Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Practical Barriers in Cancer Immunotherapy Treatment

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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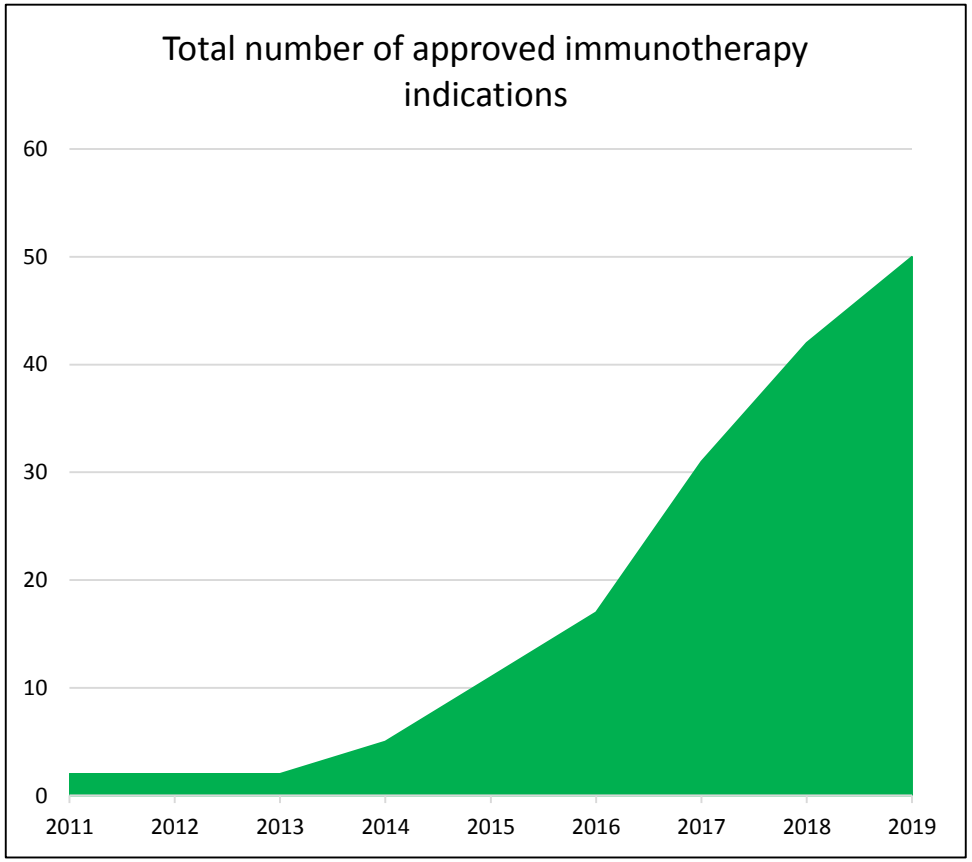
Disclosures

- I have the following disclosures:
  - Speakers Bureau for Exelixis, Inc
  - Advisory board for Array BioPharma
- 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!)

