

ENHERTU | J9358

2026 Commercial Payer Intelligence Report

Source Note

The findings in this report are drawn from the complete claim correspondence record across oncology practices — every prior authorization, EOB, remittance, denial letter, appeal, uphold, internal inquiry response, portal document, and physical mailer — read as a forensic system.

This is primary source intelligence from the claim file level. It is not derived from clearinghouse aggregations, hub data, or payer-reported metrics.

Claim-level correspondence at the practice level is structurally inaccessible to manufacturers. They cannot execute appeals, access portal correspondence, or read the EOB on a practice's behalf. This intelligence does not reach the manufacturer side through any other channel. That is why the findings in this report do not exist in any product currently in a manufacturer's market access stack.

Executive Summary

Commercial payers are failing oncology practices on Enhertu from two directions simultaneously. Both failure points hit the same practice on the same drug at the same time. Neither appears correctly in any clearinghouse report, hub data set, or field analytics product.

Failure Point One — Front End

- 15% to 25% of prior authorization requests rejected before treatment begins
- Automated UM portals running clinical criteria that predate current FDA labels
- Drug never ordered. Revenue never materializes. Patient treatment delayed or blocked
- Produces zero data points in any clearinghouse report

Failure Point Two — Back End

- Enhertu post-approval claim denial rate ran 7% to 9% in 2026
- Authorization was approved. Drug was administered. Claim came back denied anyway
- Immediate cash freeze of \$20,000+ per Enhertu cycle
- Practice cannot balance-bill. Funds locked for 45 to 90 days while distributor credit runs on 15 to 30 day clocks

What Happens To These Denials

- 50% to 60% are never appealed — written off silently as contractual adjustments — invisible in every reporting system
- Standard internal appeals succeed 40% to 45% on first line cases — declining rapidly on multi-stage cases
- Majority of standard appeals fail — clinical arguments applied to denials that were never clinical determinations
- Contradiction-based escalation across appeals, physician to physician review, expedited pathways, and IMR achieves approximately 74% recovery
- 15% to 20% of denied claims permanently abandoned — drug purchased on credit, administered, revenue written off as capital loss

The Manufacturer Blind Spot

- The accounts absorbing these losses adjust ordering behavior accordingly
- That adjustment appears in field data as unexplained volume decline

The cause is not a clinical preference shift. It is unrecovered capital loss on administered drug. That distinction is the difference between a sales problem and a payer blockade problem. Only one of them is visible in your field data. Neither of them is visible in your clearinghouse data.

- That signal does not appear in any data source between the manufacturer and the practice

The Portfolio Implication

- These mechanisms are not specific to Enhertu
- Every drug in an oncology portfolio with a recently expanded indication is subject to the same failure modes
- Enhertu is the documented example — the full portfolio is the scope

Key Findings

Enhertu post-approval denial rate ran 7% to 9% in 2026 — dual indication expansion timelines creating two simultaneous denial populations

Front end PA denial rate runs 15% to 25% — UM portals running pre-2026 criteria blocking treatment before it begins

50% to 60% of post-approval denials are never appealed — written off silently — invisible in every reporting system

Standard internal appeals succeed 40% to 45% on first line cases — declining rapidly on multi-stage denial cases — failing because clinical arguments are applied to non-clinical denials

Contradiction-based escalation achieves ~74% recovery — appeals, P2P review, expedited pathways, IMR

15% to 20% of denied claims permanently abandoned — capital loss on administered drug driving ordering behavior change invisible in manufacturer field data

True clinical rationale behind majority of post-approval denials never reaches the clearinghouse — locked in portal correspondence and medical director letters no aggregate system touches

Every oncology drug with a recently expanded indication is subject to the same mechanisms documented in this report

THE INTELLIGENCE GAP

Two Failure Points. Both Invisible To Aggregate Reporting.

Failure Point One — Front End PA Denial Rate: 15% to 25%

- Between 15% and 25% of PA requests rejected before treatment begins
- Automated UM portals running clinical criteria that predate current FDA labels
- 2026 Enhertu early stage approvals not yet recognized by significant portion of payer authorization systems
- Failure happens entirely outside the clearinghouse ecosystem
- PAs processed through Availity, CoverMyMeds, RadMD, direct payer portals — clearinghouses only touch HIPAA 837 claims
- Front end rejection rate produces zero data points in any clearinghouse report
- Does not appear in hub data. Does not appear in field analytics.

Failure Point Two — Post-Approval Claim Denial Rate

- Enhertu: 7% to 9% of claims with approved authorizations denied at adjudication
- Authorization approved. Drug administered. Claim denied anyway.
- Cash freeze of \$20,000+ per Enhertu cycle
- CO contractual obligation group code — practice cannot balance-bill
- Dispute pipeline runs 45 to 90 days against 15 to 30 day distributor credit terms
- 50% to 60% written off without appeal — logged as contractual adjustments — closed
- 15% to 20% permanently abandoned after failed appeals — capital loss on administered drug

Why Clearinghouse Data Misses Both

Three structural blind spots — not one

Blind Spot One — The Syntax Check Problem

- Clearinghouses confirm valid HCPCS format and populated fields — nothing more
- No visibility into whether payer will honor the authorization or apply correct fee schedule 14 days later
- When ERA returns CO-50 or CO-96 — one denial unit recorded
- A denied \$150 office visit and a denied \$20,000 Enhertu administration recorded identically
- Dollar weight, appeal timeline, working capital impact, authorization context — all invisible
- Front end PA denials never create a claim — clearinghouse never sees them at all

Blind Spot Two — The Multi-Stage Denial Loop

> The post-approval denial rates above do not represent claims receiving a single denial. They represent claims cycling through sequential evolving rationales that clearinghouse dashboards record as separate unrelated transactions.

