

Practical Barriers in Cancer Immunotherapy Treatment

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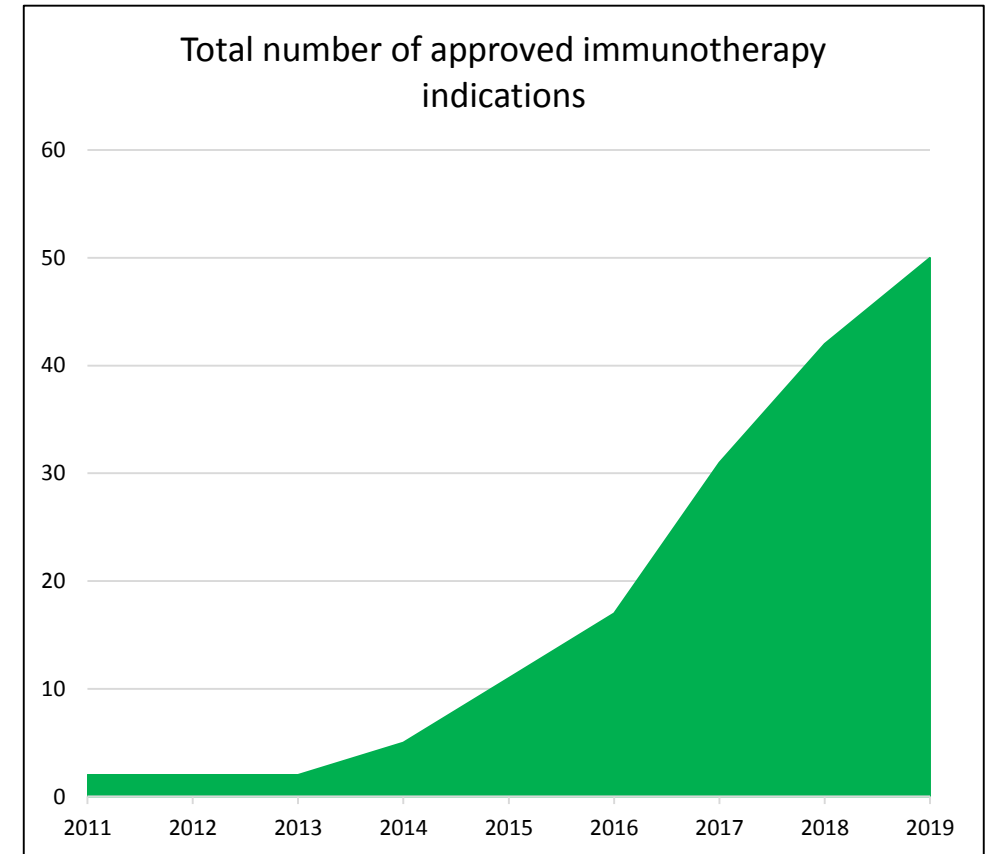
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Disclosures

- APP Oncology Summit: Committee member
- Partner Therapeutics, LLC: Advisory Board Member
- True Learn, LLC: Item writer
- I will be discussing non-FDA approved indications during my presentation.

IO Pipeline and Research

- Current products on the market are the “tip of the iceberg” when looking at manufacturers’ Immuno-Oncology (I-O) pipelines
- During the next few years, we can expect a new IO product or indication every few months
- Not only new products, but a myriad of new combinations and regimens



