns should be interpreted against current guideline recommendations, which position aspirin, P2Y12 inhibitors and dual antiplatelet therapy according to indication, ischemic risk, bleeding risk and treatment phase (1, 2). Clopidogrel remains highly relevant in practice, but its effect may be influenced by CYP2C19 genotype, and selective platelet function or genetic testing may be considered in specific PCI scenarios (10, 11).

Evidence-based positioning of market findings

The market distribution should be interpreted against the differentiated evidence base of antiplatelet agents. Clopidogrel has broad secondary prevention evidence and generic availability. Ticagrelor has a stronger acute coronary syndrome evidence base than clopidogrel in PLATO but is more expensive

and is associated with tolerability issues such as dyspnea. Short-term dual antiplatelet therapy after minor ischemic stroke or high-risk transient ischemic attack is supported by CHANCE, POINT and THALES, but the bleeding signal differs by regimen and duration (Table IV).

Table IV

Selected clinical evidence relevant to interpretation of B01AC market dynamics

Study	Population	Comparison	Main efficacy result	Main safety signal
caprie (3)	atherosclerosis (MI/stroke/PAD)	clopidogrel *vs* aspirin	annual event risk 5.32% *vs* 5.83%; RRR 8.7%	comparable bleeding profile
cure (4)	non-ST elevation ACS	clopidogrel + aspirin *vs* aspirin	CV death/MI/stroke 9.3% *vs* 11.4%; RR 0.80	major bleeding 3.7% *vs* 2.7%
triton-timi 38 (5)	ACS undergoing PCI	prasugrel + aspirin *vs* clopidogrel + aspirin	CV death/MI/stroke 9.9% *vs* 12.1%; HR 0.81	major bleeding 2.4% *vs* 1.8%; avoid after prior stroke/TIA
plato (6)	ACS	ticagrelor + aspirin *vs* clopidogrel + aspirin	CV death/MI/stroke 9.8% *vs* 11.7%; HR 0.84	non-CABG bleeding and dyspnea increased
chance (7)	minor stroke/high-risk TIA	short DAPT then clopidogrel *vs* aspirin	stroke 8.2% *vs* 11.7%; HR 0.68	moderate/severe bleeding similar
point (8)	minor stroke/high-risk TIA	clopidogrel + aspirin *vs* aspirin	major ischemic events 5.0% *vs* 6.5%; HR 0.75	major bleeding 0.9% *vs* 0.4%
thales (9)	minor stroke/high-risk TIA	ticagrelor + aspirin vs aspirin	stroke/death 5.5% vs 6.6%; HR 0.83	severe bleeding 0.5% *vs* 0.1%
pegasus-timi 54 (25)	history of myocardial infarction	ticagrelor 60 mg BID + aspirin *vs* placebo + aspirin	CV death/MI/stroke 7.77% *vs* 9.04%; HR 0.84	TIMI major bleeding 2.60% *vs* 1.06%; dyspnea increased

Legend: ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; CV = cardiovascular; DAPT = dual antiplatelet therapy; HR = hazard ratio; MI = myocardial infarction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; RR = relative risk; RRR = relative risk reduction; TIA = transient ischemic attack.

A separate implication concerns treatment individualization. Clopidogrel requires bioactivation through CYP2C19, and reduced-function genotypes can decrease platelet inhibition and increase ischemic risk in selected populations. However, both pharmacogenetic testing and platelet function testing are positioned as selective tools rather than universal routine procedures in contemporary guidance (10, 11). For Romania, this distinction is important: aggregated sales data can identify volume, value and cost patterns, but patient-level pharmacy and clinical data are required to evaluate whether treatment choices are guided by diagnosis, risk stratification, persistence or therapeutic switching. The critical gap between clinical trial data and real-life patient compliance remains a recurring challenge in pharmaceutical research, as documented in previous therapeutic efficacy reviews (20). Apart from active substance selection, the technological quality and drug-release parameters of oral dosage forms are vital components of therapeutic success, a critical relationship regularly investigated in Romanian pharmaceutical research through innovative formulation methods (21).

The European benchmark is also relevant. In a population-based study in four European countries, overall antithrombotic use declined between 2010 and 2018, mainly through reduced low-dose aspirin use, whereas oral anticoagulant uptake increased (22). In contrast, the Romanian B01AC sell-out pattern observed here remains strongly dominated by acetylsalicylic acid, suggesting that local over-the-counter access, brand penetration and prescription renewal patterns may differ from datasets based exclusively on prescriptions or medical records.

The Romanian pattern should also be interpreted in the context of broader European utilization trends, where antithrombotic use has shifted over time and aspirin exposure has declined in some settings, whereas Romanian sell-out data still show strong dominance of acetylsalicylic acid (22). This difference suggests that local over-the-counter access, brand penetration and prescription renewal patterns may contribute to a more persistent aspirin-centered market structure.

Recent evidence comparing long-term clopidogrel and aspirin monotherapy in established coronary artery disease may further influence future utilization if incorporated into guidelines and local reimbursement behaviour (23). This supports the need for continued longitudinal monitoring of clopidogrel and acetylsalicylic acid shares, particularly after guideline updates or changes in pharmacy-level availability (24).

The transition from clinical trial efficacy to real-world effectiveness is heavily mediated by the aforementioned adherence barriers. The substantial out-of-pocket costs and the twice-daily dosing regimen of ticagrelor—coupled with its complex pharmacokinetic profile as a CYP3A4 substrate and potential for adverse reactions such as dyspneea (25, 26)—can severely compromise long-term persistence compared to the once-daily, cost-effective administration of clopidogrel. This economic and tolerability pressure justifies the growing clinical implementation of therapeutic de-escalation. Transitioning patients

from ticagrelor to clopidogrel following the initial acute phase of an acute coronary syndrome is increasingly adopted in real-world practice to simultaneously mitigate major bleeding risks, alleviate financial toxicity, and ensure medication adherence.