The pattern Third Rail Intelligence consistently sees across these files:

- **Stage 1 — Administrative Rejection:** CO-16 or CO-96 — generic — missing information or non-covered service — practice corrects and resubmits
- **Stage 2 — Clinical Pivot:** CO-50 medical necessity — new rationale replaces the resolved administrative one — practice files clinical appeal
- **Stage 3 — Safety or Dosing Hold:** subsequent cycle denied — cardiac monitoring absent, modifier incorrect, quantity limit flagged

What the clearinghouse sees: three separate minor issues on three separate transactions

What the complete correspondence record shows: one coordinated sequential barrier applied to a single treatment across multiple billing cycles

The Sequential Denial Loop — Documented Transactional Path

The following sequence is documented across Enhertu claim files at multiple payers. It is not hypothetical. Each stage is drawn from actual remittance records, portal correspondence, and appeal outcomes on J9358.

```

Stage 1 — Clearinghouse Gate
Claim billed: J9358 + JZ modifier
Payer adjudication engine flags multi-vial unit math or modifier compliance error
Output: CO-16 administrative rejection on 835
Practice corrects modifier or unit calculation and resubmits
Timeline consumed: 14 to 21 days

↓

Stage 2 — Clinical Adjudication
Resubmitted claim bypasses Stage 1 administrative gate
Claims engine now evaluates clinical criteria against pre-2025 policy bulletin
Output: CO-50 endocrine sequencing lag denial
Rationale: Prior cytotoxic chemotherapy not documented
Practice files clinical appeal with January 2025 label update and NCCN Category 1 designation
Timeline consumed: 30 to 45 days

↓

Stage 3 — Safety Monitoring Hold
Appeal on Stage 2 succeeds or is pending
Payer processes next scheduled cycle
Claims engine fires subsequent CO-50 citing absent or expired LVEF monitoring
Echocardiogram already performed and documented in clinical record
Denial states monitoring is absent — it is not absent — it was not transmitted
in the format the system requires
Timeline consumed: 15 to 30 additional days
  
```

Total timeline from Stage 1 trigger to Stage 3 resolution: 60 to 96 days

What standard dashboards record: Three separate minor transactions — one modifier error, one clinical review, one safety compliance check

What the complete correspondence record shows: A single coordinated financial barrier applied sequentially to one treatment course across multiple billing cycles. The cumulative effect extends the accounts receivable window past the distributor credit clock. The practice purchased the drug on 15 to 30 day credit terms. The payer's sequential denial system runs 60 to 96 days. The practice is financing the payer's adjudication delay with its own working capital.

Why this matters for appeal success rates:

- Practice responds to current denial letter
- Payer is operating a sequential system
- Contradiction argument that reverses the denial is not in the most recent letter — it is in the complete record read against itself
- This is why standard appeal success rates decline so rapidly on multi-stage cases

HCSC — running both BCBS Illinois and BCBS Texas — is one of the most consistent sources of this pattern:

- Stage 1 CO-16 generated on 835
- True clinical pathology demands hidden inside Availity portal

- 835 shows administrative rejection — Availity portal shows actual clinical barrier
- Clearinghouse sees the code — actual barrier is in the portal

Blind Spot Three — The Correspondence Data Black Hole

|> *The 835 remittance and the actual clinical denial rationale are two different documents describing two different levels of the same denial.*

What the 835 shows:

- CO-50 with generic remark N522 — documentation does not support level of service

What the portal correspondence shows:

- Four page PDF uploaded to payer's proprietary portal or mailed to practice
- Medical director letter: "Claim denied because patient transitioned to Enhertu after failing endocrine therapy without first receiving a line of cytotoxic chemotherapy in the metastatic setting"

The result:

- 835 routes through clearinghouse — medical director letter does not
- True clinical rationale stays locked inside payer portal or sits in clinic's physical mail stack
- What aggregate data counts: CO-50 with N522
- What actually drove the denial: specific clinical policy position in a document the clearinghouse never saw
- Clearinghouse data does not just underreport these denials — it **fundamentally misrepresents their nature**

The only way to access this intelligence:

- Read every document the payer produced across every channel
- 835 remittance, portal correspondence, uphold letters, medical director determinations, internal inquiry responses, physical mailers
- Map them against each other
- That is not possible from clearinghouse data alone

What This Means For Manufacturers

- Hub data shows clean authorization rate
- Clearinghouse data shows manageable denial rate
- Neither shows practices simultaneously absorbing front end PA rejection overhead and back end post-approval cash freezes
- 50% to 60% of post-approval denials written off silently — never appear in any metric
- Ordering behavior change that follows shows up in field data as **unexplained volume decline in accounts with specific payer concentrations**
- The cause does not appear in any reporting system between the manufacturer and the practice
- It is in the correspondence

THE FINANCIAL IMPACT

Both failure points hitting the same practice simultaneously

Based on observed case data. Enhertu at \$20,000+ per administration.

