A Pharmacy Directed, Biosimilar Flexible Formulary Model Reduces Costs & Increases Reimbursement

Nathan Hartwell PharmD MPH BCOP

Assistant Director of Pharmacy – Infusion and Prior Authorization Services

Lahey Hospital & Medical Center

Beth Israel Lahey Health

Disclosures

- The presenter has no real or perceived conflicts of interest related to this presentation

Note: This program may contain the mention of suppliers, brands, products, services or drugs presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand, product, service or drug.

Learning Objectives

At the end of this session, participants should be able to:

1. Explain the evolution of the biologic and biosimilar market over the past 5 years
2. Identify factors that contribute to the complexity of the current commercial and government payor landscape
3. Describe actionable, pharmacy-driven, interdisciplinary initiatives to reduce costs and maximize reimbursement for high cost medications

Key Definitions: Biologic vs. Bio -“better” vs. Biosimilar

Biologic: A diverse category of large, complex molecules produced through biotechnology in a living system and more difficult to characterize than small molecule drugs

- Section 351(a) of the Public Health Services Act (PHSA- 1998)
- Manufacturers must submit a biologic license application (BLA) to the FDA, vs. traditional new drug application used for small molecules

Bio- “Better”: New versions of existing biologic agents that are engineered to have key differences from the originally licensed product to extend patent life/ market share

- Manufacturers also must submit a biologic license application (BLA) to the FDA

Biosimilar: biological product that it is highly similar to an already approved reference product, and that there are no clinically meaningful differences between the biologic product and the reference product in terms of safety, purity, and potency of the product

- Biologics Price Competition and Innovation Act (BPCIA -2010) as part of the Patient Protection and Affordable Care Act (ACA) established an abbreviated licensure pathway for biosimilars
- Biosimilarity is demonstrated based on the totality of the evidence across all evaluations, with each step being supported by the preceding one of the process.

US FDA. Scientific Considerations in Demonstrating Biosimilarity to a Reference Product Guidance for Industry Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Quality Considerations in Demonstrating Biosimilarity of a Therapeutic P; Guidance for Industry; FDA: Rockville, MD, USA, 2015.

Abbreviated Biosimilar Review & Approval Pathway

In order to reach the market efficiently and to avoid patent infringement Biosimilar manufacturers must reverse-engineer the original molecule and establish different processes for development.

Biosimilar manufacturers reduce costs by generally being able to avoid expensive clinical trials and instead rely on the FDA's previous determination of safety and effectiveness for the reference product.

Biosimilar evaluations are focused primarily on analytical in-vitro analysis including:

- head-to-head comparative studies for structural characterization
- functional in vitro assays
- pharmacokinetic and pharmacodynamic evaluations
- safety, efficacy and immunogenicity assessments

US FDA. Biosimilar Development, Review, and Approval; FDA: Rockville, MD, USA, 2017.

Key Definitions Continued….

Extrapolation: If the total evidence in the biosimilar application supports a demonstration of biosimilarity for at least one of the reference product's indications, then it is possible for the biosimilar manufacturer to use data and information to scientifically justify approval for other indications that were not directly studied by the biosimilar manufacturer.

Interchangeability: Biologics/biosimilar can substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

Therapeutic Substitution: The replacement of the originally-prescribed drug with an alternative molecule with assumed equivalent **therapeutic** effect. The alternative drug may be within the same class or from another class with assumed **therapeutic** equivalence.

Non-medical switching: Change of medication for reasons other than a patient's health & safety

US FDA. Considerations in Demonstrating Interchangeability with a Reference Product Guidance for Industry; FDA: Rockville, MD, USA, 2019. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-guidance-industry (accessed on 9 June 2021).

Johnston A, Asmar R, Dahlöf B, et al. Generic and therapeutic substitution: a viewpoint on achieving best practice in Europe. *Br J Clin Pharmacol*. 2011;72(5):727-730. doi:10.1111/j.1365-2125.2011.03987.

Liu Y, Yang M, Garg V, Wu EQ, Wang J, Skup M. Economic Impact of Non-Medical Switching from Originator Biologics to Biosimilars: A Systematic Literature Review. Adv Ther. 2019 Aug;36(8):1851-1877. doi: 10.1007/s12325-019-00998-3. Epub 2019 Jun 5. PMID: 31168766; PMCID: PMC6822838.

The Evolution of the Biosimilar Marketplace in the United States 2010–2021

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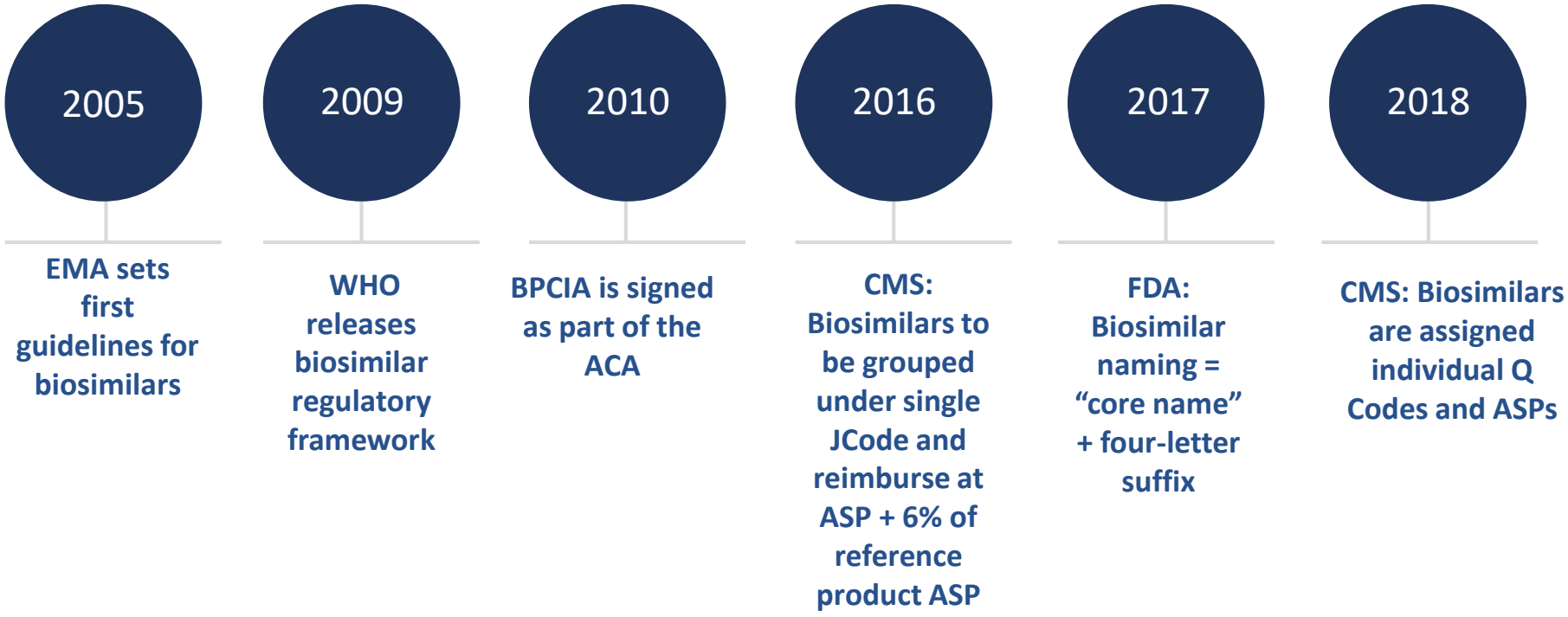
Current State of the United States Biologics Market

- An increasing number of novel biologics, “bio-betters” and biosimilars are entering the U.S. pharmaceutical market each year
  - 22 new biologics approved by the FDA in 2020
  - 29 biosimilars corresponding w/ 9 reference biologics are now approved
- Government and commercial payment structure for biologics has undergone rapid and transformative change over the past decade and will continue to evolve as the biologic and biosimilar market matures
- Through rebate and other contractual agreement Commercial payors are negotiating directly with manufacturers and establishing aggressive formulary policies that require the use of certain biologics/biosimilars over others and in some cases forcing the non-medical switching between products
- In order to control medication expenditures and increase revenue integrity hospitals, health systems, ambulatory infusion centers and physician offices must identify and implement strategies to keep pace with rapidly evolving market

Mehr S. Biosimilar Report: Where the US Biosimilars Market is Headed and When it Might Get There. 2021 Edition. Copyright 2013-2021 by SM Health. Accessed 06 June 2021

Biosimilar Regulatory Milestones



Kabir ER, Moreino SS, Sharif Siam MK. The Breakthrough of Biosimilars: A Twist in the Narrative of Biological Therapy. Biomolecules. 2019 Aug 24;9(9):410. doi: 10.3390/biom9090410. PMID: 31450637; PMCID: PMC6770099.

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Medicare Part B Reimbursement of Biosimilars…… Take 1

The 2016 Physician Fee Schedule Final Rule for Part B Biosimilar Reimbursement:

- Similar to the ASP calculation for multiple source drugs CMS will group biosimilar products that rely on a common reference product's biologics license application into the same payment calculation, and these products will share a common payment limit and HCPCS code.

- Differences from other multiple source drug reimbursement:
  - Claims for separately paid biosimilar biological products are required to include a modifier that identifies the manufacturer of the specific product.
  - Reimbursement = ASP of All Biosimilars w/ a Common Reference **+ 6 % of the Reference ASP.**
  - Example of shared HCPCS Code: Q5102 -Inflectra (Pfizer) and Renflexis (Merck- Bioepsis)

- CMS would have the ability to create one or more separate HCPCS codes "should a program need to do so arise."

Medicare Program; Revisions to Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B for CY 2016. Vol. 80, No. 220. p. 71096-99, November 16, 2015.

Medicare Part B Reimbursement of Biosimilars…Take 2

- Majority of commenters on the 2016 rule including biosimilar manufacturers and market observers opposed a single payment amount for all biosimilars that rely on a common reference product.

- Critics of the 2016 CMS single HCPCS proposal:
  - Innovation and product development will be harmed
  - Increased risk of 'death spiral' in pricing
  - Inconsistent with the statute

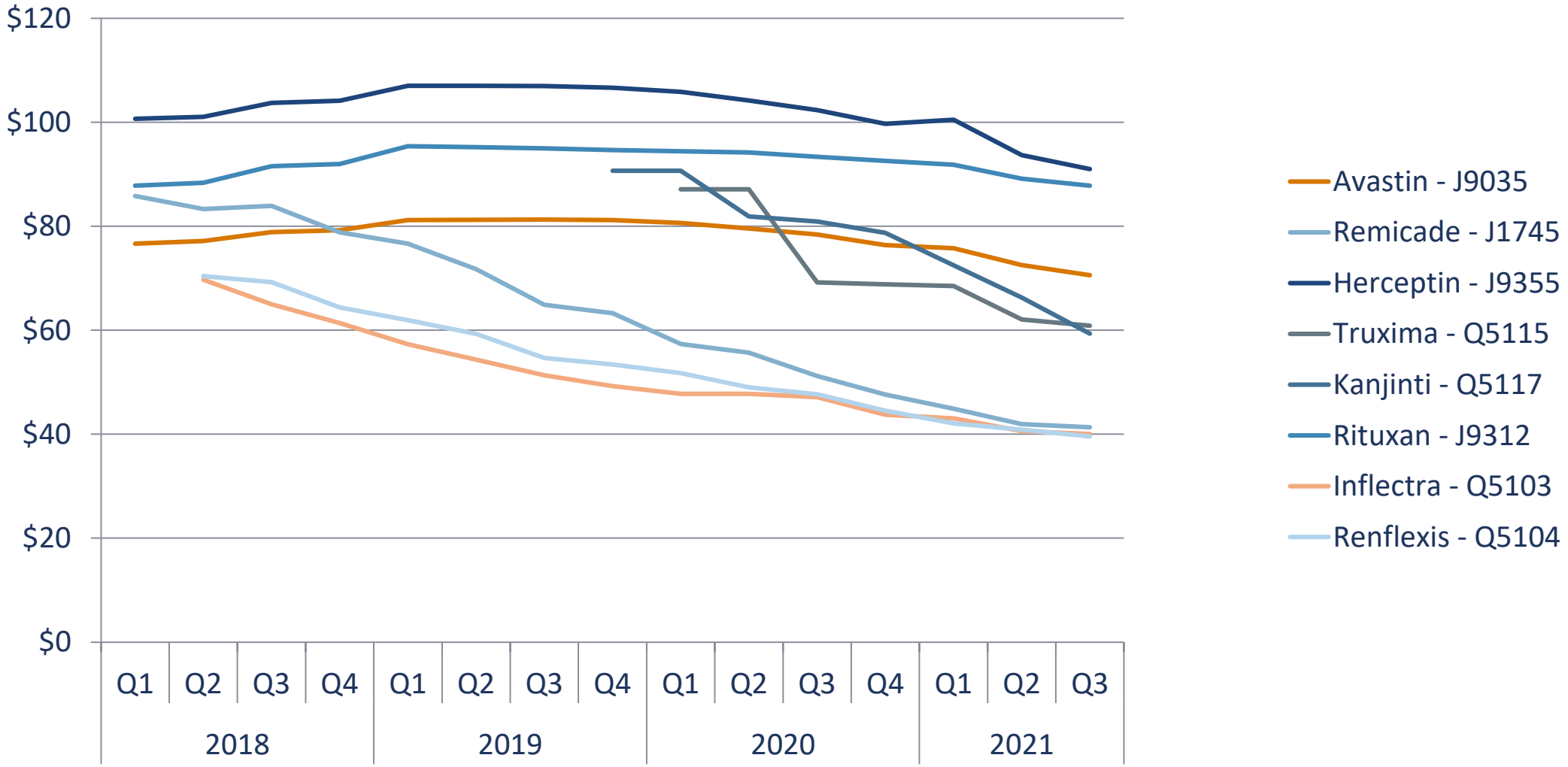
- Following pressure from stakeholders and revised estimates on savings to Medicare to exceed $65 billion vs. $50 billion under the original rule CMS was …..