Strategies for New Information

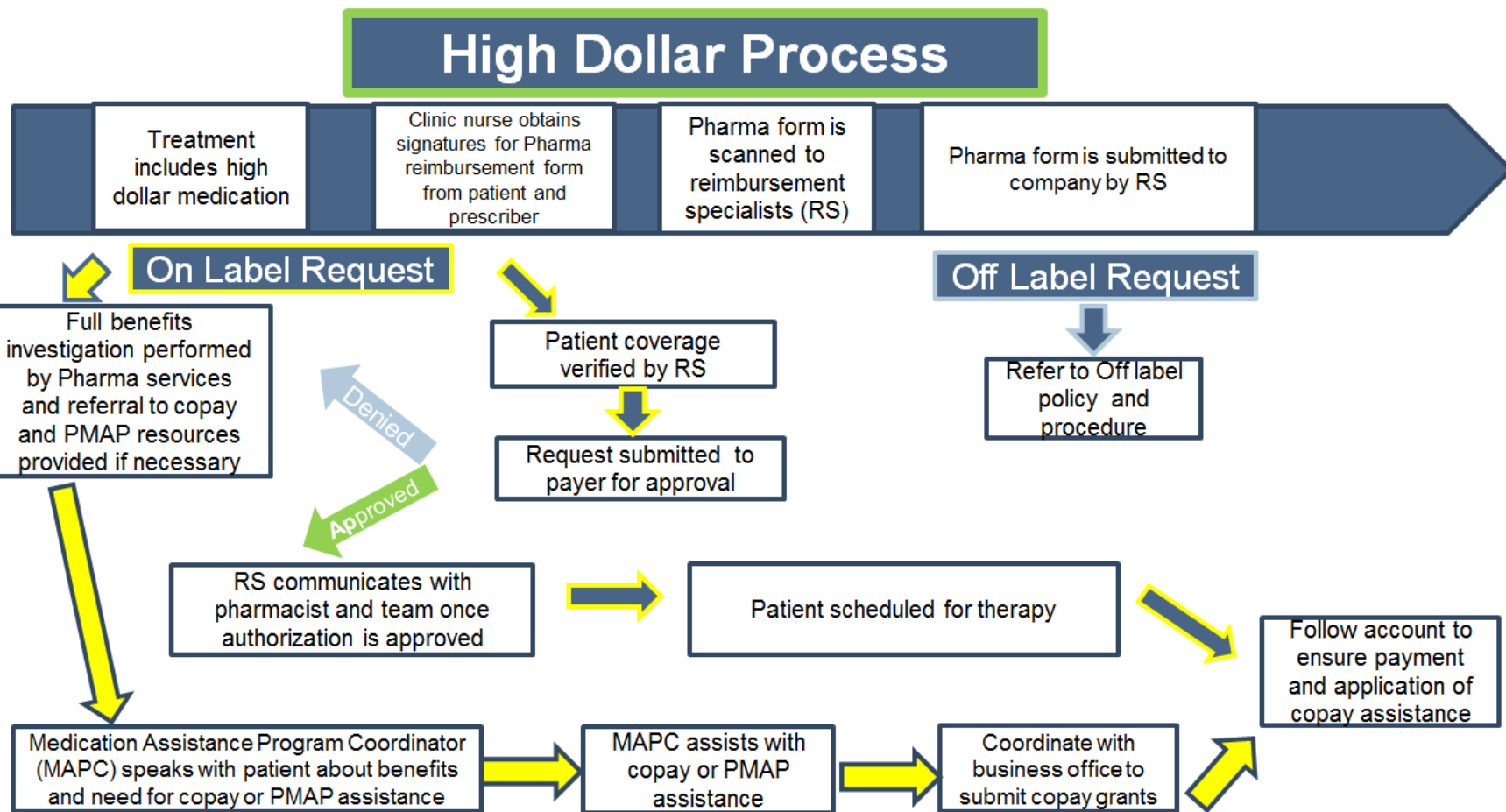
- Immuno-Oncology Champion
 - Identify an “Immuno-Oncology Champion” from among your providers to be the “I-O point person” responsible for all product questions and staff education (can be physician, advance practitioner or pharmacist)
- Education group
 - Identify a core group within your practice to manage patient education, including the review of existing patient materials and/or the development of new materials specific to I-O agents and management of their adverse effects
- Staff education
 - Proactively update staff on new information and consider use of manufacturer-provided resources including on-site training/education (or attend programs like this!)

Manage Reimbursement/Finances

- New-to-market I-O agents may not yet have specific J-Code
 - Ensure a process is in place for appropriate management/billing until J-Code is assigned or, in the case of Hospital Outpatient Prospective Payment Services, a C-Code (Temporary = C9399)
- Identify a point person from within your financial or reimbursement staff to focus on I-O agents and understand the nuances of the various patient support programs
 - Manufacturer benefits verification programs, replacement programs, co-pay support programs, co-pay foundations, and patient assistance programs
- Ensure your practice has sufficient Patient Advocacy
 - Most practices have found that Financial Counselors/Medication Assistance Coordinators pay for themselves many times over; if you are not sure if you have enough, it's a good time to conduct an analysis