Small Independent Oncology Practice — 10 to 15 active patients per quarter

Metric	Enhertu
Front end PA denials per quarter at 15-25%	2 to 4 blocked
Revenue blocked or delayed per quarter	\$40,000 to \$80,000
Post-approval denied cycles per quarter	1 to 2
Post-approval denial exposure per quarter	\$20,000 to \$40,000
Combined quarterly exposure	\$60,000 to \$120,000
Combined annual exposure	\$240,000 to \$480,000
Permanently abandoned annually at 15-20%	\$36,000 to \$96,000

Mid-Size Group Oncology Practice — 20 to 30 active patients per quarter

Metric	Enhertu
Front end PA denials per quarter at 15-25%	3 to 8 blocked
Revenue blocked or delayed per quarter	\$60,000 to \$160,000
Post-approval denied cycles per quarter	2 to 3
Post-approval denial exposure per quarter	\$40,000 to \$60,000
Combined quarterly exposure	\$100,000 to \$220,000
Combined annual exposure	\$400,000 to \$880,000
Permanently abandoned annually at 15-20%	\$60,000 to \$176,000

Large Community or Academic Oncology Center — 40 to 60 active patients per quarter

Metric	Enhertu
Front end PA denials per quarter at 15-25%	6 to 15 blocked
Revenue blocked or delayed per quarter	\$120,000 to \$300,000
Post-approval denied cycles per quarter	3 to 6
Post-approval denial exposure per quarter	\$60,000 to \$120,000
Combined quarterly exposure	\$180,000 to \$420,000
Combined annual exposure	\$720,000 to \$1,680,000
Permanently abandoned annually at 15-20%	\$108,000 to \$336,000

Regional Network Extrapolation — 30 Active Accounts Mixed Size

Drug	Combined Annual Network Exposure	Permanently Abandoned Annually
Enhertu	\$3,000,000 to \$8,000,000	\$450,000 to \$1,600,000

None of this appears in clearinghouse data. None in hub reports. None in field analytics.

- Front end PA denial population never creates a claim
- Post-approval denial population logged as denial code — stripped of dollar weight and authorization context
- Abandoned population logged as contractual adjustment — closed

THE REGIONAL PAYER RISK MAP

|> The automated systems generating these denial patterns operate identically regardless of geography. What changes by region is which payer's system generates the bulk of denial volume based on local market concentration.

Regional Risk Tier Table

Market	Primary Payers	Risk Level	Primary Denial Drivers
California	Anthem Blue Cross / Blue Shield CA	Critical	Companion diagnostic enforcement / California IMR pathway available
Texas	BCBS Texas HCSC / UHC / Aetna	Critical	HCSC Stage 1 to Stage 2 Availity pivot / front end PA lag on early stage
Northeast	Anthem Elevance / UHC / Aetna	High	Post-service AI chart scraping / endocrine sequencing lag / front end PA blocks on early stage
Midwest	BCBS Illinois HCSC / UHC / Humana	High	HCSC Availity portal black hole / multi-stage denial loop / Stage 1 CO-16 to Stage 2 CO-50
Southeast	Humana / BCBS Florida / UHC / Aetna	Moderate-High	CO-119 experimental on approved indications / Humana policy bulletin lag on May 2026 approvals
Mid-Atlantic	Highmark / Anthem / UHC / Aetna	Moderate-High	Authorization to claims disconnect
Northwest	Premiera / Regence / UHC	Moderate	Authorization to claims disconnect / CO-16 documentation denials / endocrine sequencing lag

National Overlay — UnitedHealthcare and Aetna

Both function as identical administrative layers across every region

- A practice in California and a practice in New York face the exact same automated J9358 quantity limit algorithms from both payers
- Adjudication systems nationally standardized — denial patterns consistent and predictable across every market

UHC — Primary denial patterns:

- Highest volume source of endocrine sequencing lag denials on Enhertu
- Policy bulletin not updated to reflect January 2025 indication expansion
- Every HR-positive HER2-low metastatic patient going from CDK4/6 failure directly to Enhertu at elevated denial risk — regardless of geography

Aetna — Primary denial patterns:

- Evicore authorization platform updates to current label criteria
- Aetna claims adjudication engine runs on separate bulletin
- Authorization approves — claim denies — consistent authorization to claims disconnect across every Aetna market nationally

Northeast and Mid-Atlantic — Anthem Elevance and Highmark

- Former Empire BCBS footprint now operates under Anthem Blue Cross and Anthem Blue Cross Blue Shield branding following Elevance Health transition
- Northeast now aligned with Anthem's nationally deployed **AI-assisted post-service chart scraping model**
- Chart documentation scraped after authorization approval — CO-50 denials generated post-service on claims that cleared authorization
- Portal correspondence contains specific clinical rationale — 835 shows generic remark
- Multi-stage denial loop consistent Anthem pattern across both Northeast and California
- Anthem UM portal generating front end PA rejections on Enhertu early stage indications at elevated rates
- Highmark — covering Western Pennsylvania, Delaware, West Virginia — documented source of authorization to claims disconnect denials in Mid-Atlantic market