  "persuaded that that there is a program need for assigning Part B biosimilar biological products into separate HCPCS codes, specifically that this policy change will address concerns about a stronger marketplace, access to these drugs in the United States marketplace, provider and patient choice and competition……that the change in policy will encourage innovation needed to bring more products to the market"

Medicare Program; Revisions to Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B for CY 2018. Vol. 82 No. 219. p53182- November 15, 2017

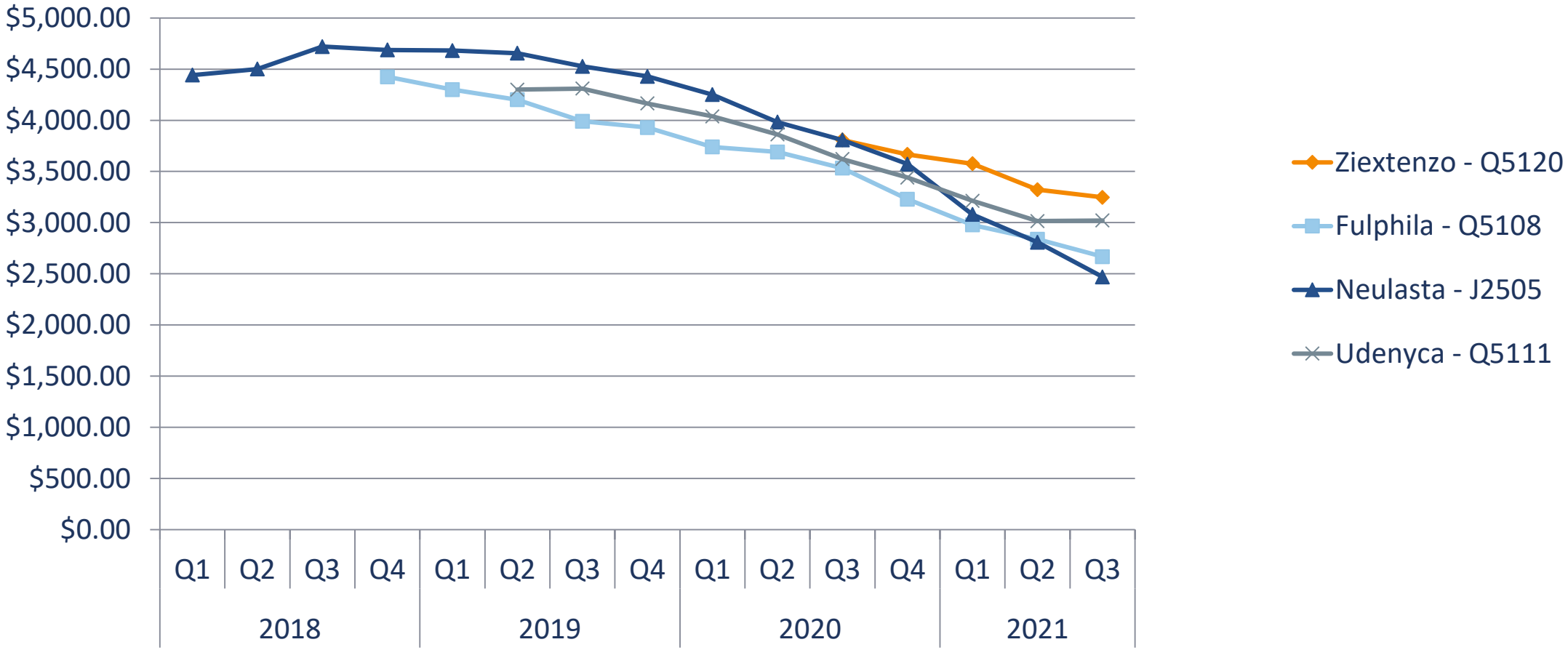
Biosimilar & Reference Average Sales Price (ASP)

2018 - 2021 (per 10 mg Billing Unit)



Pegfilgrastim Reference & Biosimilars

2018 - 2021 (per 6mg syringe)



Examples of Commercial Payor Biosimilar Formulary Policies

Standard Formulary	
Drug	Formulary Status
Aranesp®*^ (darbepoetin alfa)	Not Covered
Epogen®*^ (erythropoietin)	Not Covered
Procrit®*^ (erythropoietin)	Not Covered
Retacrit™ (epoetin alfa-epbx)	PA Required

Blue Cross Blue Shield of Massachusetts. Pharmacy Medical Policy Erythropoietin, Recombinant Human. #262 5.01.04; updated 7/2019

We may cover Neulasta® (pegfilgrastim) or **Neulasta® Onpro®** when the patient has tried **AND** failed two preferred pegfilgrastim biosimilar (Fulphila®, Udenyca™) **AND** one of the below criteria is met:

- Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (The Biosimilars are not approved for this indication and therefore would not be required)

We do not cover **Neulasta®** or **Neulasta Onpro** for other conditions not listed above unless listed in Policy 105 and reviewed through the appropriate process.

Blue Cross Blue Shield of Massachusetts. Pharmacy Medical Policy Supportive Care Treatments for Patients with Cancer. #105 updated 07/2021

UnitedHealthcare commercial plans

Medication	Category	Innovator brand(s)	Biosimilar brand(s)	Administration method	Preferred product*
Filgrastim	Cancer support	Neupogen Granix®	Nivestym Zarxio	Physician administered or self-injected	**Zarxio** Preferred product for both the pharmacy and medical benefits
Pegfilgrastim	Cancer support	Neulasta	Fulphila Nyvepria Udenyca Ziextenzo	Physician administered or self-injected	**Neulasta** and **Ziextenzo** Preferred products for both the pharmacy and medical benefits
Infliximab	Inflammatory conditions	Remicade	Avsola Inflectra Renflexis	Physician administered	**Avsola** and **Inflectra,** Preferred products for the medical benefit
Epoetin alfa	Anemia	Epogen Procrit	Retacrit	Physician administered or self-injected	**Retacrit** Preferred product for both the pharmacy and medical benefits
Bevacizumab	Cancer	Avastin	Mvasi Zirabev	Physician administered	**Mvasi** Preferred product for the medical benefit
Trastuzumab	Cancer	Herceptin	Herzuma Kanjinti Ogivri Ontruzant Trazimera	Physician administered	**Kanjinti** and **Trazimera** Preferred product for the medical benefit
Rituximab	Cancer	Rituxan	Riabni Ruxience Truxima	Physician administered	**Ruxience** and **Truxima** Preferred products for the medical benefit

United Health Care. Biosimilars Frequently asked Questions. 2021 https://www.uhcprovider.com/content/dam/provider/docs/public/resources/pharmacy/FAQ-Addendum-Biosimilars.pdf

Future State of the United States Biologics Market

With four or more biosimilars available for a particular reference product, discounts and rebates may increase quickly, perhaps reaching 50% or more within two or three years of all competitors entering the market

Increased competition from bio- “betters” and other innovative products that target the same indications will also continue to drive price, which could bolster or hurt the biosimilar

Reference Biologic and Biosimilar manufacturers may bundle sales across therapeutic areas in order to protect or grow market shares of their portfolio

“The pricing of biosimilars may not always be rational ….with developers opting to low-ball their prices to capture market share adding additional volatility for formulary decision makers“

- Mehr S. Biosimilar Report: Where the US Biosimilars Market is Headed and When it Might Get There. 2021 Edition. Copyright 2013-2021 by SM Health. Accessed 06 June 2021

Biosimilar Formulary Management

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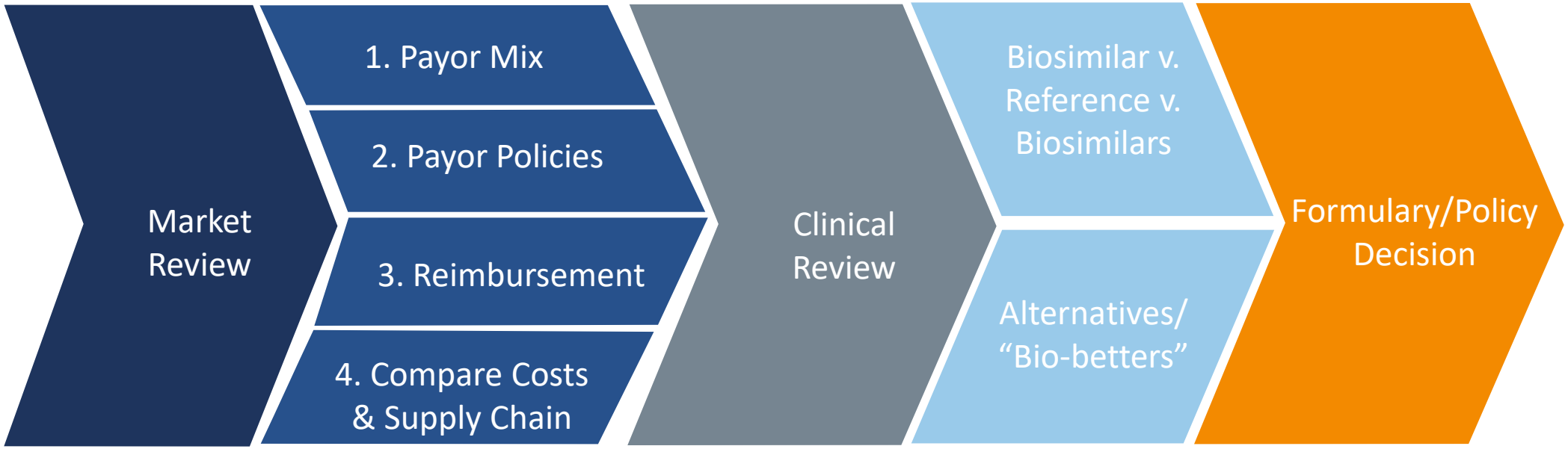
Developing Formulary Recommendations for Biosimilars