Develop Approval Process

- High dollar medication approval process
 - Full benefits investigation, utilize pharma services if offered and allowed per hospital/institution policy
 - Prioritize staff resources to enroll every viable patient into a support program, regardless of on or off-label
- Robust off-label policy and procedure
 - All off-label requests require predetermination
 - Patients are made aware of risks and benefits, including financial risk
 - Patients are required to sign an ABN or NONC
 - Peer review process for appeal if needed



Medicare

- Most Medicare Administrative Contractors (MAC) have at least one I-O agent Local Coverage Determination (LCD)
- Some MAC have separate LCD for all agents
 - Cigna Government Services (CGS) published atezolizumab LCD within the first six weeks of release of the agent
- No successful reimbursement outside the FDA label indications

Off-label medication process: *Medicare pre-treatment*

1. Before off-label use is considered, a **risk/benefit conversation** (medical, financial risks) needs to occur with the patient
2. If patient and treating physician wish to proceed, pharmacist and reimbursement specialist work together to gather **sufficient evidence** for off-label use
3. Medication assistance coordinator, reimbursement specialist, and clinical team **determine payment options**
 - Manufacturer assistance/replacement options
 - Medicare payment
4. Patient and the team decide **whether to proceed** with off-label use

Off-label medication process

5. After the patient receives off-label therapy, the **claim is submitted** to Medicare
6. If the claim is not immediately approved, up to **5 levels of appeals** are allowed
7. If claim is ultimately denied, financial counselors arrange for **payment** of the Medicare allowed amount

Commercial Payers

- Policies primarily based upon published scientific evidence
- Clinical policy guidelines and pathways
 - Vendor Pathways examples: Well Point, New Century Health, AIM
 - Clinical policies examples: Anthem, Aetna, UHC, Cigna, Humana
- Often the clinical policies require medication eligibility restrictions beyond the label and additional criteria to be met in order to assure reimbursement
 - Example: Anthem clinical policy for nivolumab includes patient's current ECOG score 0-2 be met

Commercial Payers

- Use of maximum dosages regardless of weight
 - Maximum allowable units per day and per date span for specialty drugs
- Use of National Drug Code (NDC) units versus CPT/Healthcare Common Procedure Coding System (HCPCS) units creates confusion and concern for underpayment
 - J code represents the amount of drug per billing unit
 - 1 J code per medication
 - J code established by CMS
 - NDC represents the manufacturer and size of the vial
 - 1 NDC code for each vial size for each manufacturer
 - NDC code established by FDA and manufacturer
 - Monitor closely for errors in underpayment

Commercial Payers

- Disproportionate approvals of total billing units versus doses for a specific period of time
 - Example: Authorization for 90 mg pembrolizumab for 6 infusions but date range is for nine months - Make sure that the dates and authorizations match
- Always pursue authorization/pre-determination for IO's, regardless of whether the therapy is on or off-label
 - Retrospective denials often occur, particularly for off-label uses, even when there was a pre-determination in acceptance of the use

Commercial Payers

- Billing for waste with immuno-oncology agents
 - Proper usage of the JW modifier
 - JW modifier will indicate the amount of waste volume represented
 - I-O agents that are single-use vials or single-use package for unused portion are eligible
 - Multi-dose vials are not eligible (and currently not available)
 - Not all payers will pay for waste or only pay for part
 - Some payers do not allow rounding of doses and do not pay for waste (a lose/lose situation for institutions)
 - Proper documentation necessary in the medical record for discarded waste
 - Mandated wastage rationale for any JW lines on Medicare claims on January 1, 2017

Off-label medication process: *Commercial payers*

1. Before off-label use is considered, a **risk/benefit conversation** (medical, financial risks) needs to occur with the patient.
2. Pharmacist and reimbursement specialist work together to submit **pre-determination request** to payer.
3. If denied, an **appeal** can be filed.
4. If still denied, if there is sufficient evidence for off-label use, reimbursement specialist and medication assistance coordinator **explore payment options.**

Off-label medication process: *Commercial payers*

5. Patient and team decide **whether to proceed** with off-label use
6. Managed care, reimbursement specialist, and CFO determine the appropriate amount for the **patient to deposit** toward the treatment
7. Patient submits deposit and **off-label treatment is given**