Midwest and South Central — HCSC

- BCBS Illinois and BCBS Texas both run on Health Care Service Corporation engine
- HCSC is one of the most automated adjudication systems in the commercial market
- **Primary source of the multi-stage denial loop** across these markets

The HCSC pattern:

When an Enhertu claim hits BCBS Illinois or BCBS Texas the field team's authorization screen shows a clean approval. What neither the field team nor the clearinghouse can see is that the actual clinical barrier to payment was quietly routed to the Availity portal the moment the claim was submitted. The 835 shows an administrative CO-16. The Availity portal document contains the medical director's actual clinical position. The field team has no access to either. They see an authorization win. The practice is absorbing a denial the manufacturer doesn't know exists.

California — Anthem Blue Cross and Blue Shield of California

California is a unique market for two reasons — dual payer exposure and state statutory recovery pathways

Blue Shield of California:

- Independent regional plan — aggressive companion diagnostic documentation enforcement
- Auto-denying Enhertu claims under CO-96 when exact HER2 pathology report not manually attached
- Clinical coverage policy confirms coverage — fee schedule confirms no entry
- Two internal Blue Shield systems generating contradictory determinations on the same drug on the same claim

California statutory recovery pathways — not available in other states:

- California Health and Safety Code 1367.01 — licensed clinician involvement required in utilization review decisions
- California Health and Safety Code 1367.206 — step therapy exception criteria evaluation required before denial
- Both statutes create Independent Medical Review pathways bypassing standard appeal queue
- IMR overturn rates on properly documented cases run above 70% in California
- These pathways contribute to the **74%** contradiction-based recovery rate

Southeast — BCBS Florida and Humana

BCBS Florida:

- Historically updates newly activated HCPCS codes within 14 to 30 days of activation

Humana:

- Significant presence across Southeast and nationally through Medicare Advantage
- Generating CO-50 medical necessity denials and **CO-119 experimental designations** on Enhertu early stage indications
- Policy bulletin not updated to reflect May 2026 DESTINY-Breast11 and DESTINY-Breast05 approvals
- Front end UM portal generating PA rejections on early stage Enhertu indications simultaneously
- Both failure points running simultaneously at Humana-primary practices across Southeast markets

Northwest — Premera and Regence

- Premera Blue Cross — Washington and Alaska — running endocrine sequencing lag pattern on J9358 consistent with UHC nationally
- Regence — Oregon, Washington, Utah, Idaho — generating CO-16 documentation denials on Enhertu at elevated rates
- Both payers sources of front end PA rejections on 2026 indication expansions
- Both generating authorization to claims disconnect denials consistent with national pattern

THE PORTFOLIO IMPLICATION

\> The denial mechanisms documented in this report are structural outputs of how commercial payer adjudication systems are built. Every drug in an oncology portfolio is subject to the same failure modes.

Three mechanisms that apply across every drug in the portfolio:

- **Fee schedule lag** — runs on every newly activated HCPCS code — lag window runs 60 to 90 days on average across major commercial payers — every claim in that window potentially recoverable on the CO-45 contradiction argument within timely filing period
- **Indication expansion lag** — runs on every drug with a recently expanded label — UM platform updates, claims bulletin does not — authorization clears, claim denies — correspondence contains the contradiction
- **Front end PA denial rate** — runs on every drug where UM portals have not updated to reflect current labels — every newly approved indication creates a window during which valid PA requests are rejected before treatment begins

ENHERTU | J9358

The Two-Timeline Problem

|> Enhertu's denial landscape in 2026 is the accumulated result of two separate FDA expansion timelines generating two distinct denial waves simultaneously across both failure points.

The 2025 Legacy Mismatch:

- January 2025 approval eliminated prior cytotoxic chemotherapy requirement for HR-positive HER2-low and HER2-ultralow metastatic breast cancer
- CDK4/6 inhibitor failure became sufficient prior treatment line
- Many payer adjudication engines operate on **6 to 12 month** policy bulletin update lag
- Significant portion of 2026 claims systems still running pre-2025 rules requiring documented prior cytotoxic chemotherapy
- Front end — UM portals that updated clearing these patients at authorization
- Back end — claims adjudication system running pre-2025 bulletin denying same patient post-service
- **835 shows CO-50 — portal medical director letter explains actual clinical rationale — clearinghouse sees one, complete file shows both**

The 2026 Boundary Mismatch:

- May 2026 dual approval under DESTINY-Breast11 and DESTINY-Breast05 expanded Enhertu into early stage curative intent settings
- Strictly limited to true HER2-positive disease — IHC 3-plus or ISH positive
- HER2-low — IHC 1-plus or 2-plus with ISH negative — applies only in metastatic setting
- Front end — UM portals not updated to May 2026 approvals generating PA rejections on early stage indications before treatment begins
- Back end — claims systems generating CO-50 and CO-119 on claims that cleared authorization at updated UM portal
- **Two simultaneous denial populations across both failure points — different clinical triggers — same structural cause**

The 2026 Companion Diagnostic Dictionary Failure — IHC 0 vs HER2-Ultra-Low

This failure sits between the two timeline populations and generates denials that neither timeline's standard appeal pathway addresses correctly.