Market Review Process

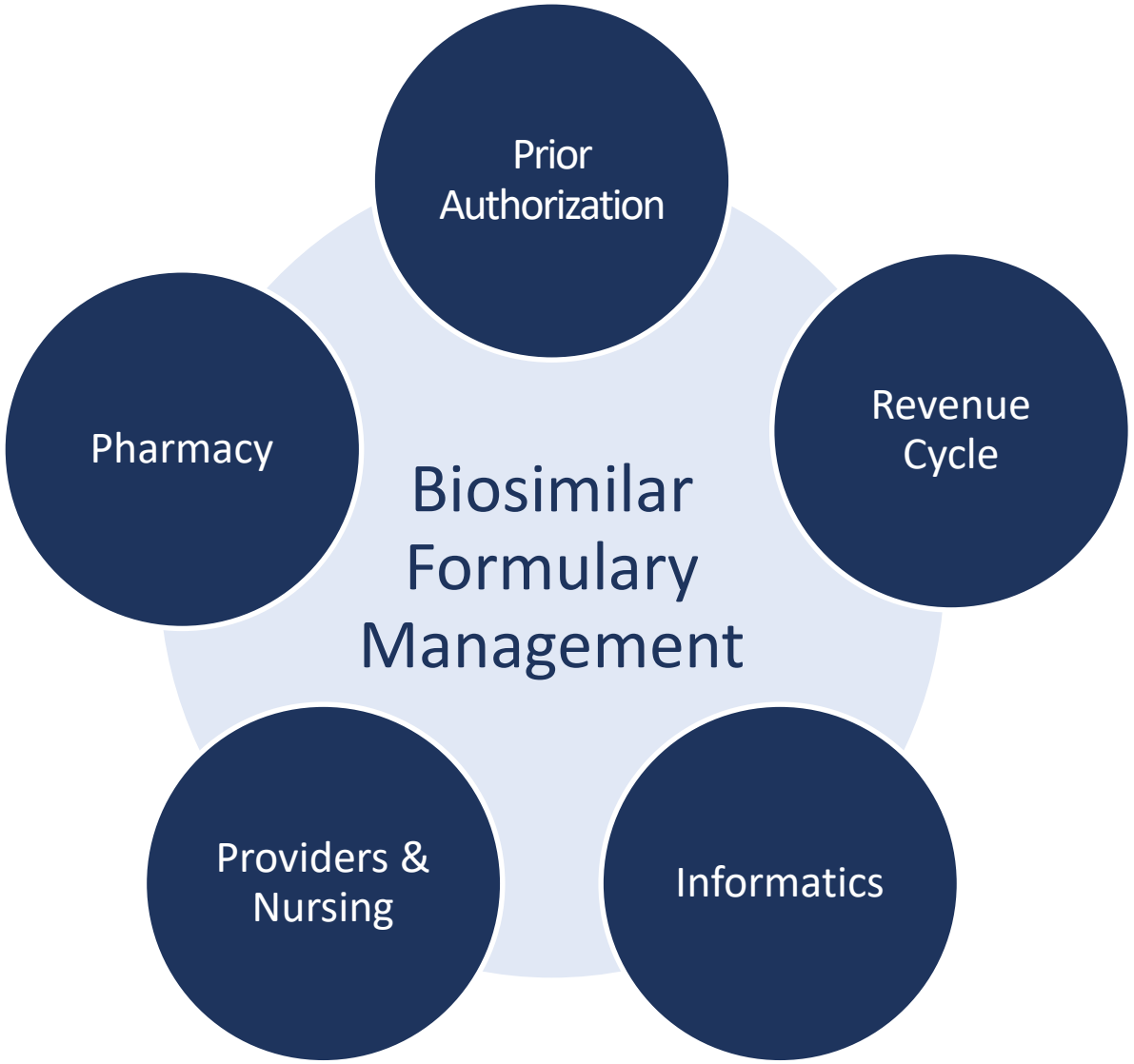
1. Establish % of Commercial vs. Government Payors
2. Identify commercial payors that require:
   - Reference vs. Biosimilar vs. Parity
   - Alternative sites of care: Home Infusion, Physician Licensed Practices vs. Hospital
   - Pharmacy vs. medical benefit coverage (i.e. White Bagging Requirements)
3. Review **CMS.gov ASP Drug Pricing Files** to determine Part B reimbursement
4. Determine the rate of reimbursement from commercial payers
   - Identify outliers – PAPE Rates*?
   - Understand contract terms and drug reimbursement
   - Monitor the pipeline through GPO or local manufacturer representatives
5. Compare costs & Supply – GPO v 340b, contracts, preferred tiers and rebate opportunities, international v. domestic production, wholesaler availability etc

*PAPE: Payment Amount per Episode

Clinical Review Process

- Formulary Review should include-
  - Head-to-head phase III clinical trials between reference and biosimilar (If completed)
  - Extrapolated Indications
  - National Compendia and Guidelines
  - Immunogenicity data (if completed)
  - Interchangeability data (if available)
  - “Switching” data – key factor if payors force non-medical switching or to help inform hospital / office decisions around non-medical switching policies
- Non-biosimilar alternatives or Bio- “betters”:
  - Delivery methods – Neulasta On Body Injector
  - Routes – Herceptin SC, Rituxan SC, Remicade SC (undergoing Phase III evaluation)
  - Formulations – Humira vs. Humira -Citrate Free
  - Competitors with alternative/novel MOA’s – Stelara , Entyvio vs. infliximab(s)

Biosimilar Formulary Management Stakeholders



Additional Stakeholders

- Quality and Safety
- Contracting
- Purchasing
- P&T Committee
- Customer Service
- Financial Counselors
- Coding
- Marketing
- Specialty Pharmacy Services or Partners
- Home Infusion Services or Partners
- Group Purchasing Organization
- **Patients and Caregivers !!!**

Establish a Biosimilar Formulary Grid & Quarterly Review Process

Brand*	Generic	Formulary	HCPCS Code	Manufacturer	Payor Preferred
Remicade*	infliximab	Y	J1745	Jansenn	HPHC/CIGNA/AETNA/Tufts/Allways
Inflectra	infliximab-dyyb	Y	Q5103	Pfizer	BCBSMA/United/MC Advantage/Fallon/THPP
Renflexis^	infliximab-abda	Y	Q5104	Merck	Tufts Medicaid/Tufts Public
Avsola	infliximab-axxq	N	Q5121	Amgen	
Herceptin*	trastuzumab	Y	J9355	Genentech	
Kanjinti^	trastuzumab-anns	Y	Q5117	Amgen	United/Fallon/HPHC
Ogivri	trastuzumab-dkst	N	Q5114	Mylan	
Trazimera	trastuzumab-qyyp	N	Q5116	Pfizer	
Ontruzant	trastuzumab-dttb	N	Q5112	Merck	
Ritxuxan*	rituximab	Y	J9122	Biogen	
Truxima ^	rituximab-abbs	Y	Q5115	Teva	Unites/Fallon
Ruxience	rituximab-pvvr	N	Q5119	Pfizer	AETNA
Riabni	rituximab-arrx	N	Q5123	Amgen	
Avastin*	bevacizumab	Y	J9035	Genentech	
MVasi^	bevacizumab-awwb	Y	Q5107	Amgen	United/Fallon/HPHC
Zirabev	bevacizumab-bvzr	N	Q5118	Pfizer	
Procrit/Epogen*	erythropoetin-alfa	N	J0885	Jansenn/Amgen	
Retacrit^	erythropoetin-alfa-epbx	Y	Q5106	Pfizer	BCBSMA/United/Fallon
Aranesp*^	darbepoetin	Y	J0881	Amgen	
Retacrit	erythropoetin-alfa-epbx	Y	Q5106	Pfizer	BCBSMA/AETNA
Neulasta^*	pegfilgrastim	Y	J2505	Amgen	United/AETNA
Udenyca	pegfilgrastim-cbqv	Y	Q5111	Coherus	BCBS MA + MC Advantage/BMC/Fallon(req)
Fulphila	pegfilgrastim-jmdb	N	Q5108	Mylan	BMC
Ziextenzo	pegfilgrsatim-bmez	N	Q5120	Sandoz	United/AETNA
Nyvepria	pegfilgrastim-apgf	N	Q5122	Pfizer	
Neupogen*	filgrastim	Y	J1442	Amgen	
Zarxio	filgrastim-sndz	Y	Q5101	Sandoz	United/Fallon/CIGNA
Granix^	tbo-filgrastim	Y	J1447	Teva	CIGNA
*Reference product					
^Hospital Preferred					

Biosimilar Formulary Management Stewardship Cycle

1. Market Review – Payors and Medicare Update Policies Quarterly
2. Clinical Review – Monitor pipeline for biosimilars and alternatives
3. Update Policy- Engage P&T and Department Leaders often
4. **Training !!** – Pharmacy, Nursing, Providers, Patient Access etc.
5. Go-Live – Establish a Strategy
   - Non-Medical Switching?
   - New starts only?
   - Conversion on insurance change or expiration of PA?
6. Monitor – Adverse Effects, Clinical Response
7. Measure - Financial and Clinical Outcomes
   - Cost savings
   - Payor policy compliance via first pass denials +/- write-offs
   - Medication Use Evaluations and Retrospective Research

Biosimilar Formulary Management: Pegfilgrastim

Provider Level Prescribing Alert

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Formulary Evaluation pegfilgrastim Biosimilars 2019

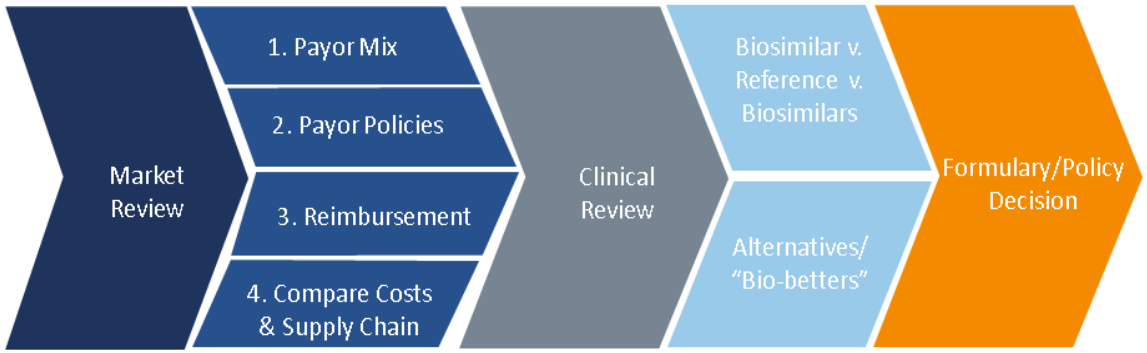
Market and Clinical Review Findings

- Payor Mix: 20% patients had a commercial payor requiring use of biosimilar
- Payor Policies: Estimated $900,000 at risk due non-compliance w/ payor policies
- Reimbursement: Comparable reimbursement for Udenyca and Neulasta
- Costs/Supply Chain: Inventory issues and coverage challenges with Fulphila

- Clinical: Neulasta OBI already accounted for >70% of use and contractual pricing offered advantage over biosimilars
  - Lack of head-to-head b/w Udenyca and Neulasta
  - NCCN: Supports use of GCSF biosimilars across all indications

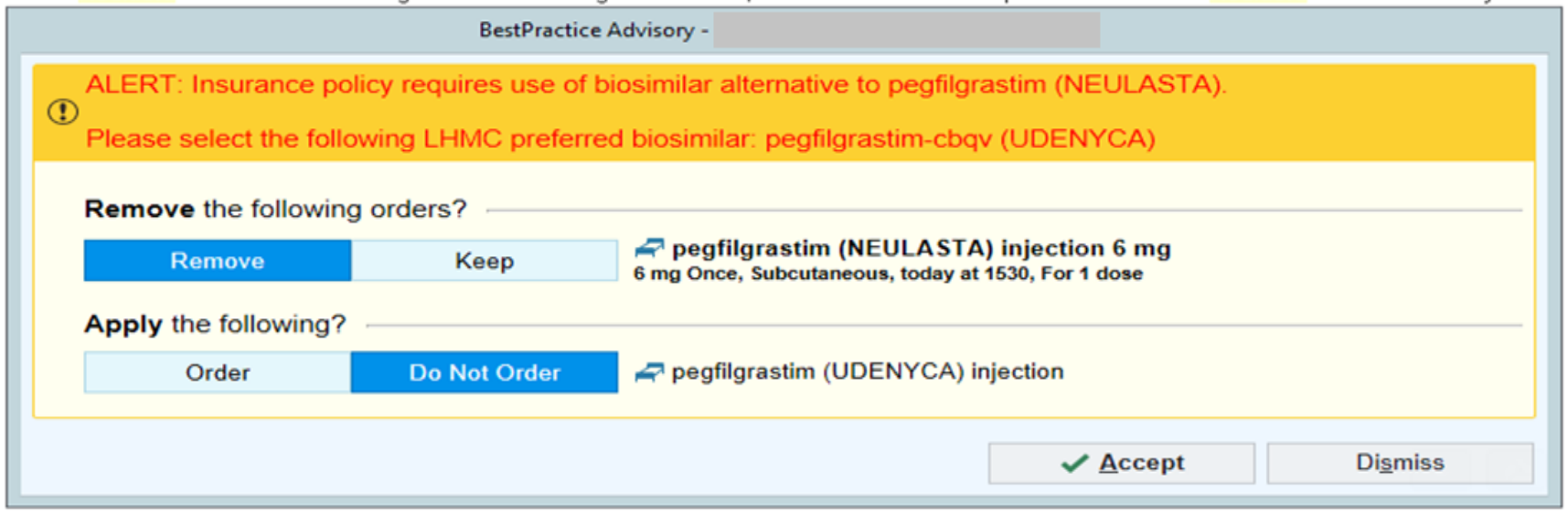
Pharmacy Formulary Recommendation:

1. Neulasta and Neulasta-OBI remain hospital preferred pegfilgrastim
2. Add pegfilgrastim – cbqv (UDENYCA) to LHMC formulary as preferred biosimilar for patients w/ insurance requiring use of biosimilar over Neulasta
3. Not eligible for Therapeutic Substitution by pharmacy due to difference in appointment scheduling for Neulasta OBI vs. syringe options
4. Develop Provider Directed Alert based on insurance coverage to drive use of Udenyca

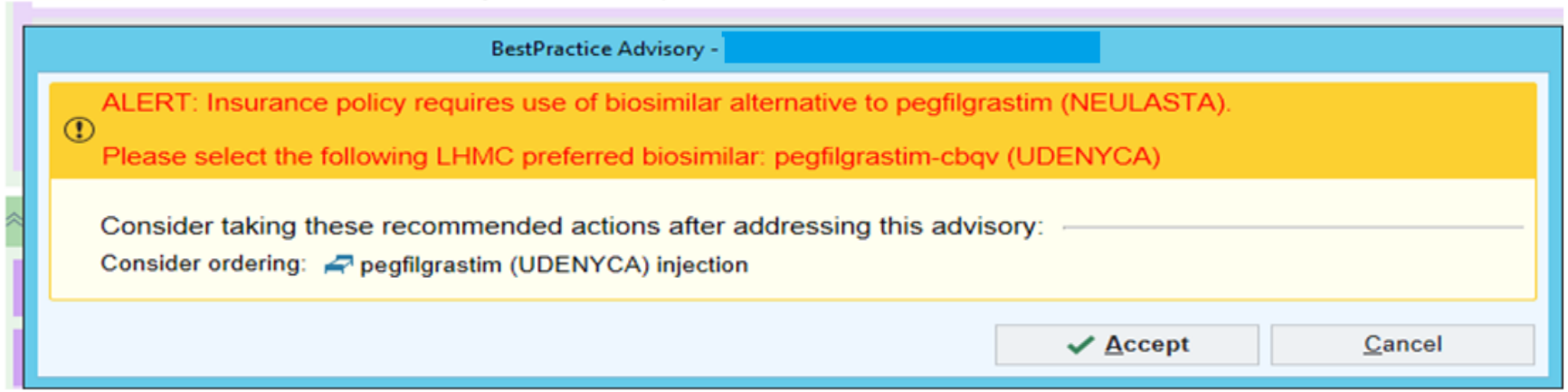


Provider Level Alerts to Drive Use of Payor Preferred Biosimilar

When Neulasta is ordered via Manage Orders or during a clinic visit, the BPA will allow the provider to remove Neulasta and order Udenyca.