Financial Considerations

Processes for High Dollar Medications

Medicare

Commercial Payers

Denials

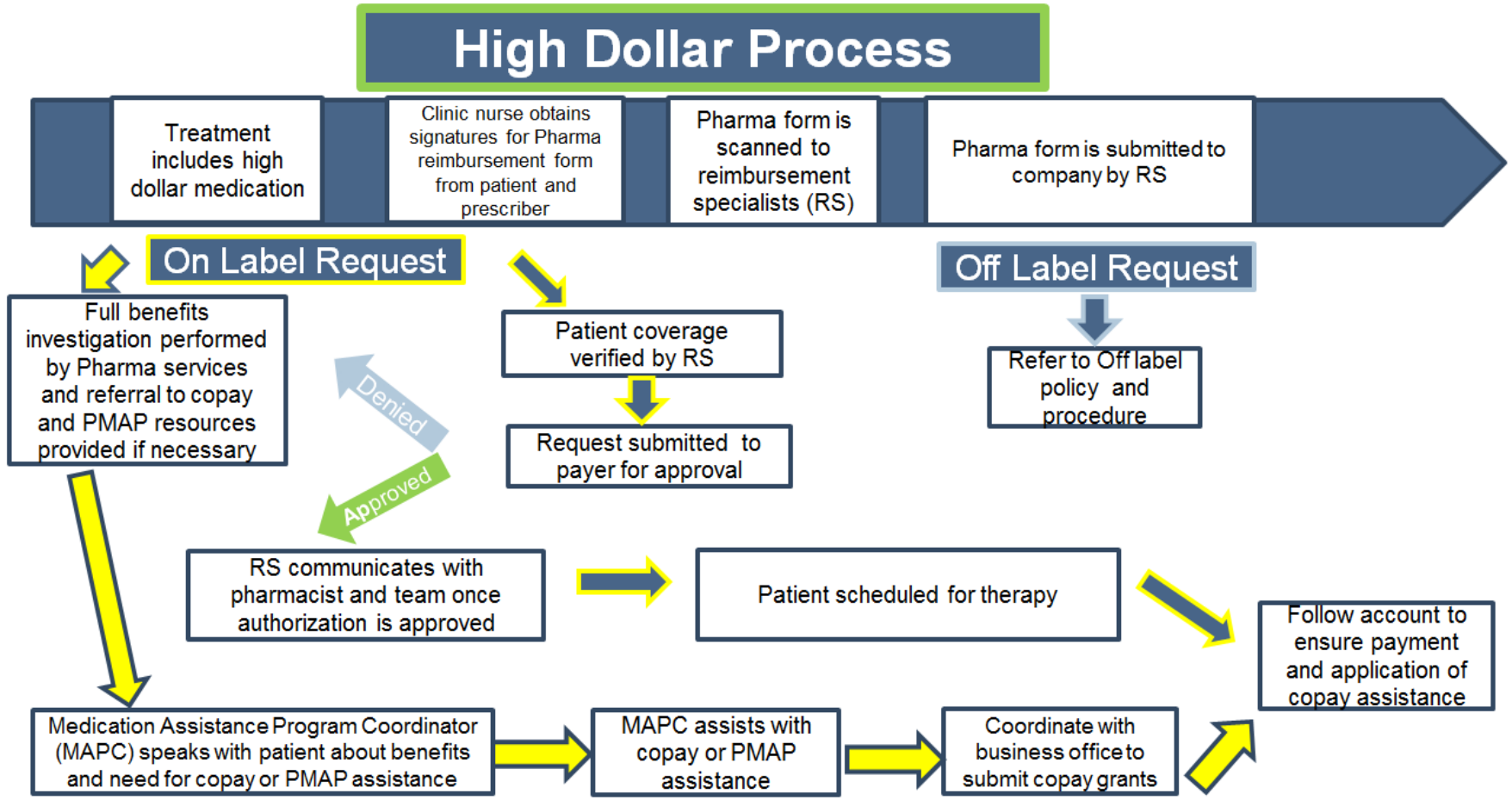
Manage Reimbursement/Finances

- 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

High Dollar Process



Medicare

- Most Medicare Administrative Contractors (MAC) have at least one I-O agent for 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 200 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

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Practical Barriers Beyond Payment

IO-Related Medical Emergencies

Biosimilars

CAR T Treatments

AAEM American Academy of Emergency Medicine
ACCC Association of Community Cancer Centers
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Management Strategies for IO-Related Medical Emergencies

Develop protocols

- Develop/revise any treatment protocols that may be impacted by the addition of new I-O therapies and/or I-O-related medical emergencies in your practice
- Develop policies/procedures to ensure appropriate and timely delivery of treatments for I-O medical emergencies and financial reimbursement thereafter