The mechanism:

The January 2025 approval created the HER2-ultra-low category for metastatic breast cancer — defined as IHC 0 with faint incomplete membrane staining. This is a clinically distinct population from IHC 0 negative. The distinction lives in the pathology narrative: the difference between “IHC 0 — no staining detected” and “IHC 0 — faint incomplete membrane staining detected in $\leq 10\%$ of tumor cells.” Both score as IHC 0 on the numeric scale. They are not the same clinical finding. The FDA label and NCCN guidelines recognize the distinction. Payer claims engines do not.

The failure point:

Payer backend claims adjudication systems use automated text-matching algorithms to parse laboratory results attached to or referenced in the claim file. These systems scan for IHC scoring values as discrete numeric fields. The text-matching dictionary is hardcoded to classify “IHC 0” as an absolute negative — no HER2 expression — which routes the claim into the non-HER2 pathway and triggers an automatic CO-50 medical necessity denial or line-of-therapy violation.

The system is structurally blind to the qualifier string. “IHC 0 with faint incomplete membrane staining” enters the text-matching engine. The engine reads “IHC 0.” The qualifier “with faint incomplete membrane staining” is not in the dictionary. It is not parsed. It is not evaluated. The system classifies the patient as HER2-negative and denies the claim.

The UM authorization portal evaluates these patients differently. The authorization system accepts the pathology narrative as a clinical document. A human reviewer or a more sophisticated clinical rules engine reads the full pathology description, recognizes the ultra-low designation, and approves the prior authorization under the January 2025 expanded indication. The authorization clears. The claims engine then receives the same patient's claim. It does not read the pathology narrative. It reads the IHC score field. It sees IHC 0. It denies.

What the correspondence shows:

- UM authorization: Approved — HER2-ultra-low metastatic indication — January 2025 pathway cleared
- Claims remittance: CO-50 — Medical necessity not established — HER2 expression does not meet threshold for Enhertu
- Portal correspondence or medical director letter: “Patient pathology reflects IHC 0 scoring. HER2 expression level does not support administration of trastuzumab deruxtecan under current coverage criteria.”

The medical director letter references IHC 0 as though it is dispositive. It does not reference ultra-low. It does not reference faint membrane staining. It does not reference the January 2025 label expansion that created the category. The denial is generated by the same dictionary limitation that generated the automated flag — the human reviewer is reading the system’s output, not the pathology report.

Documented Contradiction:

UM authorization	Approved — HER2-ultra-low — faint membrane staining documented — January 2025 indication cleared
Claims remittance and portal correspondence — same patient	CO-50 — IHC 0 does not meet HER2 expression threshold — medical necessity not established

- Authorization system evaluated the full pathology narrative and approved
- Claims engine evaluated the numeric IHC score field and denied
- **The authorization is the payer’s own documentation that this patient qualifies. The denial contradicts it on the basis of a text-matching limitation in the payer’s own claims software.**

Why this matters for Enhertu specifically:

The HER2-ultra-low population is the fastest-growing segment of Enhertu’s metastatic prescribing base. Every patient in this population scores IHC 0 on the numeric field. This denial population does not appear correctly in any aggregate data source — it looks like a clinically appropriate denial. It is not. It is a text-parsing limitation denying a patient who was approved under the correct indication by the same payer’s own authorization system.

The Denial Landscape

Denial Category	Primary Codes	Root Cause	Failure Points
HER2 boundary conflict — early stage	CO-50 / CO-119	May 2026 IHC threshold enforcement	Front end PA and post-approval
Companion diagnostic dictionary failure — HER2-ultra-low	CO-50	IHC 0 text-matching limitation in claims engine — blind to ultra-low qualifier	Primarily post-approval
Endocrine sequencing lag — metastatic	CO-50	January 2025 policy bulletin lag	Primarily post-approval
Billed units vs authorized quantity — multi-vial rounding	CO-50 / CO-197	Weight-based dosing variability, vial rounding, and full-line rejection logic	Post-approval
JW/JZ modifier compliance	CO-16	Single dose vial waste documentation failure	Post-approval — frequently Stage 1 of multi-stage loop
Missing molecular pathology report	CO-16 / M28	Raw pathology source document required	Front end PA and post-approval
LVEF monitoring gap	CO-50	Cardiotoxicity compliance audit	Post-approval — frequently Stage 3 of multi-stage loop

The multi-stage denial loop runs across all seven categories. A claim beginning as CO-16 becomes CO-50 after correction and becomes a safety monitoring hold on the next cycle. Clearinghouse logs three separate transactions. Complete file shows one coordinated sequential barrier.