Denials – Common Reasons

- Lack of pre-certification or authorization
- Medical necessity
- Experimental and investigational
- Requires additional information
- Non-covered service/medication on the plan benefit
- Out of network provider
- Timely filing of claims
- Multiple diagnoses coding for disease states and metastases - payer does not apply correct codes to medications
- Error in number of units billed to payer
- Insurance duplicity or delay

General Rules for Denials

- Discover the root cause of the denial
 - Review payer-specific policy, local coverage determinations, national coverage determinations (LCDs & NCDs)
 - Determine if pre-certification or prior authorization was completed
 - Review documentation
 - Reimbursement is linked to the quality of the bill
 - Coders obtain information from medical record but sometimes required information is missing
- Look for denial trends with payers
 - Drugs, diagnosis, charge threshold
- Exceeds total units allowable

Handling Denials

- Work with Finance to develop a method for routing denials to appropriate personnel
 - Leverage IT to create work queue and notification process
- Consider appropriateness of resources
 - Workload (average number of denials/appeals)
 - Strict appeal timelines of many payers
- Consider training/experience of personnel
 - Ideally a nurse, pharmacist, or pharmacy technician with oncology experience
 - Ability to learn and understand financial systems and processes
 - Ability to navigate electronic medical record

Handling Denials

- Request medical peer-to-peer interaction
 - Offer additional information and rationale to discuss with clinical reviewers who made initial determination
- Monitor for trends
 - Increased denials for repetitive reasons may require payer, billing or provider education
- Hold payer accountable
 - Regardless of the size of the organization
 - Example: Payer not recognizing authorization because it came from a third party administrator and denying claims for reason of “lack of pre-certification”

Handling Denials

- Challenge outdated payer policies
 - Develop reconsideration packet (for both commercial payer and Medicare) with evidence to support addition of covered diagnoses and/or regimens excluded from payer policies

Practical barriers beyond payment

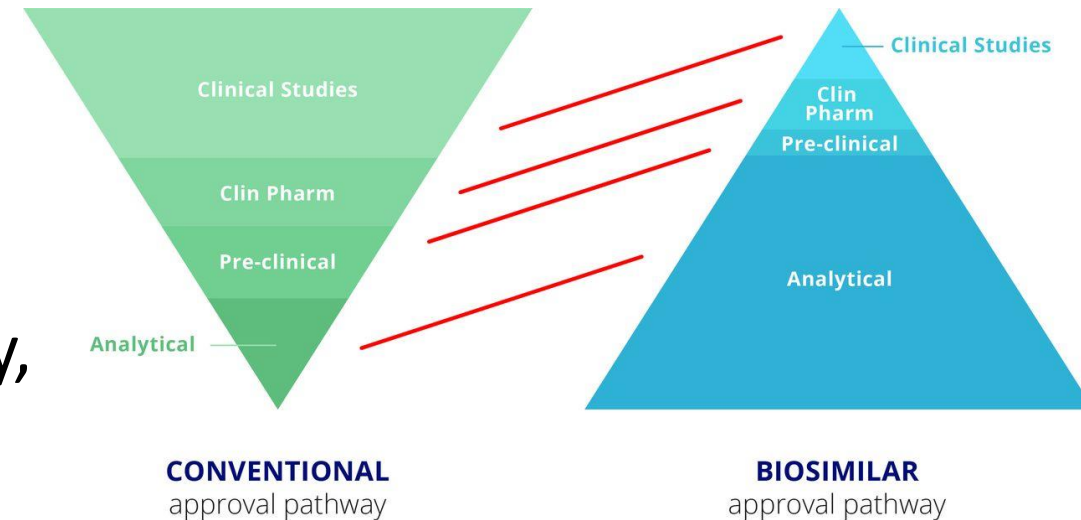
- IO-related medical emergencies
- Biosimilars
- CAR T treatments

IO Management Strategies

- Develop protocols
 - Use your “I-O Champion” to take the lead in developing/revising any treatment protocols that may be impacted by the addition of new I-O therapies in your practice
- Patient education
 - Educate all patients on an I-O therapy to clearly identify themselves as such; make sure that these patients can be quickly identified as being on an I-O therapy in their medical record
- Staff education
 - Ensure staff understand and can identify the most common adverse events associated with I-O products, and know when these events could be potentially be life-threatening and/or require immediate clinical attention