Patient education

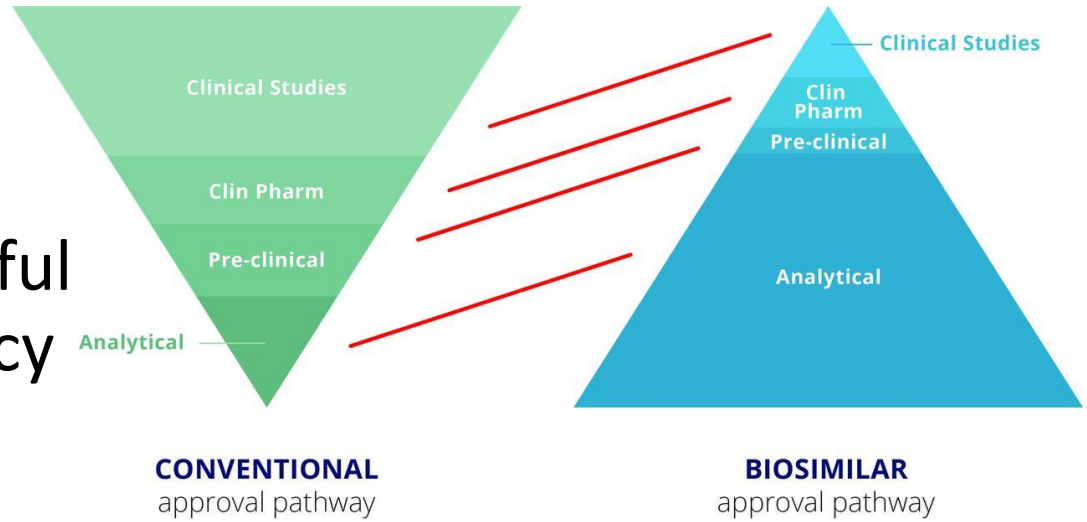
- Educate all patients on an I-O therapy to clearly identify themselves as such and to recognize adverse events
- Ensure that these patients can be quickly identified as being on I-O therapy in their medical record

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
- Educate staff on policies/procedures regarding treatment of and financial reimbursement for medical emergencies

Biosimilars

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



Isaacs *et al*, Consid Med 2017.

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
  - Vary by institutional policies (e.g. Pharmacy and Therapeutics committee may approve products to be interchanged by pharmacist without prescriber approval)
- Incentives to prescribe biosimilars from Medicare
- Formulary product (reference or biosimilar) varies by insurance company
  - Product (reference or biosimilar) preferred by insurance company may change with limited or no notice