Furthermore, when placed in a broader European epidemiological context, the Romanian market exhibits specific structural rigidities. While overall antithrombotic use in several Western European countries declined between 2010 and 2018, primarily due to an evidence-based reduction in the prophylactic use of low-dose aspirin (22), the Romanian B01AC market remains heavily dominated by acetylsalicylic acid. This structural inertia is exacerbated by delayed patient access to innovative therapies. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA) W.A.I.T. Indicator 2024 survey, Romania registers significant administrative delays regarding the pricing and reimbursement of new medicines (17, 25). This systemic reimbursement delay, compounded by a strong reliance on out-of-pocket payments for cost-effective legacy molecules, perpetuates a delayed epidemiological transition compared to Western European healthcare systems.

Implications for pharmacy-based real-world data

A national pharmacy chain can substantially strengthen this research by providing pseudonymized transaction-level data. The minimum dataset should include patient hash, dispensing date, pharmacy and county, SKU, active substance, concentration, pack size, number of packages, retail price, reimbursement/copayment status and prescription/over-the-counter flag. Additional variables such as prescriber specialty, diagnosis code, patient age band and sex would permit clinically meaningful subgroup analyses.

With such data, the next analytical layer could estimate medication possession ratio, proportion of days covered, persistence, gaps, switching from ticagrelor to clopidogrel or from dual therapy to monotherapy, and differential cost exposure by patient group. If diagnosis codes are available, analysis by acute coronary syndrome, percutaneous coronary intervention, ischemic stroke/transient ischemic attack and peripheral artery disease would become feasible. Without diagnosis codes, disease-specific interpretation remains inferential and should be limited to treatment pattern proxies.

Without patient-level linkage, sell-out data remain useful for describing market structure, but they cannot distinguish between appropriate use, nonadherence, stock-driven substitution or prescribing shifts. This limitation is especially important in antiplatelet therapy, where adherence, persistence and regimen changes are strongly shaped by affordability, access and clinical indication (17-19). To move beyond descriptive market surveillance, future studies should combine dispensing records with diagnosis, copayment and prescriber data so that treatment duration, switching, persistence and indication-specific use can be measured more accurately. Without such linkage, sell-out data remain informative for market monitoring but cannot determine whether observed patterns represent optimal care, substitution pressure or access constraints (15, 18, 27, 28).

Limitations

The analysis is based on aggregated sell-out data and cannot identify diagnosis, indication, prescriber intention, adherence at patient level, clinical outcomes, bleeding events or actual platelet response. Cost estimates represent direct drug costs only and do not incorporate reimbursement, copayment variability, adverse-event management, laboratory testing or hospitalization. The price-volume correlation is exploratory and may reflect product mix, seasonality, stock availability or market access rather than true demand elasticity. Additionally, B01AC includes prostacyclin-pathway agents such as iloprost and selexipag that are indicated for pulmonary arterial hypertension and are not antiplatelet drugs in the conventional thrombosis-prevention sense; their market presence is negligible but readers should be aware that the ATC class definition is broader than the clinical category of antiplatelet agents. Finally, the clinical evidence map is selective and intended to contextualize utilization rather than replace a systematic review.

Conclusions

The Romanian B01AC market during August 2022–July 2025 showed moderate growth, high concentration and clear dominance of acetylsalicylic acid, with clopidogrel and ticagrelor defining the most relevant prescription segment. The latest 12-month window reached 19.43 million packages and 378.27 million RON in manufacturer-level value. Market value increased faster than volume, indicating a combined effect of consumption and price or product mix. Treatment costs differed markedly across schemes, from low-cost acetylsalicylic acid to substantially more expensive ticagrelor-based dual therapy. Clinical trial evidence supports differentiated use by diagnosis and risk profile; therefore, market share alone cannot be interpreted as appropriateness. The next step should be patient-level pharmacy research, linking dispensing episodes, persistence, switching and cost exposure to diagnosis and prescriber variables when available.

The Romanian B01AC market during August 2022-July 2025 showed moderate growth, high brand concentration and a clear two-component structure. Acetylsalicylic acid accounted for 81.17% of packages and 58.91% of manufacturer-level value, whereas ticagrelor accounted for only 1.09% of packages but

12.36% of value. In the latest 12-month window, the market reached 19.43 million packages and 378.27 million RON in manufacturer-level value. Value increased faster than volume, and approximately 43% of retail-value growth was attributable to price or product mix. Direct treatment costs ranged from low-cost acetylsalicylic acid to ticagrelor-based dual therapy, which was approximately 4.2-fold more expensive annually than clopidogrel-based dual therapy. These findings quantify utilization, concentration and cost but cannot determine clinical appropriateness. Patient-level dispensing data linked, where possible, to indication, procedure, prescriber and reimbursement variables are required to evaluate persistence, switching, treatment duration and alignment with evidence-based care.

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Availability of data and materials

The aggregated results generated in the present study are included in the figures and/or tables of this article. The underlying sell-out dataset is not publicly available because it contains commercially sensitive aggregated market information; additional data may be requested from the corresponding author subject to data-use permissions.

Ethics approval and consent to participate

Not applicable.

AI use disclosure

During the preparation of this manuscript, the authors used AI-assisted tools for language improvement and generation of graphical representations from aggregated quantitative data. The authors reviewed and revised all outputs and take full responsibility for the final content of the work.

Conflict of interest

The authors declare no conflict of interest.

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