If Neulasta is ordered via a Treatment Plan, you can not swap the meds within the BPA.



Pegfilgrastim Biosimilar Implementation Timeline

June 2018: Market review revealed that Part B Reimbursement accounted for only 88% of pegfilgrastim cost to the organization followed by contract w/ Amgen established to reduce cost on Neulasta

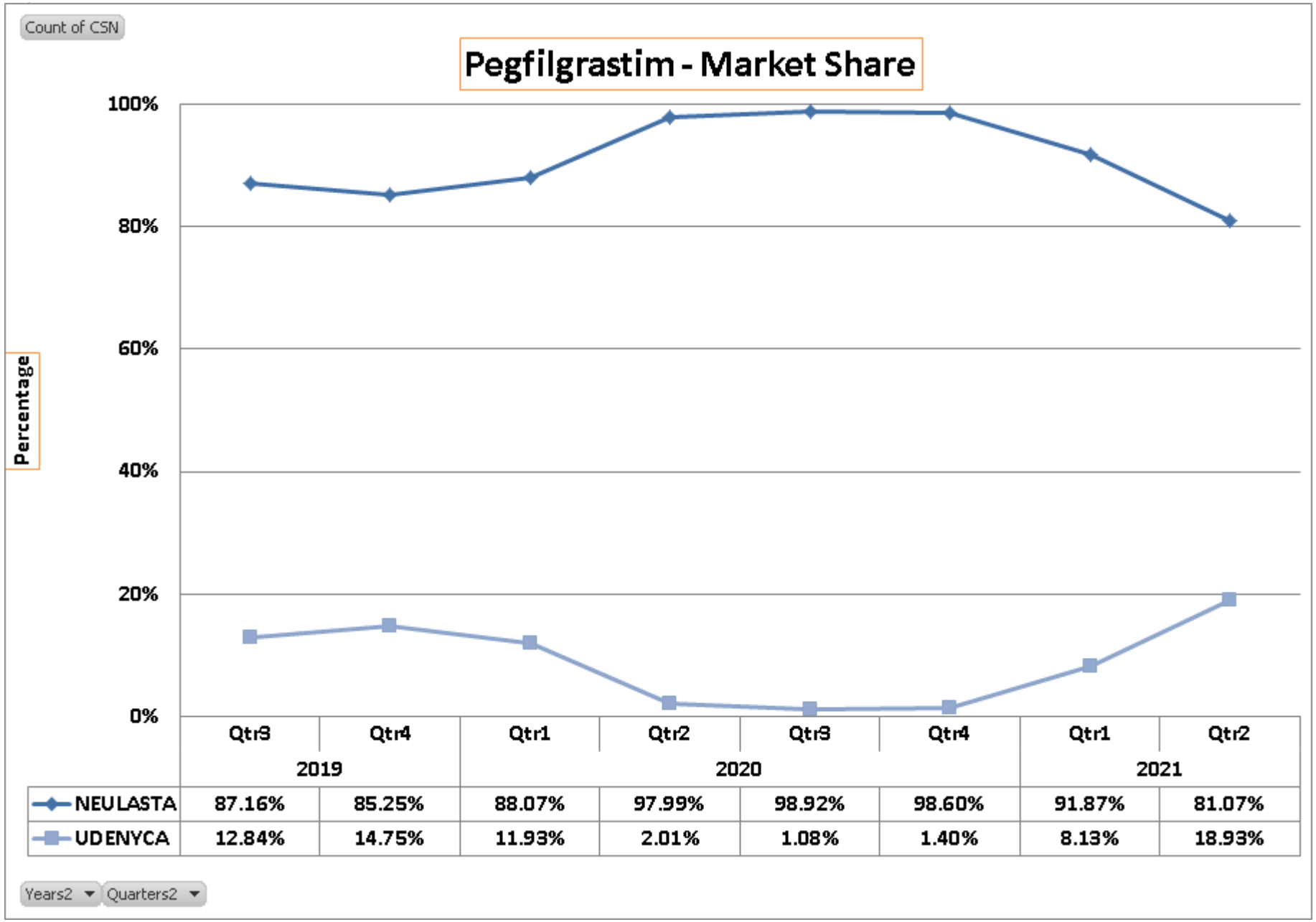
June 2019: Udenyca added to LHMC formulary as preferred biosimilar for patients w/ insurance requiring use of biosimilar over Neulasta

August 2019: Provider Level Prescribing Alert implemented

March 2020: Due to COVID-19 pandemic commercial payors grant waivers for Neulasta OBI use to prevent need for return visit for biosimilar for administration

March 2021: Commercial payors reinstate policies requiring use of pegfilgrastim biosimilars

July 2021: Fulphila to replace Udenyca as preferred hospital biosimilar due to new GPO opportunity and changes in ASP- reimbursement



	Qtr3	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2
	2019		2020				2021	
NEULASTA	87.16%	85.25%	88.07%	97.99%	98.92%	98.60%	91.87%	81.07%
UDENYCA	12.84%	14.75%	11.93%	2.01%	1.08%	1.40%	8.13%	18.93%

Biosimilar Formulary Management: Infliximab

Therapeutic Substitution by Pharmacy at Treatment Initiation

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Formulary Evaluation infliximab Biosimilars 2019

Market and Clinical Review Findings

- Payor Mix: 20-25 % patients had a commercial payor requiring use of biosimilar or reference;
- Payor Policies: Estimated >$500k at risk due non-compliance w/ payor policies
- Reimbursement: Remicade reimbursement 70% of medication cost – $1.2 million dollar gap in the Medicare population
- Cost/Supply Chain: Biosimilars priced at 30-35% Less than Remicade; estimated cost savings > $150k / month
- Clinical: Clinical trial data available to support use across indications and EU data to support successful non-medical switching

Pharmacy Formulary Recommendation:

1. Add Renflexis as hospital preferred infliximab product
2. Add Inflectra to formulary and restrict to patients subject to commercial payors requirements
3. Restrict Remicade to patients subject to commercial payor requirements
4. Initiate non-medical switching (w/MD and Patient consent) to align with hospital and commercial payor requirements
5. Implement Therapeutic Substitution by Pharmacy at initiation of infliximab therapy

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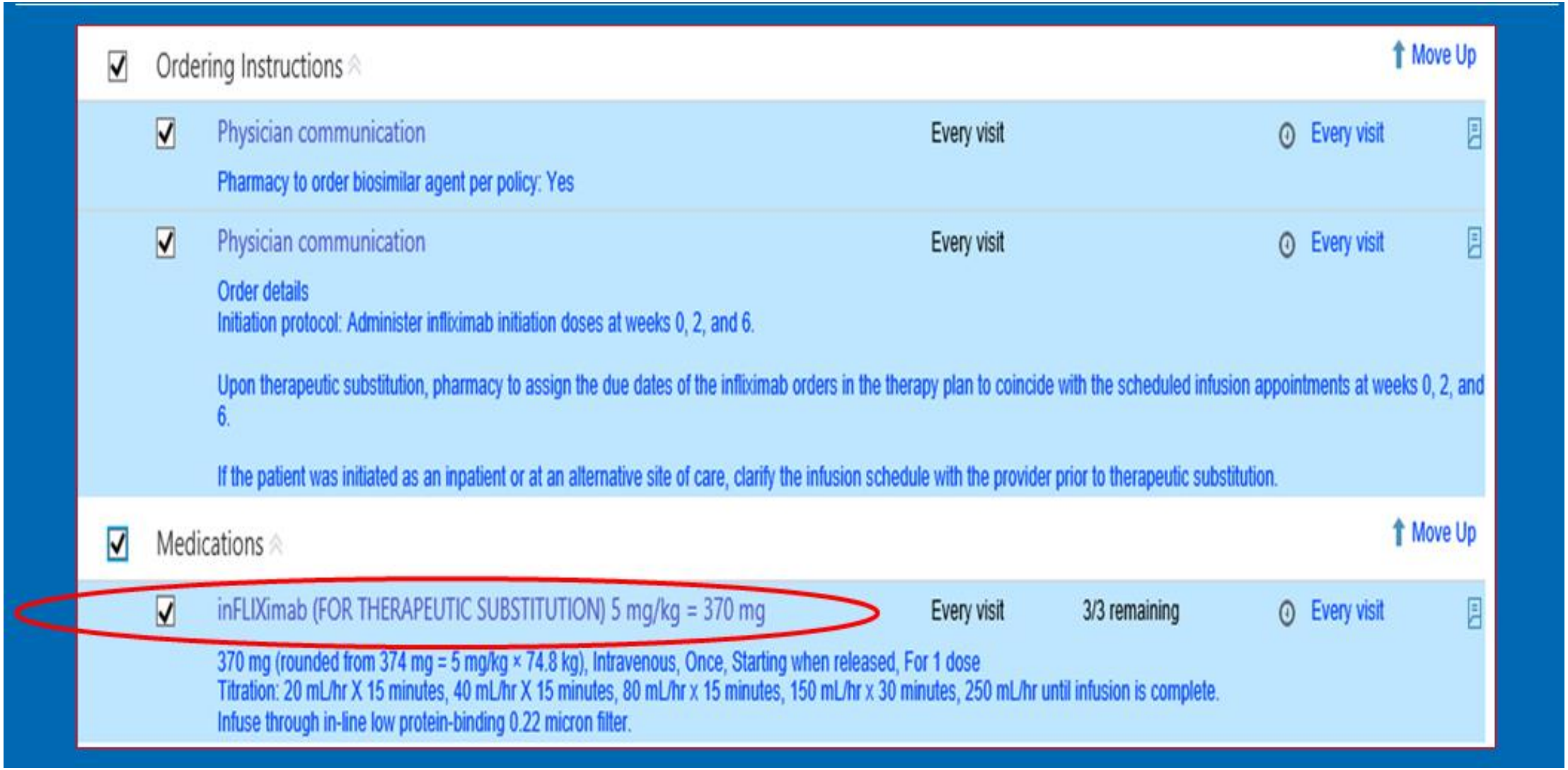
Biosimilar Therapeutic Substitution Policy

Who may initiate the Therapeutic Substitution Procedure: Pharmacist at Lahey Hospital and Medical Center in Burlington or Lahey Medical Center, Peabody

Ambulatory Process:

- Provider will enter biosimilar order FOR THERAPEUTIC SUBSTITUTION with default instruction: *Pharmacy to order preferred biosimilar agent per policy*
- Preferred biosimilar medication will be dictated by the patient's insurance policy
- If the patient's insurance policy does not specify a preferred biosimilar medication patient to receive Hospital Pharmacy and Therapeutics designated preferred biosimilar medication
- Pharmacist will enter biosimilar medication in patient Therapy Plan or Treatment Plan
- Order will be placed using order mode "Pharmacy per Policy"
- Provider may request a formulary alternative biosimilar but must provide clinical rationale for that alternative
- Delivery of formulary alternative is contingent upon pre-approval from patient's insurance carrier

FOR THERAPEUTIC SUBSTITUION Order to Trigger Payor Policy Review Process



Prior Authorization & Payor Policy Review

- FOR THERAPEUTIC SUBSITITUION order triggers the Patient Access team to attempt to obtain prior authorization for the hospital preferred product.
- If the payor requires use of a formulary alternative then authorization will be obtained for the alternative, without additional discussion with the provider
- The Authorized product is listed in a communication by the Patient Access team in the authorization notes
- The note is referenced by the Pharmacist when completing the Therapeutic Substitution process ***prior*** to the patients first infusion appointment

Referral Notes Number of Notes: 3

Type	Date	User	Summary	Attachment
General	08/05/2019 9:07 AM		-	-

Note
InFLIXimab agent preferred by the patient's insurance plan policy:
inFLIXimab (REMICADE) - J1745

Approved - after clinical review
Case has been approved after review of clinical documentation
RTE Status:E-verified
Auth #:CV1638107
CPT codes approved:J1745- Remicade
Validity dates:08/02/2019-08/01/2020
Facility:LCH