Pattern One — Early Stage HER2 Boundary Conflict

Code: CO-50 / CO-119 — Front end PA and post-approval

The mechanism:

- Automated claims software issues CO-50 or CO-119 when early stage claim submitted without confirmed true HER2-positive documentation or when pathology reflects HER2-low scoring
- System enforces binary boundary without clinical review — IHC 3-plus or ISH positive clears — anything below in early stage context denies
- Front end — UM portals not updated to May 2026 approvals generating PA rejections
- Back end — claims system generating same denial on claims that cleared at updated UM portal

What the correspondence shows:

- 835 shows CO-50 with N522 or CO-119 with generic remark
- Portal correspondence contains medical director letter specifying patient's HER2-low pathology score does not meet IHC 3-plus threshold
- **Clinical specificity of actual rationale is in portal document — clearinghouse only sees the code**

Documented Contradictions — Pattern One

Contradiction-based escalation on this denial class achieves approximately 74% recovery

Contradiction 1 — UM authorization approving early stage indication vs CO-50 or CO-119 denial

Carelon or Eviti authorization	Early stage HER2-positive indication approved — DESTINY-Breast11 or DESTINY-Breast05 pathway cleared
Claims remittance and portal correspondence — same patient	CO-50 or CO-119 — Medical necessity not established / Experimental investigational

- UM vendor updated to reflect May 2026 approvals — claims bulletin did not
- Authorization cleared patient under current label — denial applies pre-approval criteria
- **Both from same payer. They cannot coexist.**

Contradiction 2 — CO-119 experimental on FDA approved indication

FDA approval May 2026	Enhertu approved neoadjuvant and adjuvant early stage HER2-positive breast cancer
Payer remittance — same indication	CO-119 — Experimental / investigational

- CO-119 on FDA approved indication is automated output of policy bulletin that has not been updated
- **Not a clinical determination**

Contradiction 3 — N522 duplicate remark on new indication claim

Remittance remark N522	Duplicate of a claim processed or being processed
Claim record	New indication — new clinical pathway — no prior identical claim

- Adjudication engine flagging early stage claim as duplicate of prior metastatic claim for same drug on same patient
- System cannot distinguish between indication pathways
- **The claims are not duplicates**

Pattern Two — Metastatic Endocrine Sequencing Lag

Code: CO-50 — Primarily post-approval

This is the highest volume authorization to claims contradiction on J9358 in 2026

The mechanism:

- Claims adjudication engines running on pre-2025 bulletins still requiring documented prior cytotoxic chemotherapy
- Patient record shows CDK4/6 inhibitor or endocrine failure without prior chemo line — engine flags line of therapy violation — CO-50 fires automatically
- UM authorization issued under updated 2025 criteria — claims engine running on criteria that predate those criteria by at least a year

What the correspondence shows:

- 835 shows CO-50 with generic remark
- Medical director correspondence names actual clinical rationale
- **Both required to build the contradiction argument — neither alone is sufficient — clearinghouse sees one — complete file shows both**

Documented Contradictions — Pattern Two

Contradiction-based escalation on this denial class achieves approximately 74% recovery

Contradiction 1 — Authorization under 2025 endocrine failure criteria vs CO-50 under pre-2025 chemotherapy requirement

Carelon or Eviti authorization	HR-positive HER2-low metastatic — endocrine failure pathway approved — no prior chemo required
Claims remittance and portal medical director letter — same patient	CO-50 — Medical necessity not established — prior cytotoxic chemotherapy not documented

- Authorization reflects current criteria
- Portal correspondence names actual clinical rationale the 835 does not show
- Authorization is direct documentation correct updated pathway was evaluated and patient cleared
- Claims denial applies superseded criteria
- **Both from same payer. Neither alone tells the full story.**

Contradiction 2 — CO-50 line of therapy denial on NCCN Category 1 indication

NCCN guidelines 2025 onward	Enhertu HR-positive HER2-low metastatic after endocrine failure — Category 1 recommendation
Payer remittance and portal correspondence	CO-50 — Does not meet medical necessity criteria — line of therapy violation

- CO-50 on NCCN Category 1 indication is not a defensible clinical position
- Payer's own UM platform recognized the designation and approved the treatment
- **Claims system applied pre-2025 criteria against post-2025 Category 1 approved pathway**

Pattern Three — Billed Units vs Authorized Quantity — The Multi-Vial Rounding Rejection

Code: CO-50 / CO-197 — Post-approval

The mechanism:

- J9358 billed at one unit equals one milligram
- Dosing weight-based — 5.4 mg/kg breast cancer indications — 6.4 mg/kg select GI and lung indications
- PA approved based on baseline weight at submission
- Enhertu distributed in single dose 100 mg vials — clinic must round to the nearest full vial
- Patient weight gain between PA and administration, or clinic rounding to nearest full vial per

institutional safety protocol, causes billed units to exceed authorized quantity ceiling

The multi-vial math error:

A 70 kg patient authorized at 5.4 mg/kg requires 378 mg per cycle. The practice opens four 100 mg vials — 400 mg total. Administers 378 mg. Discards 22 mg under JW modifier. Claims engine authorized 378 units. Practice billed 400 units (administered) plus 22 units (waste on JW line). Total units on claim: 422. Authorized ceiling: 378.

The same patient gains 2 kg between PA submission and cycle 3 administration. New weight: 72 kg. New dose: 388.8 mg. Practice rounds to 400 mg — four vials. Authorized ceiling has not been updated. The claim now exceeds the authorized quantity by 22 mg on the administered line alone before the waste line is even calculated.

