

# FDA Summary and Discussion Topics

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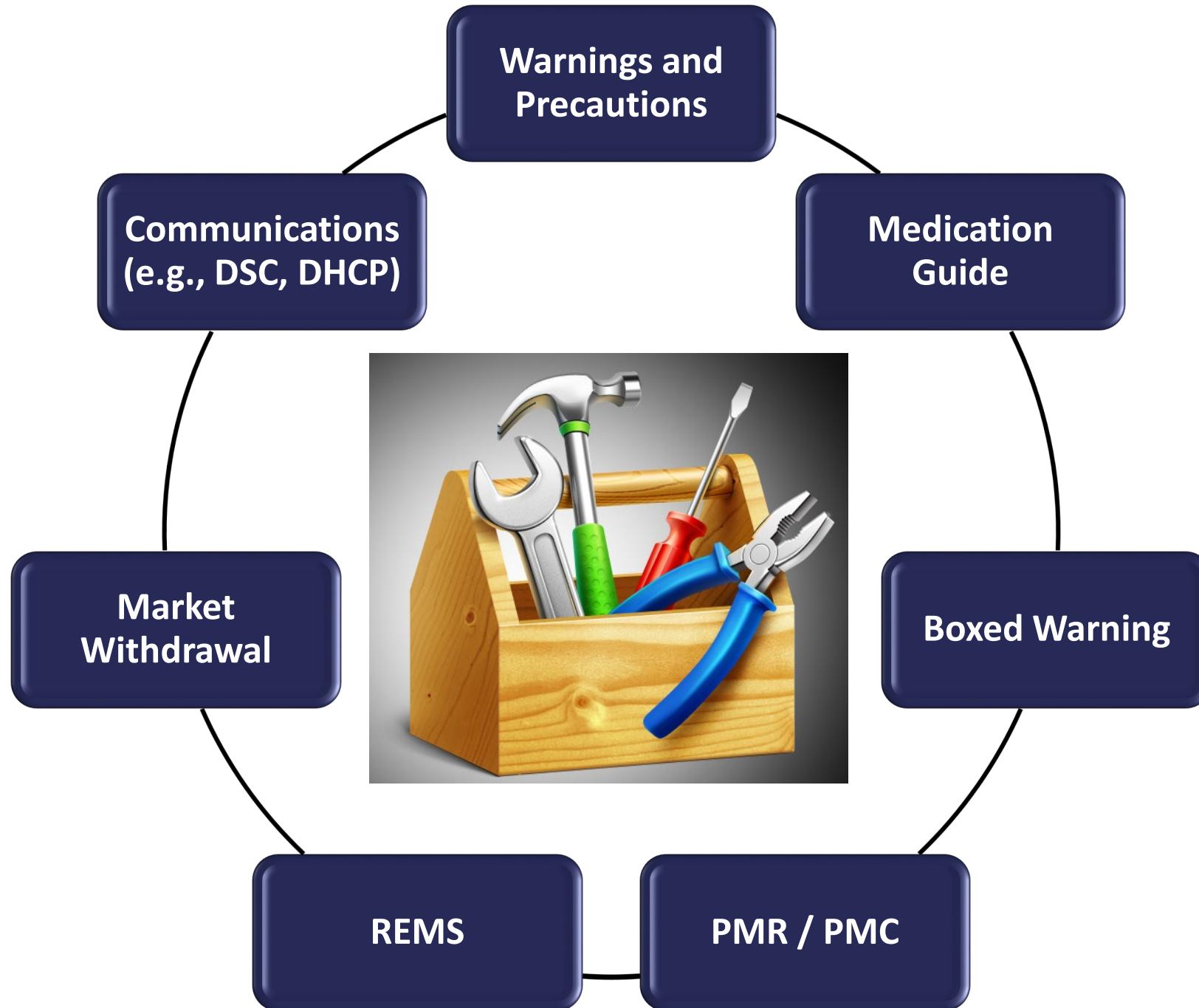