Buy and Bill

Type	Date	User	Summary	Attachment
General	08/02/2019 9:54 AM		-	-

Note
InFLIXimab agent preferred by the patient's insurance plan policy:
inFLIXimab (REMICADE) - J1745

Pending- Auth initiated
Insurance verified and authorization was initiated for CPT: J1745
Clinical information has been faxed to the payer and additional review is needed

Type	Date	User	Summary	Attachment
General	08/01/2019 10:19 AM		-	-

Note
Pending- Auth initiated
Insurance verified and authorization was initiated for CPT: Q5104
Clinical information has been faxed to the payer and additional review is needed

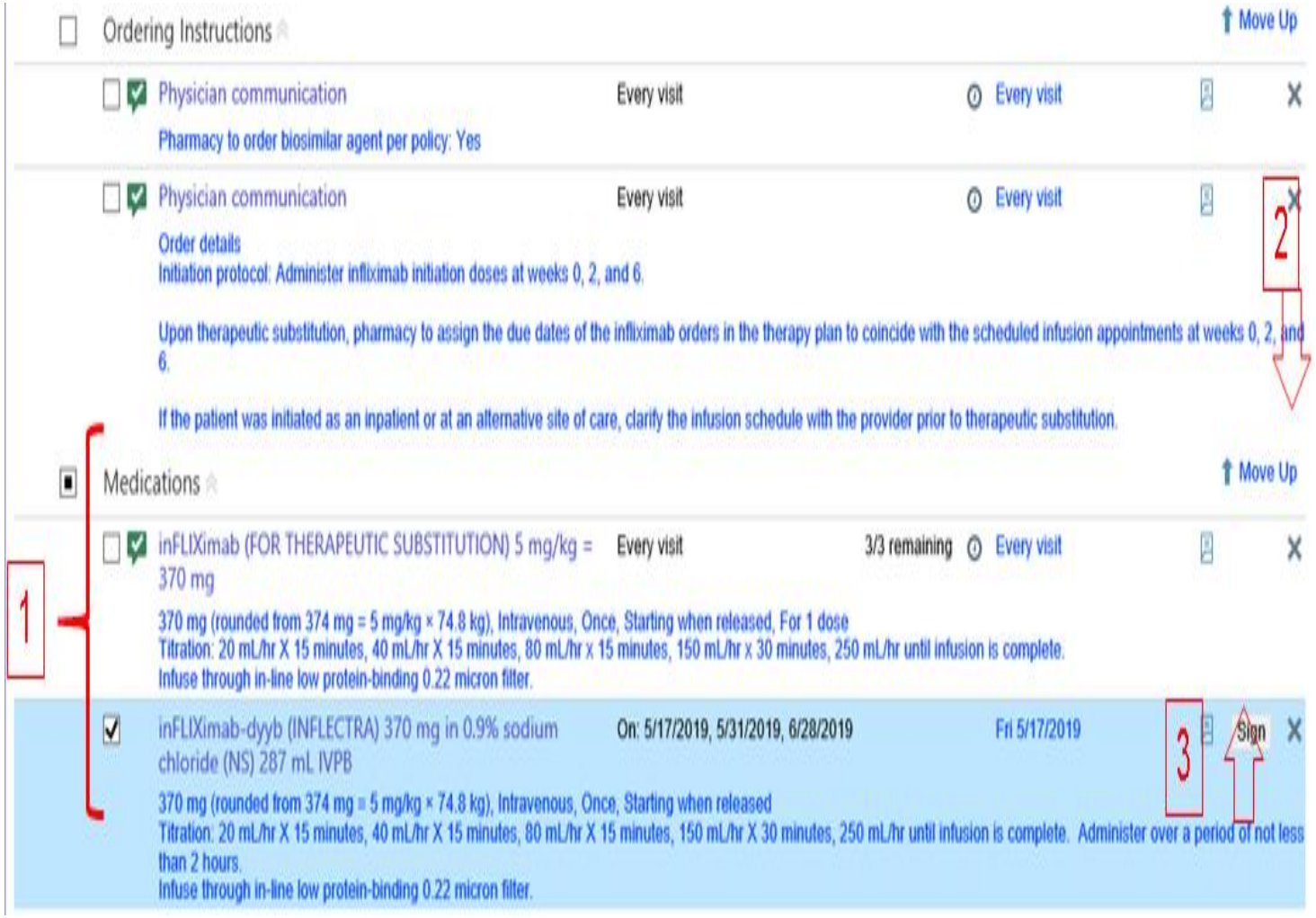
Therapeutic Substitution Process

1) The referral note is reviewed by the RPh and a New – “real” order for biosimilar order is added to the protocol, dose is and infusion dates are transcribed from the FOR THERAPEUTIC SUBSTITUTION order

2) The FOR THERAPEUTIC SUBSTITUION order is removed from the protocol

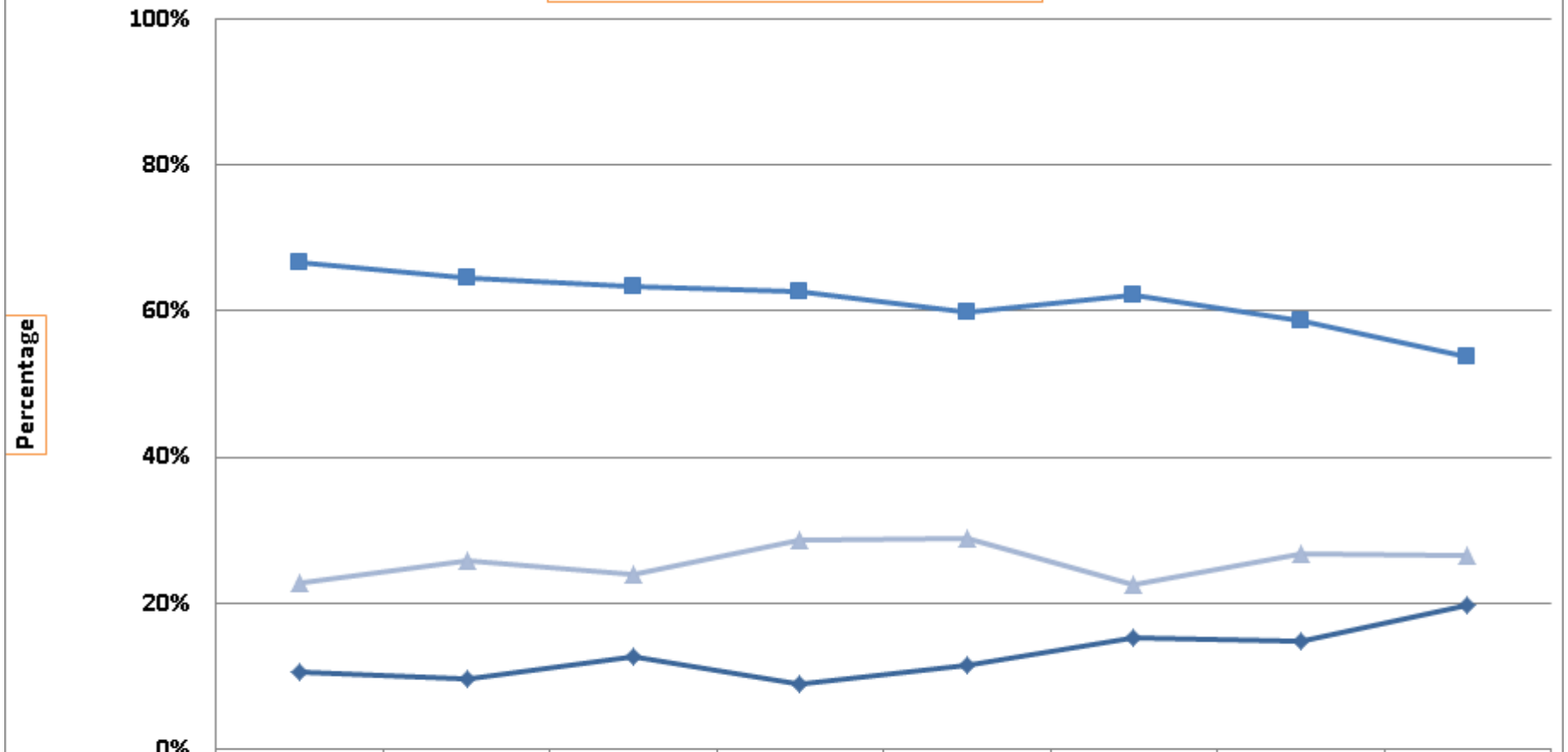
3) The new “real” order is signed by the pharmacist under “Pharmacy per Policy”

4) A communication is sent to the prescriber to inform them of the brand the patient will receive.



Count of CSN

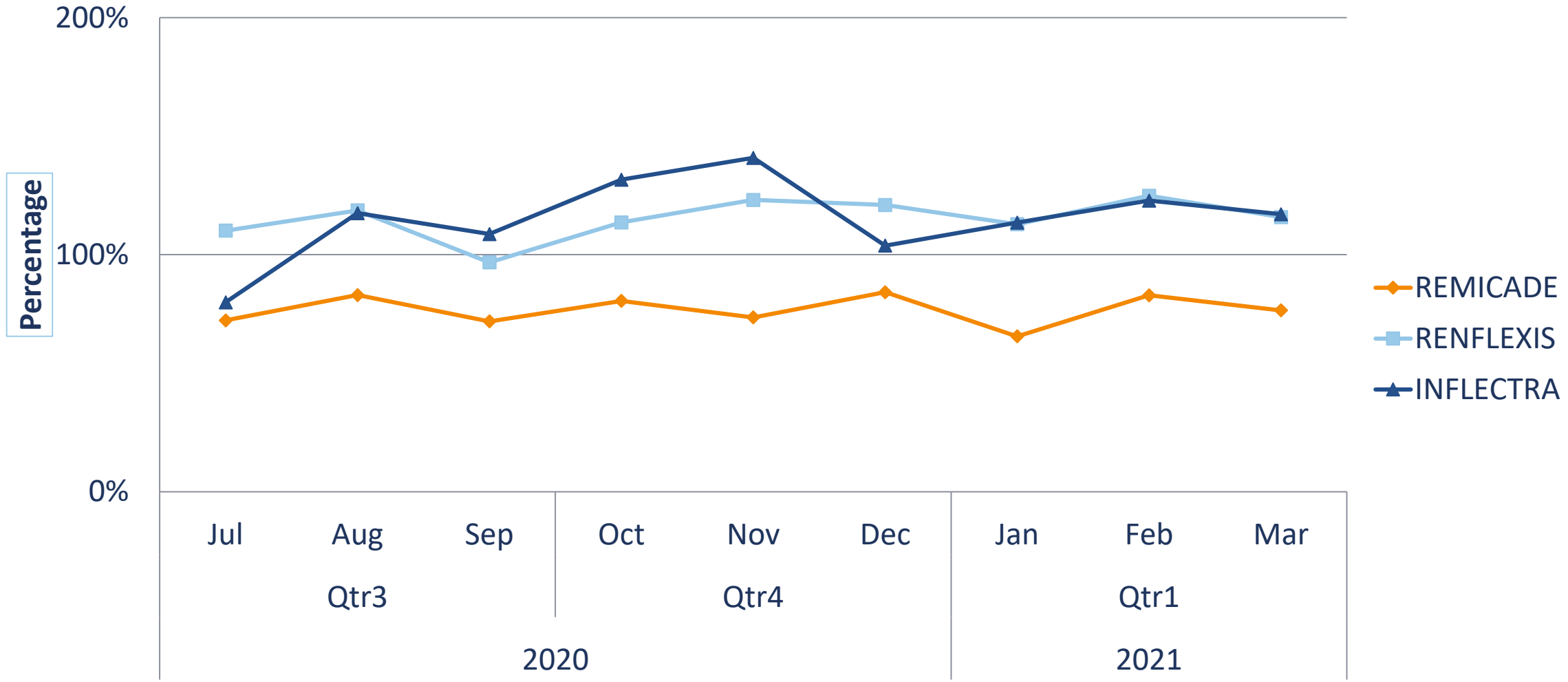
Infliximab - Market Share



	Qtr3	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2
	2019		2020				2021	
INFLECTRA	10.44%	9.65%	12.72%	8.81%	11.38%	15.22%	14.71%	19.79%
REMICADE	66.76%	64.61%	63.36%	62.58%	59.88%	62.23%	58.56%	53.71%
RENFLEXIS	22.80%	25.74%	23.92%	28.62%	28.74%	22.55%	26.74%	26.50%

Years2 Quarters2

Infliximab Cost: Reimbursement Ratio



Infliximab Biosimilar Implementation Timeline

- **January 2018:** CMS Announces Biosimilars to be given independent QCodes and ASP
- **April 2018:** Two large regional Payors (~10% of patient volume combined) announce new policy: Remicade to be preferred over biosimilar alternatives
- **July 2018:** Largest commercial payor (~15 % of patient volume) implements policy: Inflectra or Renflexis will be preferred for new starts over Remicade
- **January 2019:** Largest commercial payor revises policy: Inflectra preferred over others
- **July 2019:** Implementation of the Biosimilar Therapeutic Substitution Program is launched in parallel with Non Medical Switching of Active infliximab patients
- **October 2020:** Largest commercial payor revises policy ***again***– All patients even those previously on Remicade must try Inflectra followed by Renflexis before approval of Remicade
- **July 2021:** Non-Medical Switching Phase II and update to Therapeutic Substitution Process → Moving from substitution at Treatment Initiation to ***every*** Order Verification