Biosimilars

- FDA requires biosimilars to be highly similar, but not identical, to reference product
- Has to demonstrate no clinically meaningful differences in efficacy, safety, and potency
- Primarily tested through non-clinical pathways – examining structural and functional nature of the product



Biosimilars approved by the FDA

Cancer-related Biosimilar	Reference Product	Approval Date
Zarxio (filgrastim-sndz)	Neupogen (filgrastim)	March 2015
Mvasi (bevacizumab-awwb)	Avastin (bevacizumab)	September 2017
Ogivri (trastuzumab-dkst)	Herceptin (trastuzumab)	December 2017
Fulphilia (pegfilgrastim-jmdb)	Neulasta (pegfilgrastim)	June 2018
Nivestym (filgrastim-aafi)	Neupogen (filgrastim)	July 2018
Truxima (rituximab-abbs)	Rituxan (rituximab)	November 2018
Herzuma (trastuzumab-pkrb)	Herceptin (trastuzumab)	December 2018
Ontruzant (trastuzumab-qyyp)	Herceptin (trastuzumab)	March 2019
Kanjinti (trastuzumab-anns)	Herceptin (trastuzumab)	June 2019

Biosimilar	Reference Product	Approval Date
Inflectra (infliximab-dyyb)	Remicade (infliximab)	April 2016
Erelzi (etanercept-szzs)	Enbrel (etanercept)	August 2016
Amjevita (adalimumab-atto)	Humira (adalimumab)	September 2016
Renflexis (infliximab-abda)	Remicade (infliximab)	May 2017
Cyltezo (adalimumab-adbm)	Humira (adalimumab)	August 2017
Ixifi (infliximab-qbtx)	Remicade (infliximab)	December 2017
Retacrit (epoetin alfa-epbx)	Procrit (epoetin alfa)	May 2018
Hyrimoz (adalimumab-adaz)	Humira (adalimumab)	October 2018
Udenyca (pegfilgrastim-cbqv)	Neulasta (pegfilgrastim)	November 2018
Eticovo (etanercept-ykro)	Enbrel (etanercept)	April 2019

Biosimilars – practical considerations

- Healthcare providers, pharmacists, and patients are critical for biosimilar acceptance and usage
- Substitution policies vary by state – “interchangeable products” can be substituted without prescriber input
- Incentives to prescribe biosimilars from Medicare



Unique considerations for CAR T therapies

- Large up-front cost instead of smaller costs over time
- Potential side effects can lead to large costs as well
- Medicare coverage:
 - National coverage determination in August 2019
 - Will be covered by Medicare if administered in health care facilities that follow FDA REMS (risk evaluation and mitigation strategies)
 - May be covered for off-label indications

UC San Diego Health Practices

- Checkpoint inhibitors
 - Infusion Center RN assesses patient if not seen by the physician or advanced practice provider (APP) within 7 days of administration
 - If iRAE symptoms present, physician contacted regarding decision to proceed
- Approval of biosimilars via Pharmacy & Therapeutics (P & T) interdisciplinary committee
 - Currently only one of the 18 FDA-approved biosimilars are approved by P & T
 - Insurance approves biosimilar ONLY vs reference product → requires pharmacy approval
- CAR-T
 - Process of eligibility analogous to BMT eligibility (i.e. caregiver support required)
 - Lymphodepletion chemotherapy administered outpatient followed by inpatient admission for 7 days for infusion & monitoring
 - Patients remain at UC San Diego for first 8 weeks
 - Insurance authorization to letter of agreement (between insurance and hospital) can be challenging
 - i.e. Insurance associated with various states
 - Tisagenlecleucel (Kymriah)
 - HIV/Hep B/Hep C + → Infectious disease hold and cells cannot be shipped for processing
 - Axicabtagene ciloleucel (Yescarta)
 - Fresh product, timing is KEY for collection (requires significant coordination with apheresis and company)

Future Considerations

- Payer ability to keep up with accelerating evidence-based new indications (e.g., new lines of therapy, new tumor types)
- Increasing utilization of checkpoint inhibitors in combination with a host of agents (e.g., chemo, targeted, immunotherapeutic)
- Potential for coverage policies to be biomarker driven (e.g., PD-L1 overexpression)
- Financial implications of agents becoming first line
- Emergence of biosimilars and CAR T treatments