# Summary

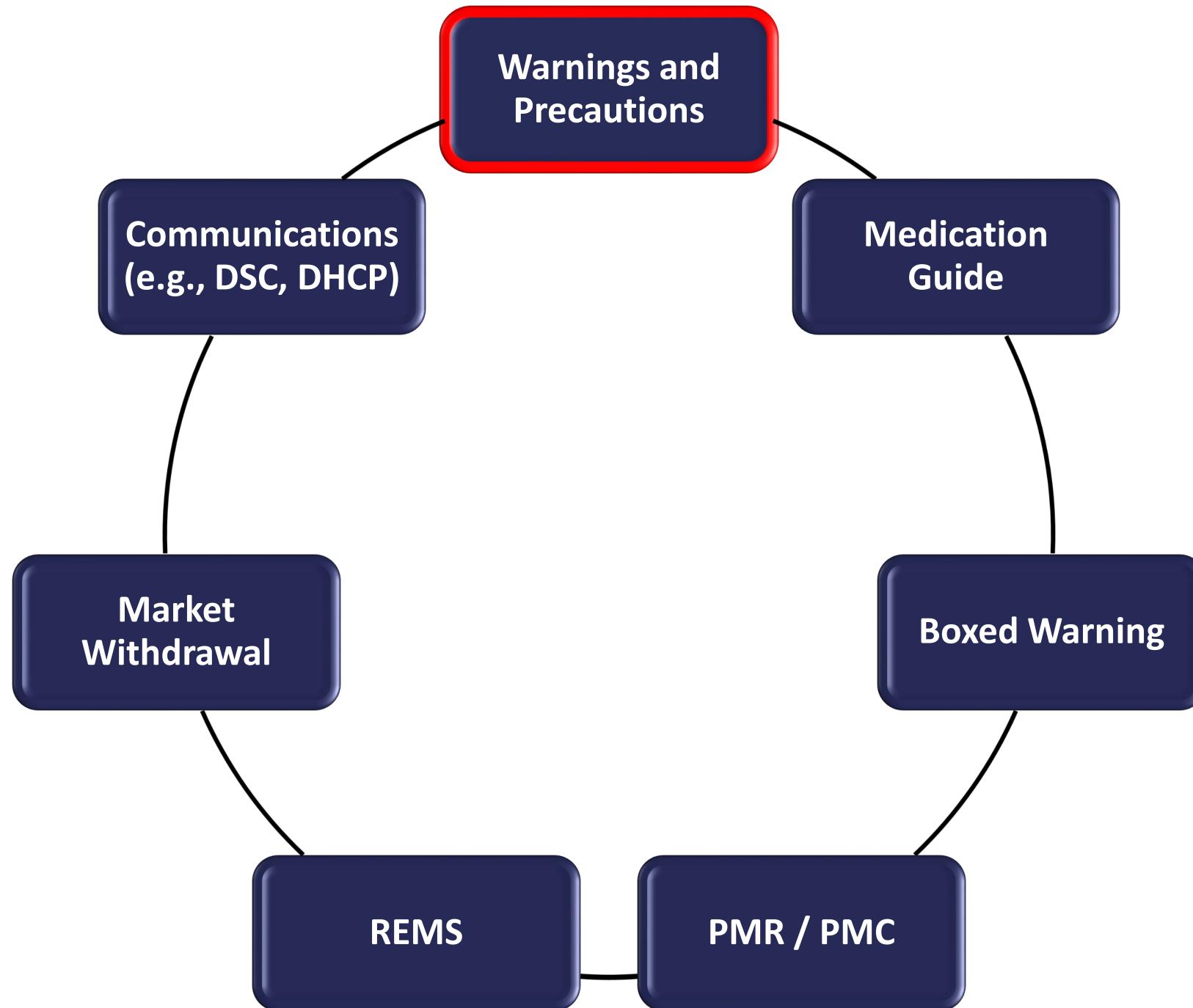
- Long-standing safety issue with montelukast and neuropsychiatric events
- Absence of strong safety signal in clinical