The rejection logic:

The payer's claims engine does not pay up to the authorized ceiling and deny the excess. It rejects the entire claim line. The full \$20,000+ cycle is denied — not the \$200 overage. The system treats a 22 mg variance on a 400 mg administration as grounds to freeze the entire claim value.

The denial does not distinguish between clinical overuse and administrative rounding variance. A \$20,000 claim denied over a rounding difference that reflects standard pharmacy practice.

Documented Contradictions — Pattern Three

Contradiction 1 — Authorization approving Enhertu for this patient vs CO-50 or CO-197 on quantity grounds

UM authorization	Enhertu approved for this patient at this indication
Claims remittance	CO-50 or CO-197 — Billed units exceed authorized quantity

- Authorization approved the drug — denial does not challenge clinical appropriateness
- Authorization is a clinical approval — quantity discrepancy is an administrative calculation mismatch
- **Resolvable through amendment or reauthorization — not a medical necessity denial on a clinically approved drug**

Contradiction 2 — Prior cycle payment at identical or higher unit count vs CO-197 on subsequent cycle

Remittance records prior cycles — same authorization	Paid — 400 units — no quantity flag triggered
Remittance current cycle — same authorization, same or lower unit count	CO-197 — Billed units exceed authorized quantity

- Payer paid identical unit count on prior cycles without triggering quantity limit
- Same unit count on subsequent cycle denied
- **Inconsistent enforcement of quantity ceiling across cycles under same authorization is adjudication inconsistency — prior payment is the contradiction**

Pattern Four — JW/JZ Modifier and Vial Wastage Compliance

Code: CO-16 — Post-approval — frequently Stage 1 of multi-stage loop

The mechanism:

- Enhertu distributed in single dose **100 mg vials**
- Discarded drug — administered amount on one claim line — discarded remainder on second line with **JW modifier**
- Zero waste — claim line must include **JZ modifier** confirming zero waste
- Incorrect modifier, absent modifier, or incorrect unit math between administered and waste lines — CO-16 or automated claim kick-out

What Third Rail Intelligence consistently sees in these files:

- Modifier compliance failure is frequently **Stage 1 of the multi-stage denial loop**
- CO-16 correction leads to CO-50 on resubmission
- **The modifier issue was not the real barrier — it was the first gate in a sequential denial sequence**

Pattern Five — Missing Molecular Pathology Report

Code: CO-16 / M28 — Front end PA and post-approval

The mechanism:

- Payers require original diagnostic pathology report confirming:
 - IHC membrane staining scores with specific percentage values
 - FISH or ISH gene amplification ratios at ratio ≥ 2.0 or gene copy number ≥ 6.0
- Clinical summary note does not satisfy the requirement
- CO-16 fires when raw source document absent — generates both front end PA rejections and post-approval claim denials
- For first cycle new patients — documentation path — raw pathology source report must be in submission
- **Contradiction surfaces mid-cycle**

Documented Contradictions — Pattern Five

Contradiction 1 — Prior cycle payment under identical documentation vs CO-16 on later cycle

Remittance records cycles 1 through 3 — same authorization

Paid — no pathology documentation flag triggered

Remittance cycle 4 or later — same authorization, same documentation

CO-16 — Claim lacks information — raw pathology report absent

- Documentation sufficient for cycles one through three cannot be insufficient for cycle four without identified change in what was submitted or required
- Prior payment record is the contradiction
- **Inconsistent enforcement of documentation standard across cycles under same authorization is adjudication inconsistency payer is required to explain**
- Mid-cycle CO-16 frequently becomes **Stage 1 of the multi-stage loop** — documentation correction leads to different denial rationale on resubmission

Pattern Six — LVEF Monitoring Compliance

Code: CO-50 — Post-approval — frequently Stage 3 of multi-stage loop

The mechanism:

- Multi-cycle reauthorizations beyond **3 to 6 months** of active therapy require documented cardiac safety monitoring
- Specific LVEF thresholds vary by payer policy
- Documented decline or failure to submit current monitoring results within required window triggers denial

- **This pattern frequently appears as Stage 3 of the multi-stage denial loop — earlier stages resolved — safety monitoring hold is the final barrier**

Documented Contradictions — Pattern Six

Contradiction 1 — Reauthorization approved after monitoring window closed vs CO-50 citing absent monitoring

UM reauthorization for the denied cycle Approved — no cardiac monitoring flag at reauthorization

Claims remittance	CO-50 — Documentation does not support continuation — cardiac monitoring absent or not current
-------------------	--

- Cardiac monitoring status was a barrier to continuation — reauthorization system should have flagged it before approving
- It did not — reauthorization cleared the patient
- Claims system applied requirement the authorization system did not invoke
- **Both from same payer. Both in the correspondence.**

Contradiction 2 — Cardiac monitoring performed and charted vs CO-50 citing absent monitoring

Clinical record and EHR Echocardiogram or MUGA scan performed within required window — documented in chart

Claims remittance	CO-50 — Cardiac monitoring not documented — documentation does not support continuation
-------------------	---

- Monitoring was performed — record contains it — denial states it is absent
- **This is a submission gap not a clinical gap. The documentation exists. The denial does not reflect the actual clinical record.**

The Structural Problem

> Every denial pattern in this report is the same structural failure expressed through different clinical content.