Biosimilar Formulary Management: Trastuzumab Bevacizumab & Rituximab

Therapeutic Substitution by Pharmacy at Order Verification

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Formulary Evaluation Trastuzumab, Bevacizumab & Rituximab Biosimilars

Market & Clinical Review:

- Payor Mix: 5 % of patients had a commercial payor requiring use of biosimilar;
- Payor Policies: Estimated $150 k / year at risk due non-compliance w/ payor policies
- Reimbursement: Generally positive margin for reference and biosimilars
- Cost/Supply Chain: Biosimilars priced at 10 – 25% less than reference products; estimated cost savings = $75k / month

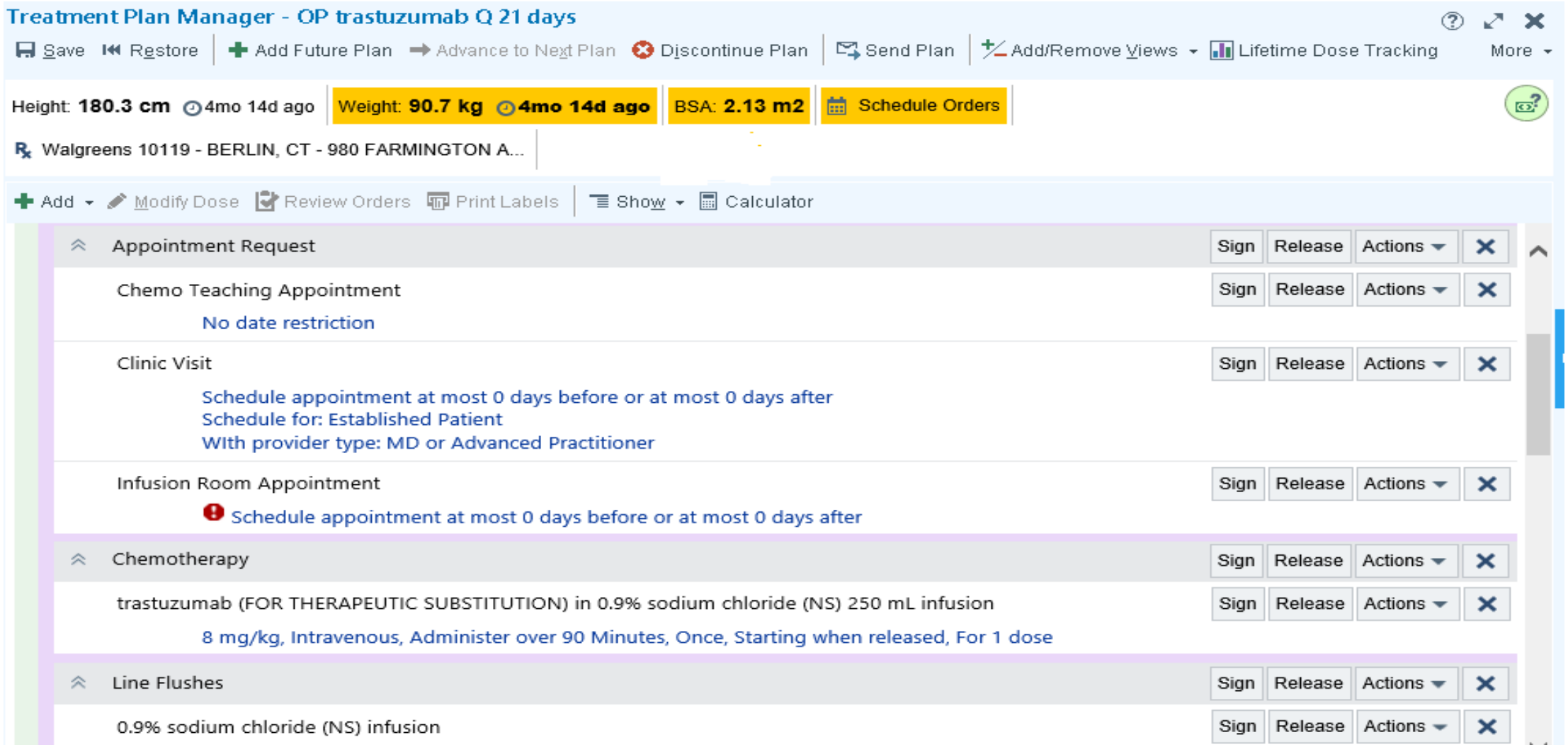
- Clinical: Clinical trial data available to support use across indications –
  - Except: Orphan indication (Avastin) & lack of non-hematology data for Truxima at launch
  - NCCN supported biosimilar use across all malignancies
  - Truxima data in Rheumatoid Arthritis was available mid 2020 after which P&T extended approval to all indications

Formulary Evaluation Trastuzumab, Bevacizumab & Rituximab Biosimilars Continued….

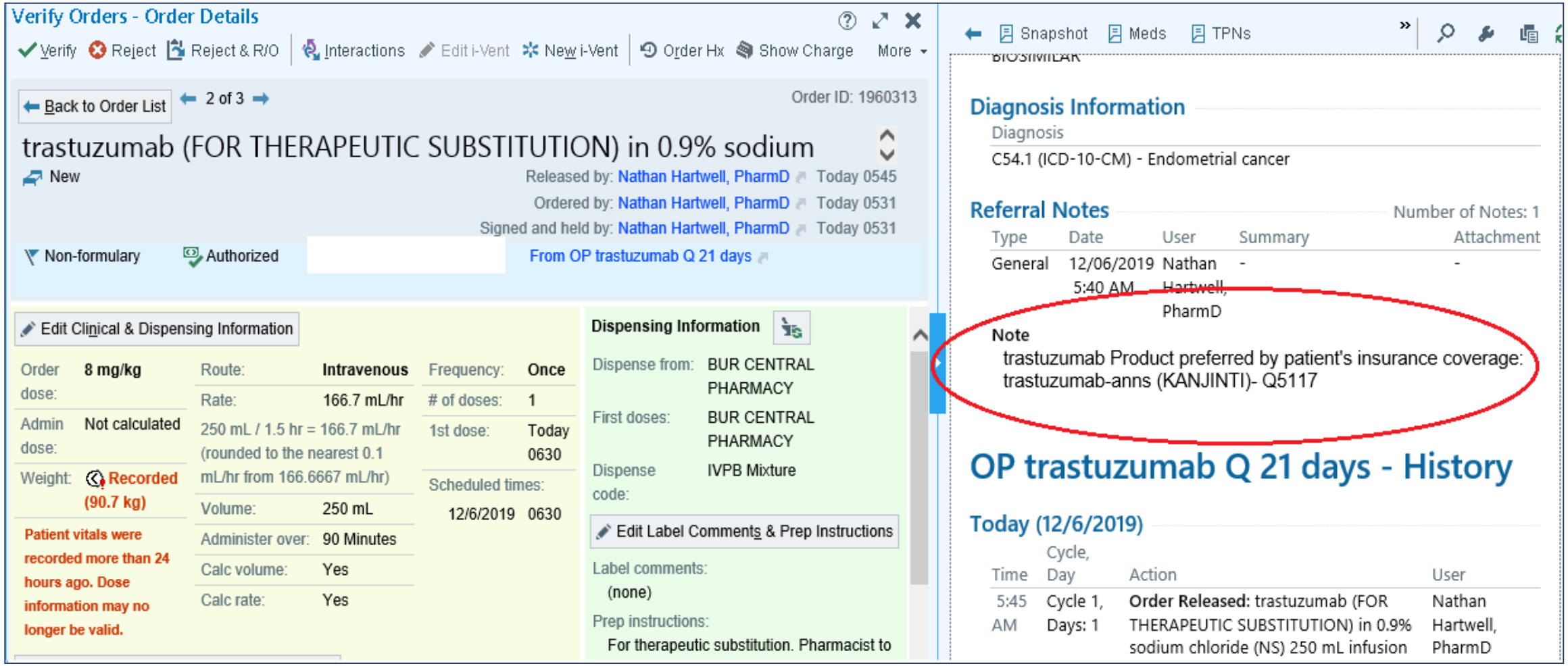
Formulary Recommendation by Pharmacy:

1. February 2020: Add Mvasi & Kanjinti to Formulary as hospital preferred bevacizumab and trastuzumab
2. April 2020: Add Truxima to Formulary as preferred rituximab but restricted to hematologic malignancies
3. September 2020: Expand Truxima as preferred for all indications
4. Restrict reference products to patients on active therapy or that are subject to commercial payor requirements
5. Approved only for new patients; non-medical switching not allowed unless dictated by payor
6. Pharmacist to review authorization and perform Therapeutic Substitution at the time of ***every*** order verification

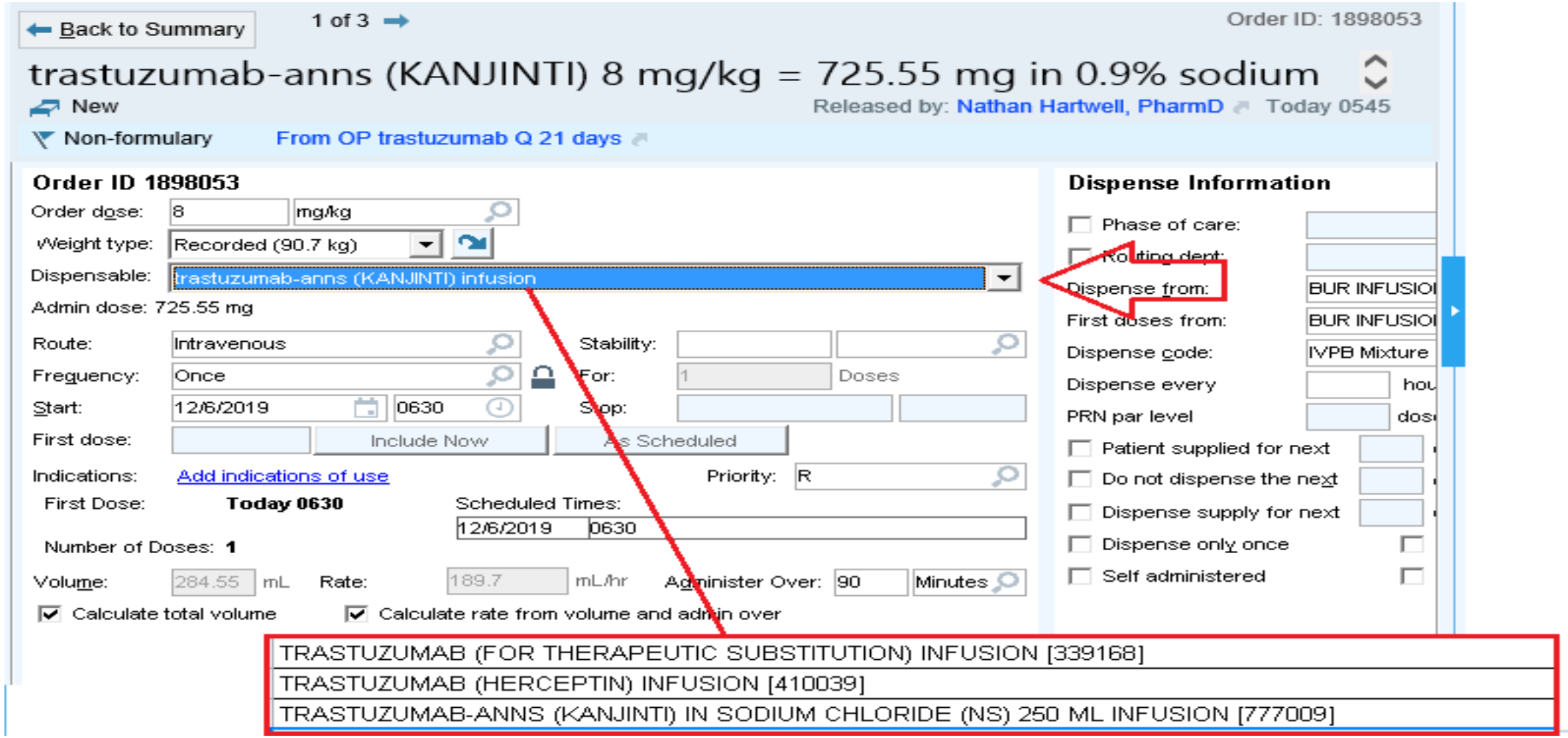
FOR THERAPEUTIC SUBSTITUION Order to Trigger Payor Policy Review