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

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Local Practices

Pharmacy Patient Assistance Program

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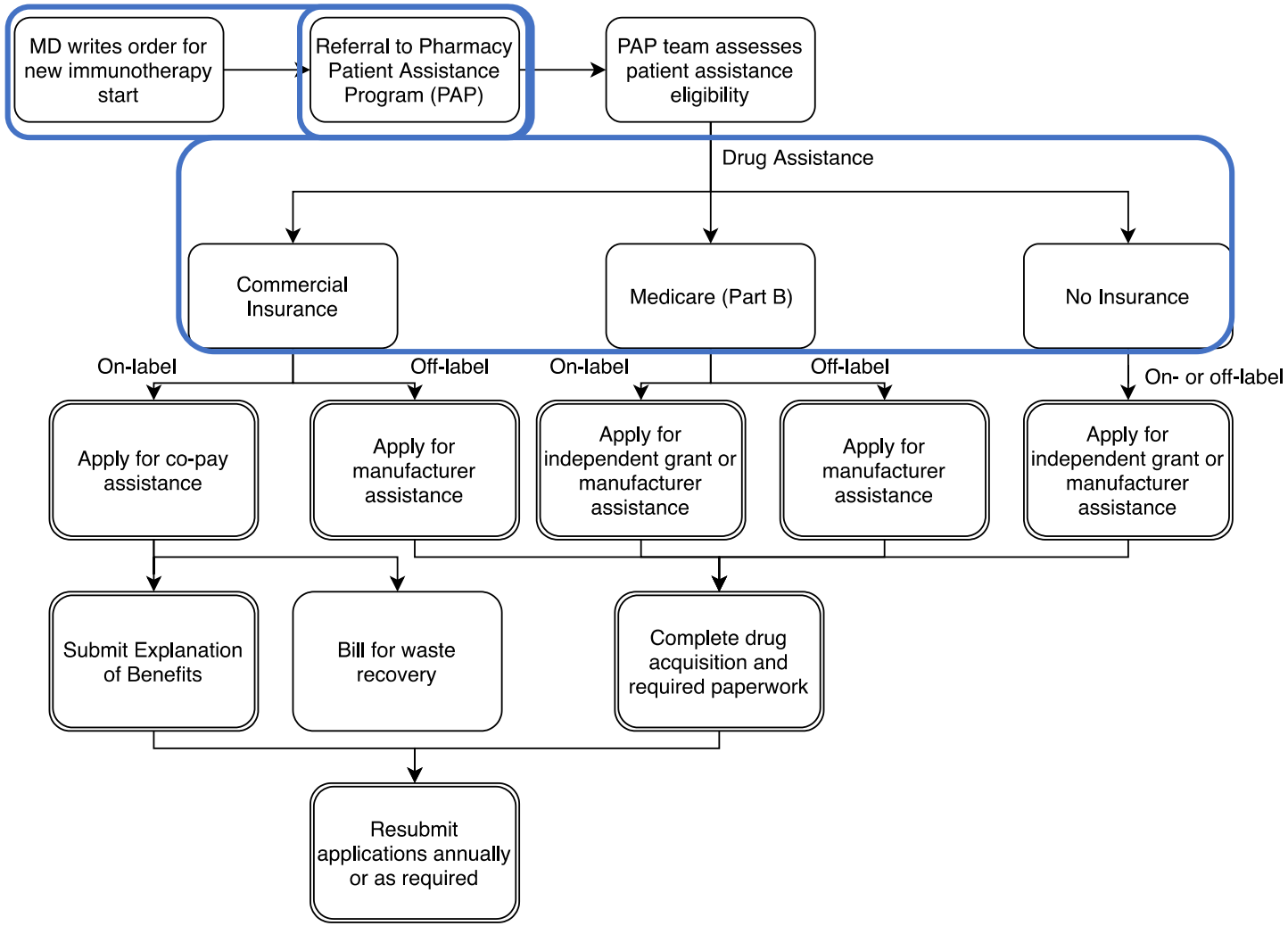
All patients (new starts) are referred to PAP team through electronic medical record

PAP team comprised of pharmacy technicians

PAP team assists with drug assistance and waste recovery for all intravenous therapy