trials for allergic rhinitis and asthma
- FAERS postmarketing reports
  - Wide range of events
  - Sparse information regarding withdrawal
  - Limitations
- Literature review
  - Mixed results from observational studies

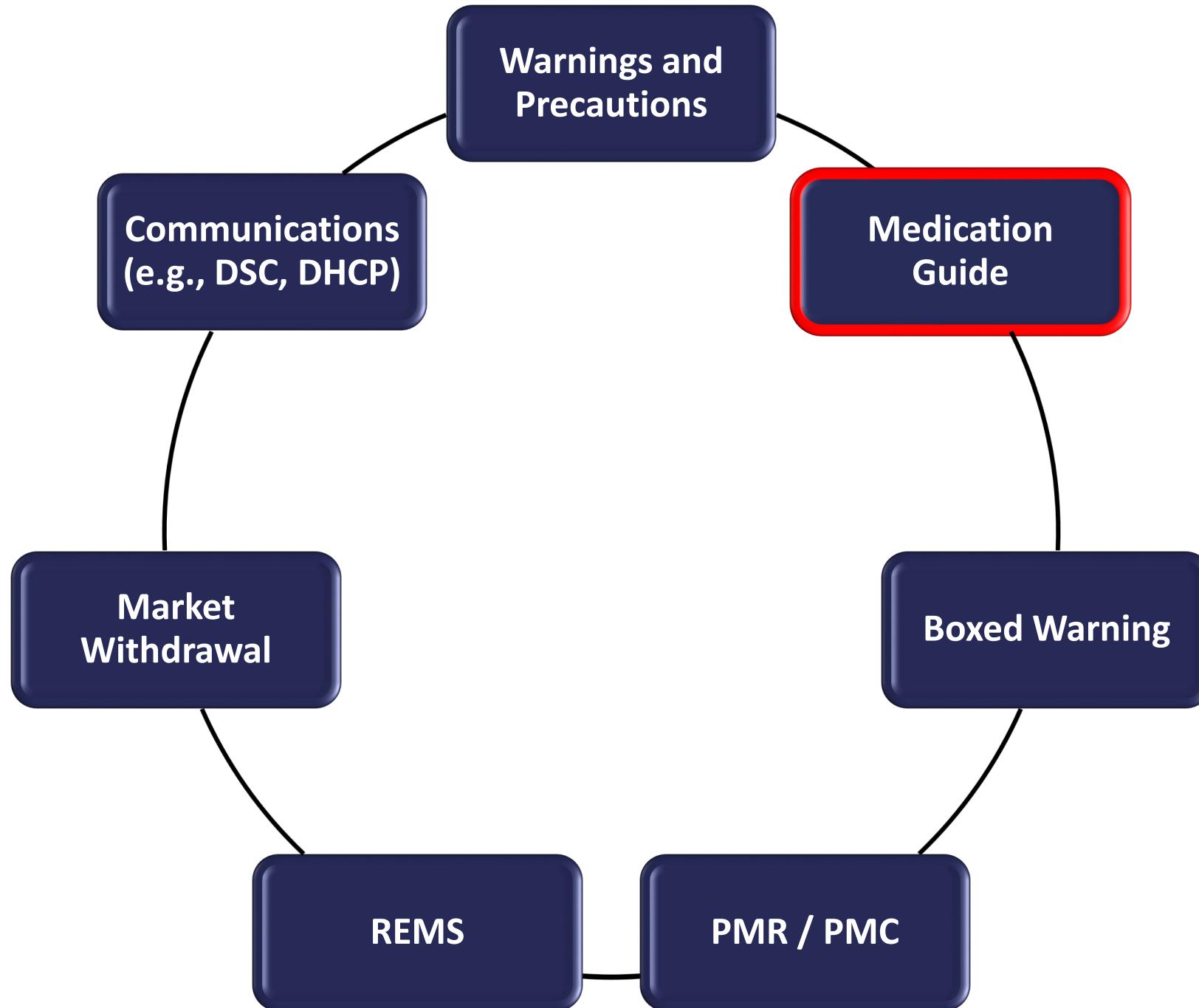
# Summary

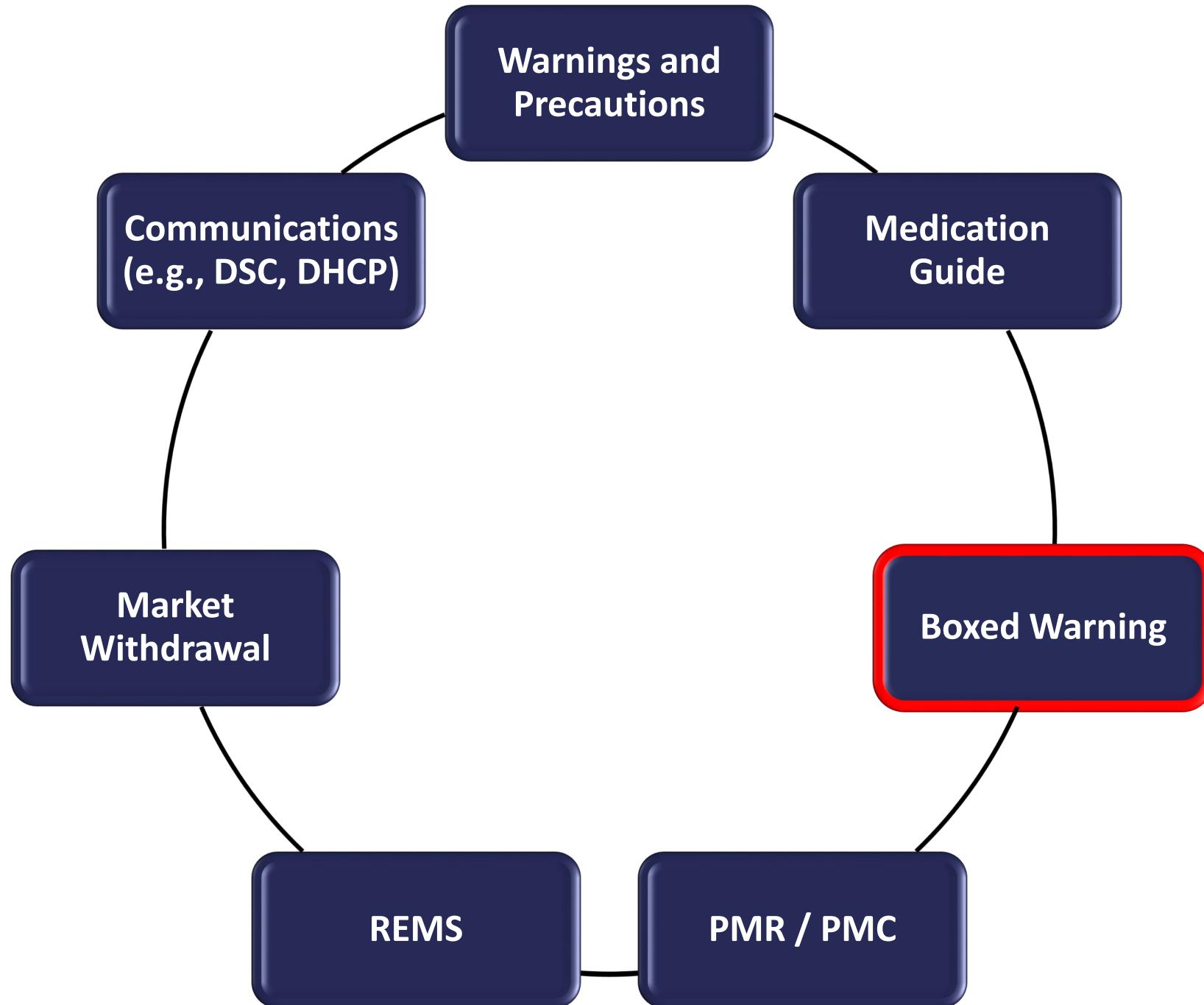