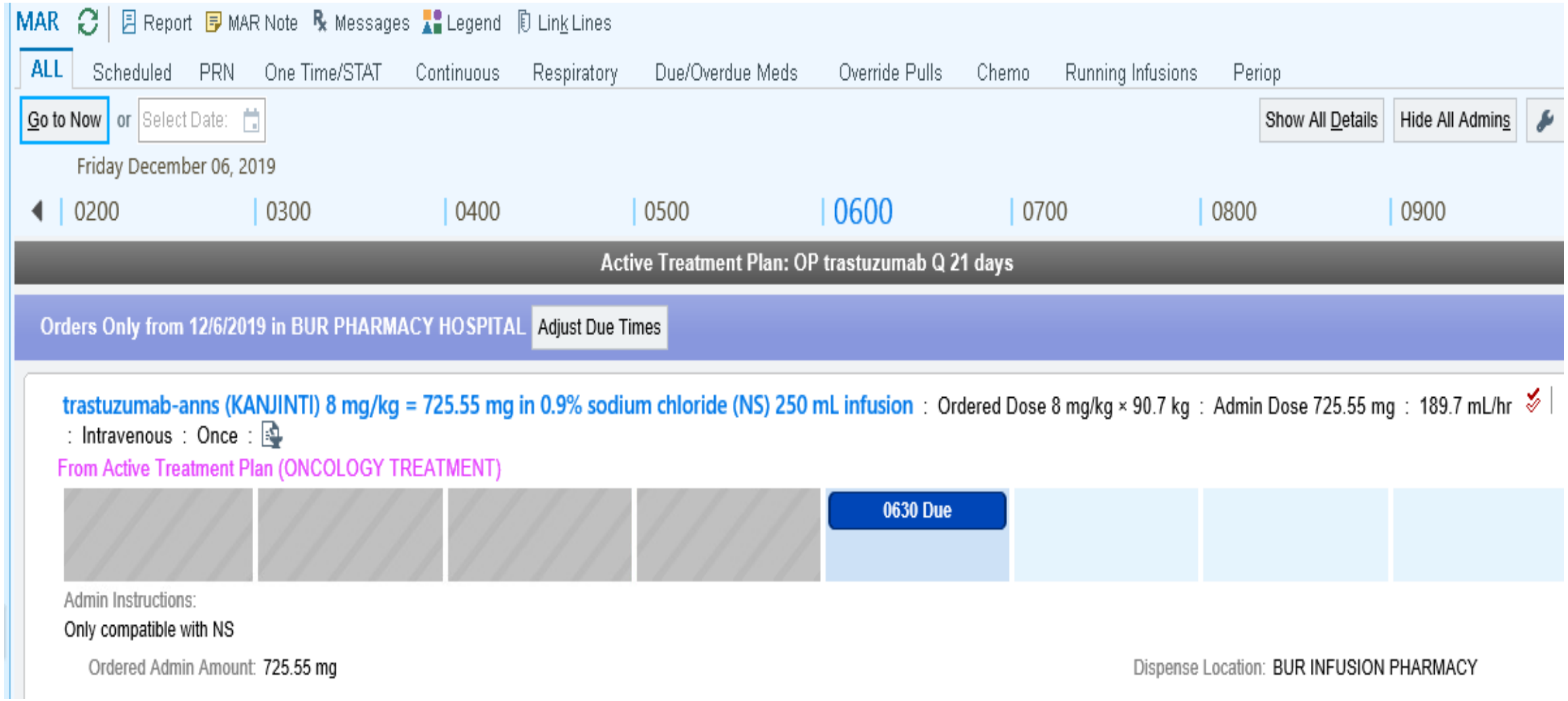
Prior Authorization & Payor Policy Review