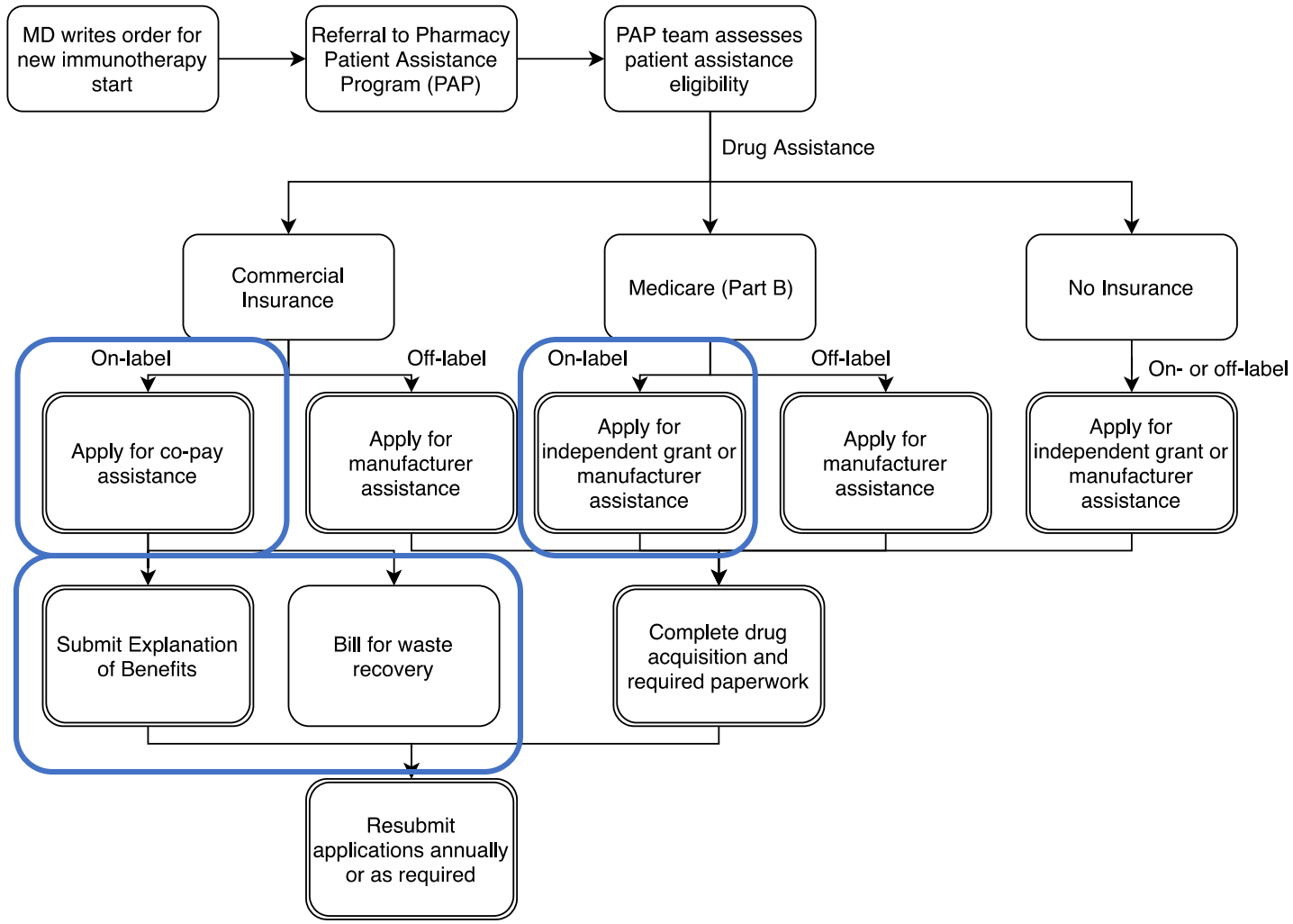


Levine Cancer Institute

On-label processes

Commercial insurance: patients may qualify for co-pay assistance

Commercial insurance:
-submit EOB
-bill for waste recovery



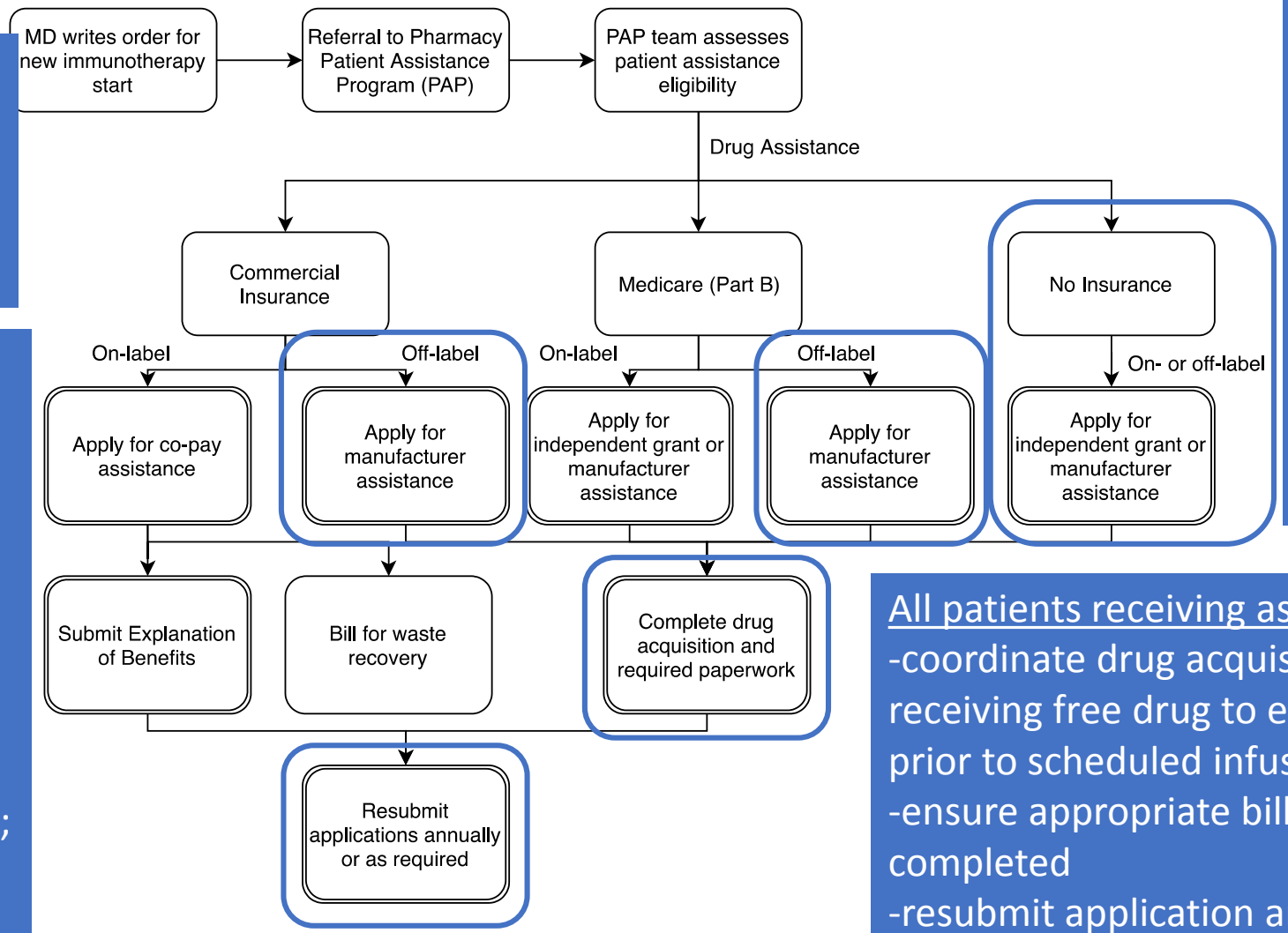
Medicare (or other government insurance):
-will not qualify for co-pay assistance through manufacturer
-may qualify for independent grants or free drug through manufacturer based on income
-per institutional policy, not allowed to pursue assistance for on-label indications for Medicare patients

Levine Cancer Institute

Off-label processes

Commercial insurance: will need denial from insurance prior to obtaining free drug from manufacturer

Medicare (or other government insurance):
-denial from insurance is difficult to obtain prior to drug administration as Medicare does not require prior authorizations
-may need to obtain drug coverage through manufacturer retroactively; need to confirm with manufacturer



No insurance:
-will need to apply for manufacturer assistance or independent grants for all drugs regardless of indication
-typically approved with limited barriers unless very income (above manufacturer or grant income limits)

All patients receiving assistance:
-coordinate drug acquisition for patients receiving free drug to ensure drug availability prior to scheduled infusion time
-ensure appropriate billing and paperwork is completed
-resubmit application annually

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 other 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