- Sentinel study
  - No statistical association with montelukast use and neuropsychiatric events of inpatient depressive disorder and self-harm
  - Death due to suicide was rare and limited to adults with a prior psychiatric history
- Communication is a challenge
  - Existing safety issue
  - Available data have limitations and/or inconclusive

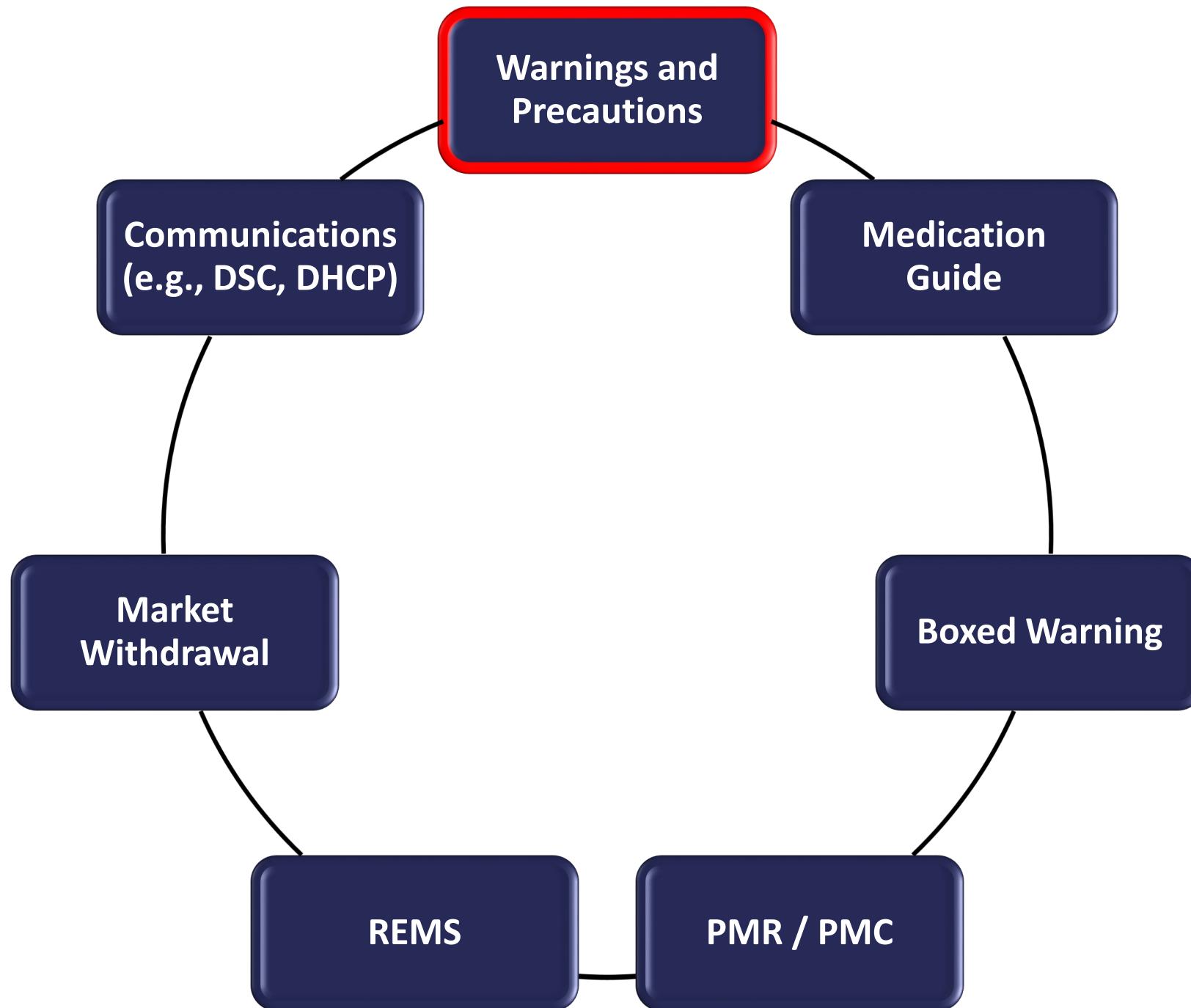
# Regulatory considerations

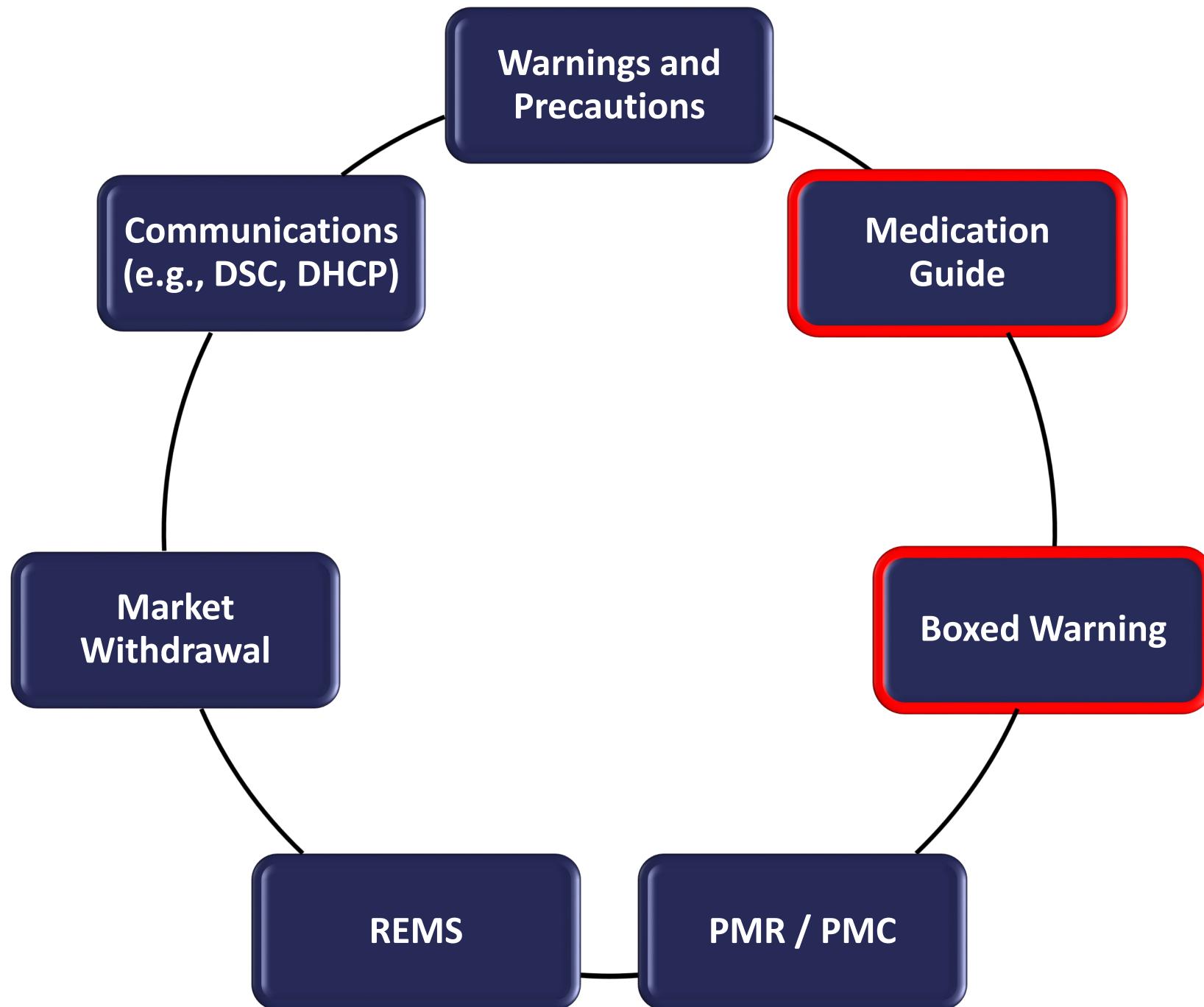