Therapeutic Substitution Process *(No Transcription Required)*

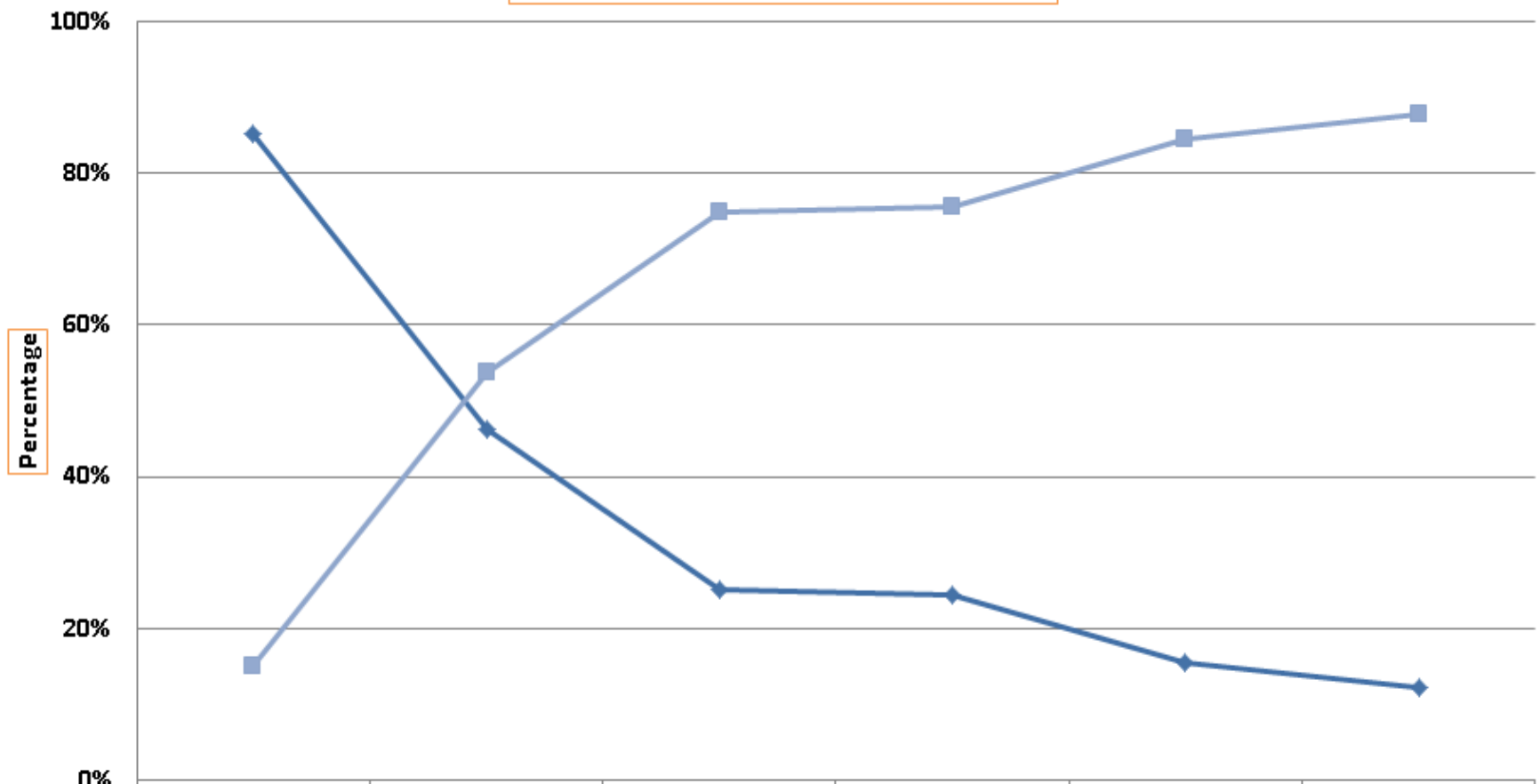


Medication Administration Record Display following Therapeutic Substitution



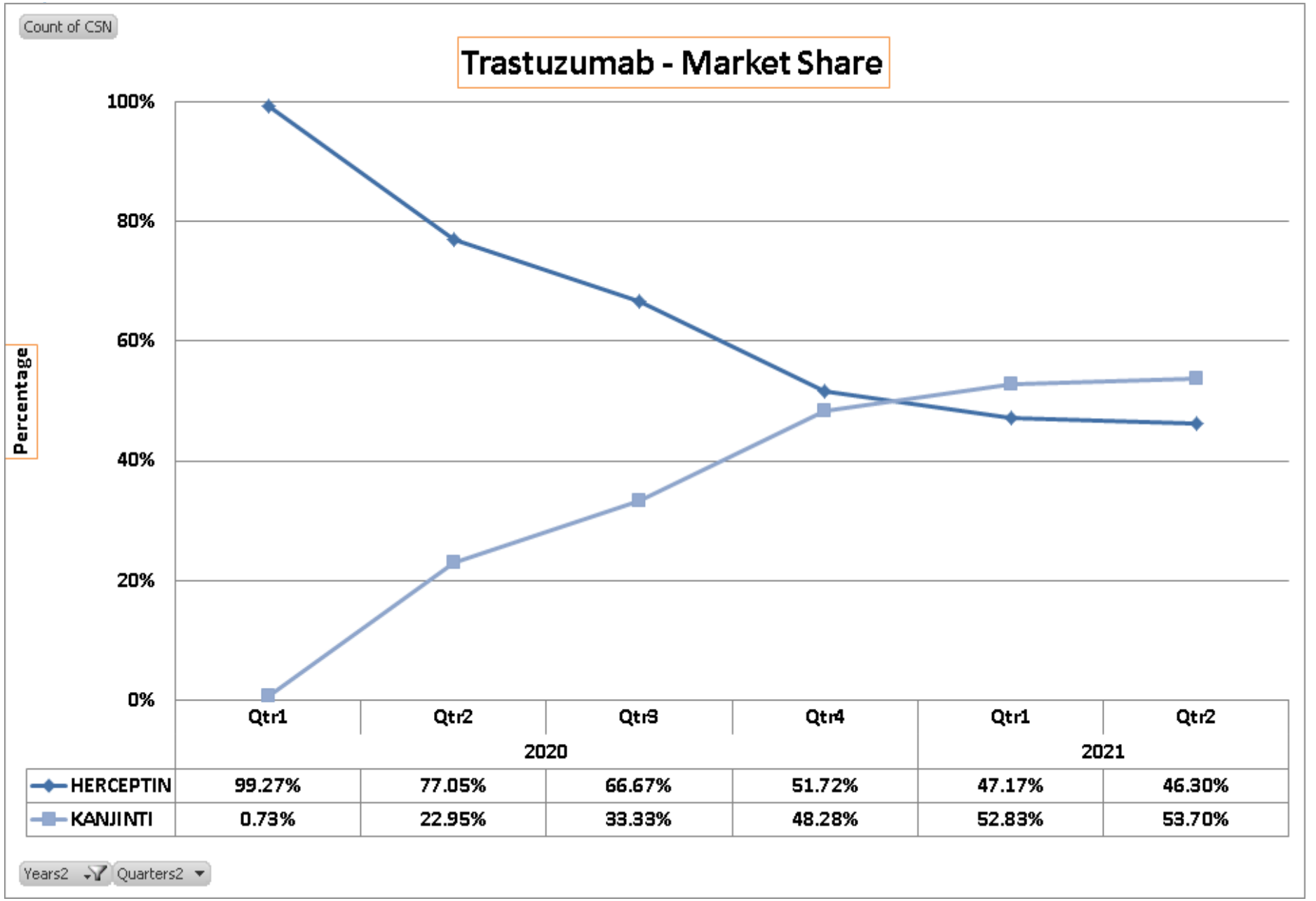
Count of CSN

Bevacizumab - Market Share



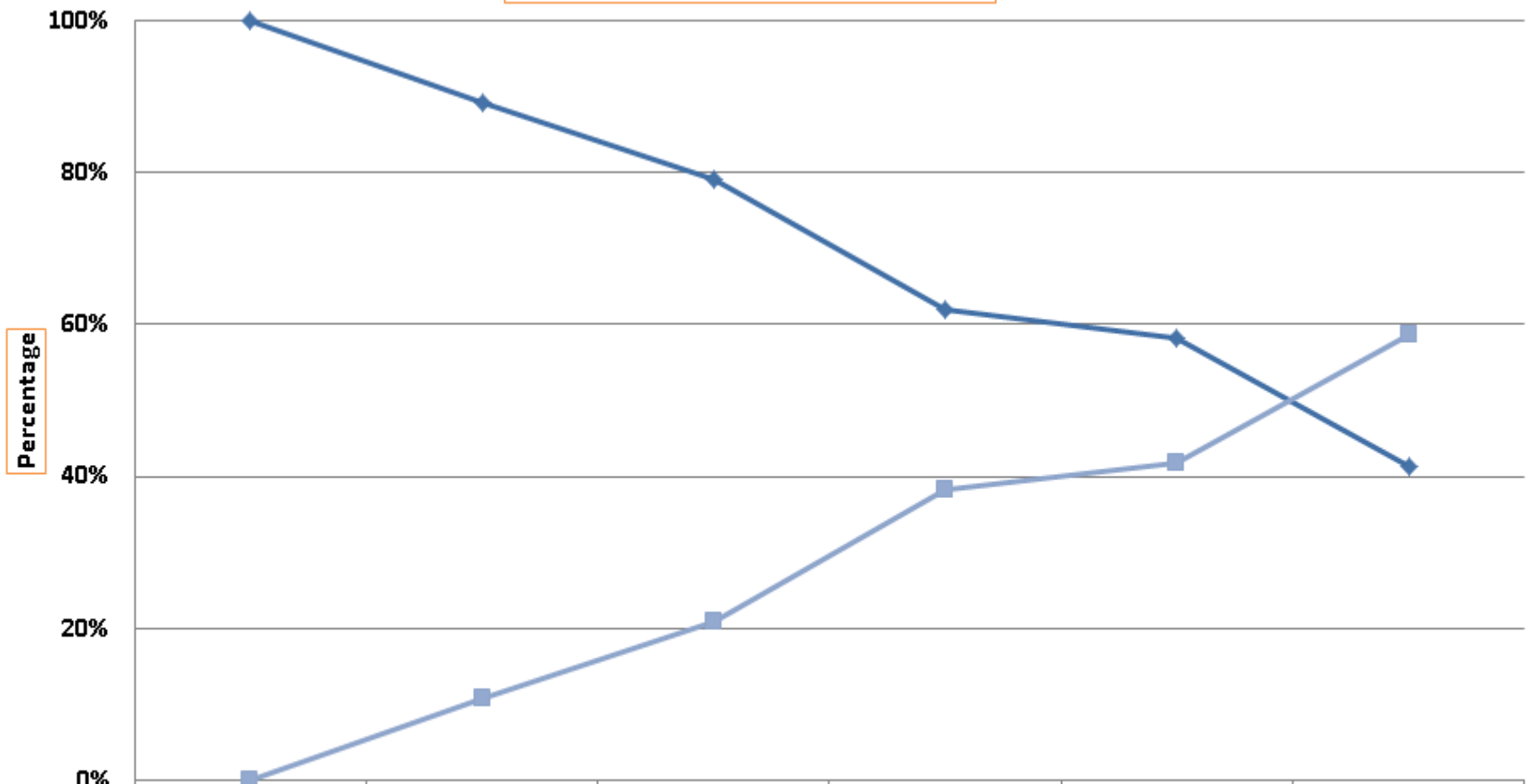
	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2
	2020				2021	
AVASTIN	85.09%	46.23%	25.20%	24.37%	15.48%	12.28%
MVASI	14.91%	53.77%	74.80%	75.63%	84.52%	87.72%

Years2 Quarters2


Count of CSN
Trastuzumab - Market Share
100%
80%
60%
40%
20%
0%
Percentage
Qtr1
Qtr2
Qtr3
Qtr4
Qtr1
Qtr2
2020
2021
HERCEPTIN 99.27% 77.05% 66.67% 51.72% 47.17% 46.30%
KANJINTI 0.73% 22.95% 33.33% 48.28% 52.83% 53.70%
Years2
Quarters2

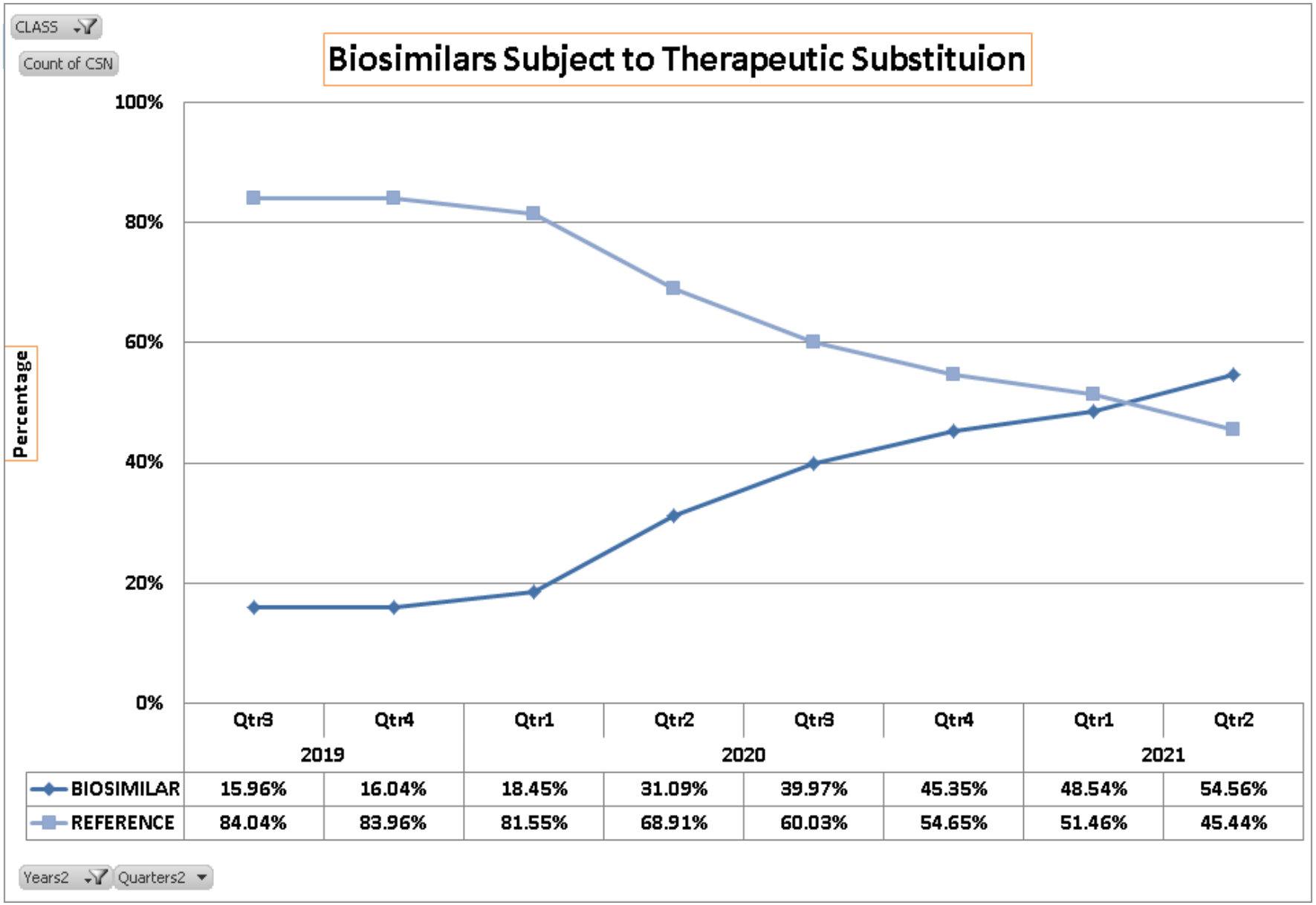
Count of CSN

Rituximab - Market Share



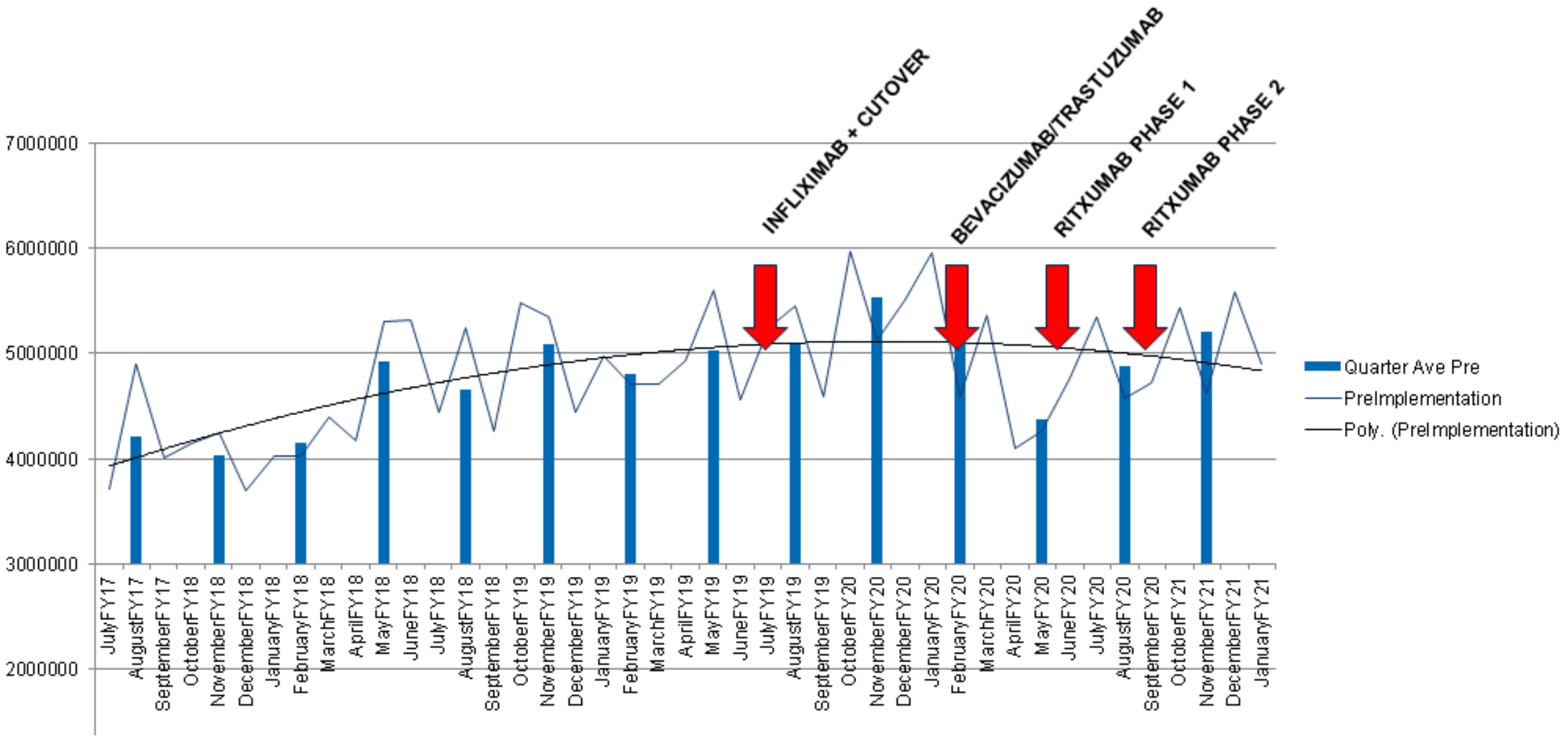
	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2
	2020				2021	
RITUXAN	100.00%	89.29%	79.08%	61.88%	58.20%	41.32%
TRUXIMA	0.00%	10.71%	20.92%	38.13%	41.80%	58.68%

Years2 Quarters2



	Qtr3	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2
	2019		2020				2021	
BIOSIMILAR	15.96%	16.04%	18.45%	31.09%	39.97%	45.35%	48.54%	54.56%
REFERENCE	84.04%	83.96%	81.55%	68.91%	60.03%	54.65%	51.46%	45.44%

Overall Infusion Center Medication Expenditures & Biosimilar Therapeutic Substitution



Comparing Biosimilar Substitution Models

Provider Level Prescribing Alert

- **Pros-** More real-time feedback and puts the decision in the hands of the provider, helps with One-Off orders if med is added to the plan after the fact
- **Cons –** Requires Continuous IT Maintenance, Potential Alert Fatigue, Difficulty to operationalize depending on the EHR

Therapeutic Substitution by Pharmacy prior to Treatment Initiation

- **Pros-** Less maintenance, better ensures compliance with hospital and payor policies, hard stop
- **Cons-** Requires transcription, Adds cooks to the kitchen, May not be feasible depending on the EHR, Does not accommodate transfer of established patient or non-medical switching due to insurance or insurance policy changes

Therapeutic Substitution by Pharmacy at Order Verification

- **Pros-** Less maintenance, better ensures compliance with hospital and payor policies, hard stop, no transcription, less risk of error due to insurance or authorization status change
- **Cons-** Selection error, requires manual review of authorization status

Assessment Question #1 of 3

In 2020 how many new biologics were approved by the FDA?

a. <5
b. <10
c. <15
d. >20

Assessment Question #2 of 3

Understanding the percent of commercial versus government payers is essential for:

- Market review
- Better pricing
- Adverse event reporting
- ASP

Assessment Question #3 of 3

What is an example of a pharmacy-driven, interdisciplinary initiatives to reduce costs and maximize reimbursement for high cost medications?

a. Provider Level Prescribing Alerts
b. Therapeutic Substitution by Pharmacy at Treatment Initiation
c. Therapeutic Substitution by Pharmacy at Order Verification
d. All of the above

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Thank you…

- Nancy Huff PharmD – Director of Pharmacy Services - Lahey Hospital and Medical Center
- Brigitte Gil PharmD BCPS BCOP – Clinical Informatics Coordinator for Hematology/Oncology & Infusion Services – Lahey Hospital and Medical Center
- Matthew Ho CPhT MBA – Pharmacy Finance Manager – Lahey Hospital and Medical Center
- HeideMarie McMaster PharmD – Clinical Pharmacy Manager – Lahey Hospital and Medical Center
- Davina Wolcik RN – EHR Applications Analyst - Lahey Health Shared Services
- Sean Scott – EHR Applications Analyst - Lahey Health Shared Services

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