The core failure:

- Payer organizations operate multiple internal systems that do not communicate in real time
- Authorization system and claims system run on different update cycles with different data sources and different decision criteria
- When those systems produce contradictory outputs the financial consequence lands on the practice

Why standard appeals fail:

- Billing teams read documents individually and respond to them
- Reading CO-50 — argue clinical necessity
- Reading CO-96 — argue coverage
- Neither argument addresses the actual problem
- The actual problem is in the relationship between what one payer document says and what another payer document says about the same claim

What the complete correspondence record consistently shows:

- Authorization approved days before claims engine denied same patient as non-contracted
- Reauthorization issued with no cardiac monitoring flag while claims denial cites absent monitoring
- Internal portal correspondence confirming fee schedule gap while uphold letter cites contracting deficiency
- Medical director letter naming specific clinical rationale while 835 shows only generic remark code

None of these require new clinical documentation to argue. They require reading the complete record as a system.

REVENUE CLAWBACK HORIZON — TIMELY FILING THRESHOLDS

The 50% to 60% of Enhertu denials that are silently written off by practices are not permanently lost. They are sitting in clinic billing archives inside active timely filing windows. The contradiction arguments documented in this report apply retroactively to every claim within that window.

The Filing Windows

Payer Category	Typical Timely Filing Window from Original ERA	Notes
Commercial — Anthem / Elevance	90 to 180 days from ERA date	Varies by state and contract — California provider agreements typically 180 days
Commercial — UnitedHealthcare	90 to 120 days from ERA date	Standard commercial contract — Medicare Advantage contracts may differ
Commercial — Aetna / CVS Health	90 to 120 days from ERA date	Evicore authorization platform — claims engine on separate bulletin — both timelines apply
Commercial — HCSC (BCBS IL / BCBS TX)	120 to 180 days from ERA date	Availity portal correspondence must be included in contradiction filing
Commercial — Humana	90 to 180 days from ERA date	Medicare Advantage timely filing may follow CMS 365-day standard
Commercial — Blue Shield of California	180 days from ERA date	California statutory pathways extend effective recovery window through IMR
Commercial — Highmark	90 to 120 days from ERA date	Mid-Atlantic contracts — varies by plan
Medicare Advantage — all payers	365 days from date of service per CMS regulation	Federal standard overrides commercial contract terms on MA plans
California IMR pathway	No strict timely filing limitation once CDI complaint accepted	IMR process runs on regulatory timeline independent of commercial contract filing

What This Means

Every Enhertu denial written off by a practice in 2026 that falls within these windows is potentially recoverable using the contradiction arguments documented in this report. The claims are not expired. The billing system logged them as closed. The correspondence file still contains the contradictions. The payer's own documents still say opposite things about the same claim.

The scale of the opportunity:

- 50% to 60% of post-approval Enhertu denials are written off without appeal
- At a mid-size practice administering Enhertu to 20 to 30 patients per quarter that represents \$60,000 to \$176,000 in permanently abandoned claims annually — per practice
- Across a 30-account regional network that represents \$450,000 to \$1,600,000 in abandoned claims annually
- A significant portion of those claims are still inside timely filing windows right now
- The contradiction arguments do not require new clinical documentation — they require reading what the payer already wrote

For practices:

Your write-off queue contains claims with active timely filing windows and documented contradictions in the payer's own correspondence. The billing system closed them. The filing window has not.

For market access teams:

The write-off population is invisible in every data source between the manufacturer and the practice. It does not appear in hub data. It does not appear in clearinghouse reports. It does not appear in field analytics. It appears as unexplained volume decline in accounts with specific payer concentrations. The claims are sitting in practice archives. The contradictions are documented. The filing windows are open. A forensic retrospective review of the correspondence record across your prescriber base identifies which claims are recoverable, which practices are carrying the exposure, and what the aggregate recovery opportunity looks like by region and by payer.

That is what a Veriscope regional intelligence engagement produces.

For Oncology Practices

- Recognizing these denial patterns in your write-off queue?
- The claims may not be as closed as your billing system indicates
- The argument to recover them does not require new clinical documentation in most cases
- It requires reading what the payer already wrote and finding where it contradicts itself
- Third Rail Intelligence will review your claim correspondence at no cost
- Findings delivered regardless of whether you engage for recovery work
- Nothing is owed unless money is actually returned

For Market Access Teams

- The denial patterns in this report are what is happening to your drug at the adjudication level after your hub confirms the authorization
- Front end PA denial rate and post-approval claim denial rate together represent a combined access and revenue failure your clearinghouse data, hub reports, and field analytics were not built to detect
- **Clearinghouse data shows what payers reported. It does not show what payers wrote.**
- The portal correspondence, medical director letters, internal inquiry responses — that is where the true picture lives
- A complete adjudication correspondence analysis can be produced for Enhertu across any region
- Output maps payer behavior at the claim level in the payer's own language across every correspondence channel
- Identifies where that behavior is creating access failures and ordering friction your current data cannot explain
- **Enhertu is the documented example. Your full portfolio is the scope.**