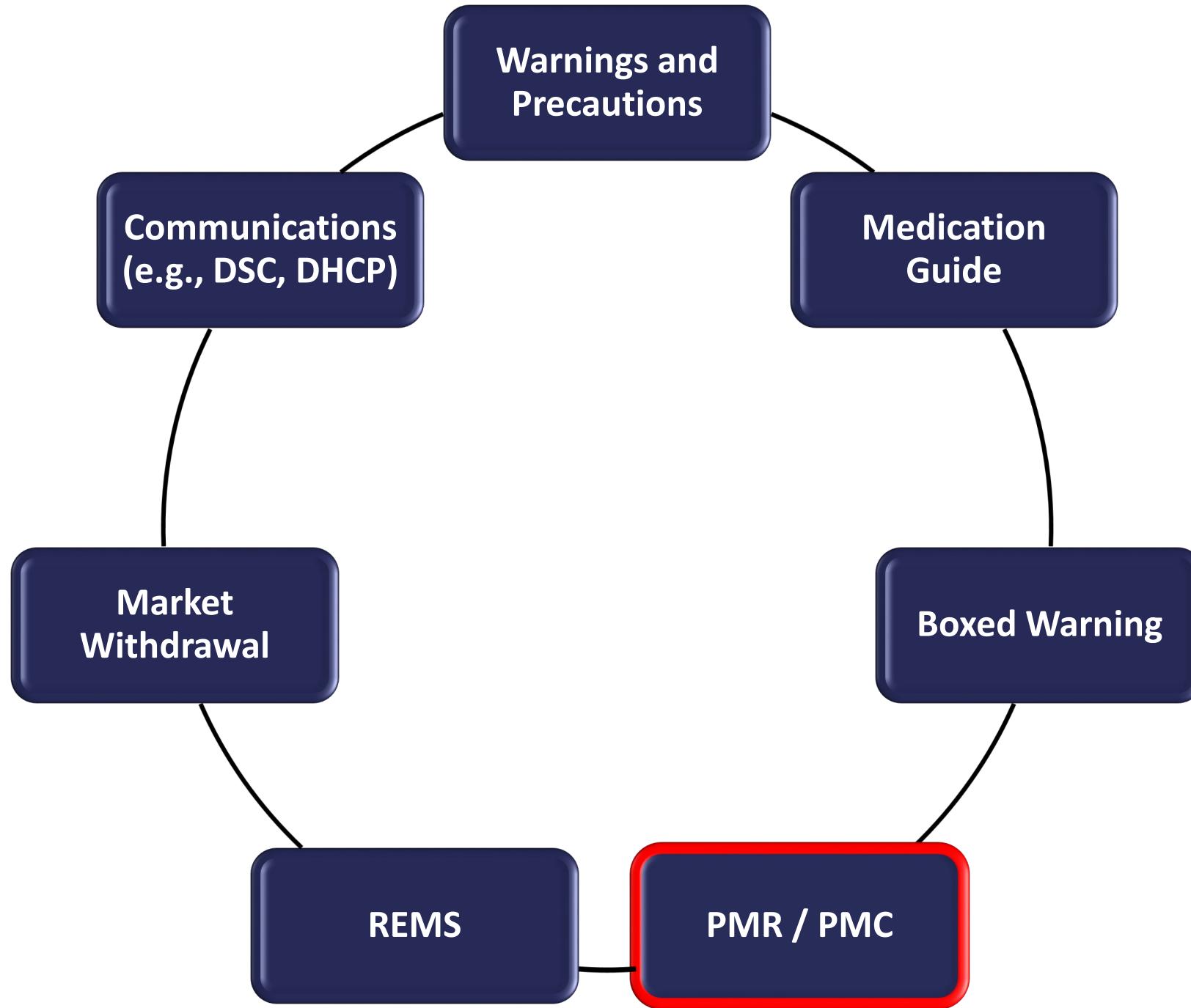


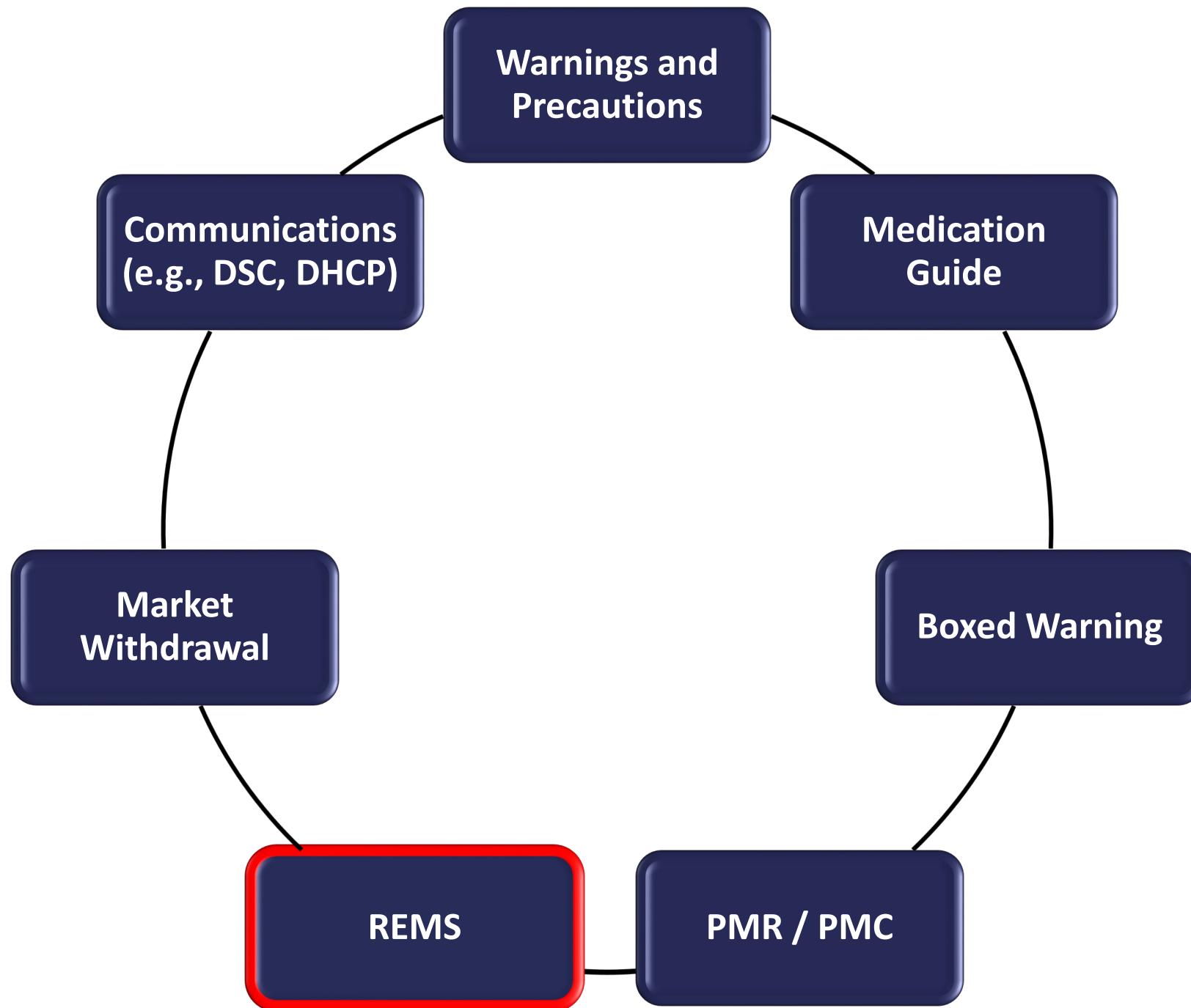


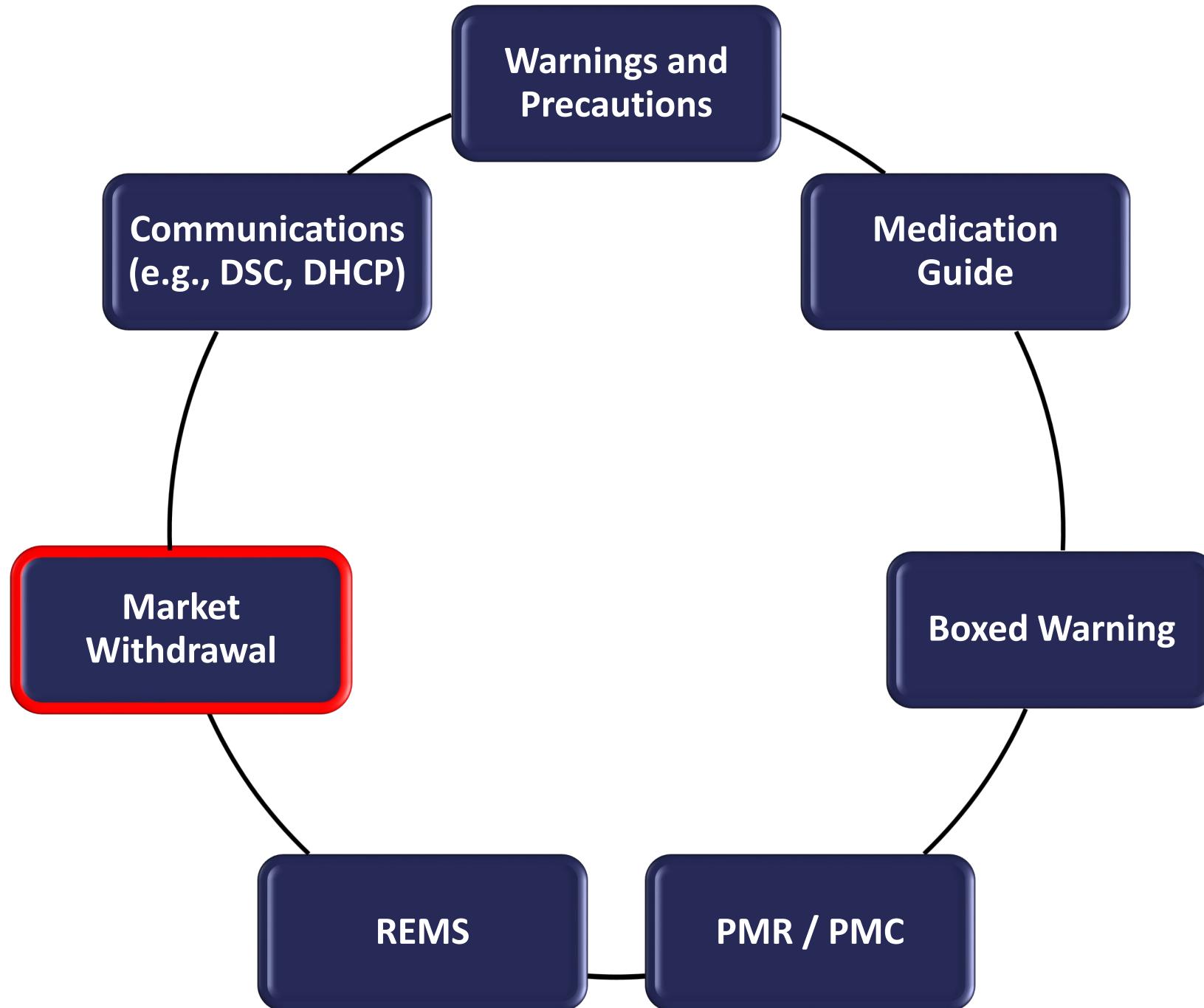


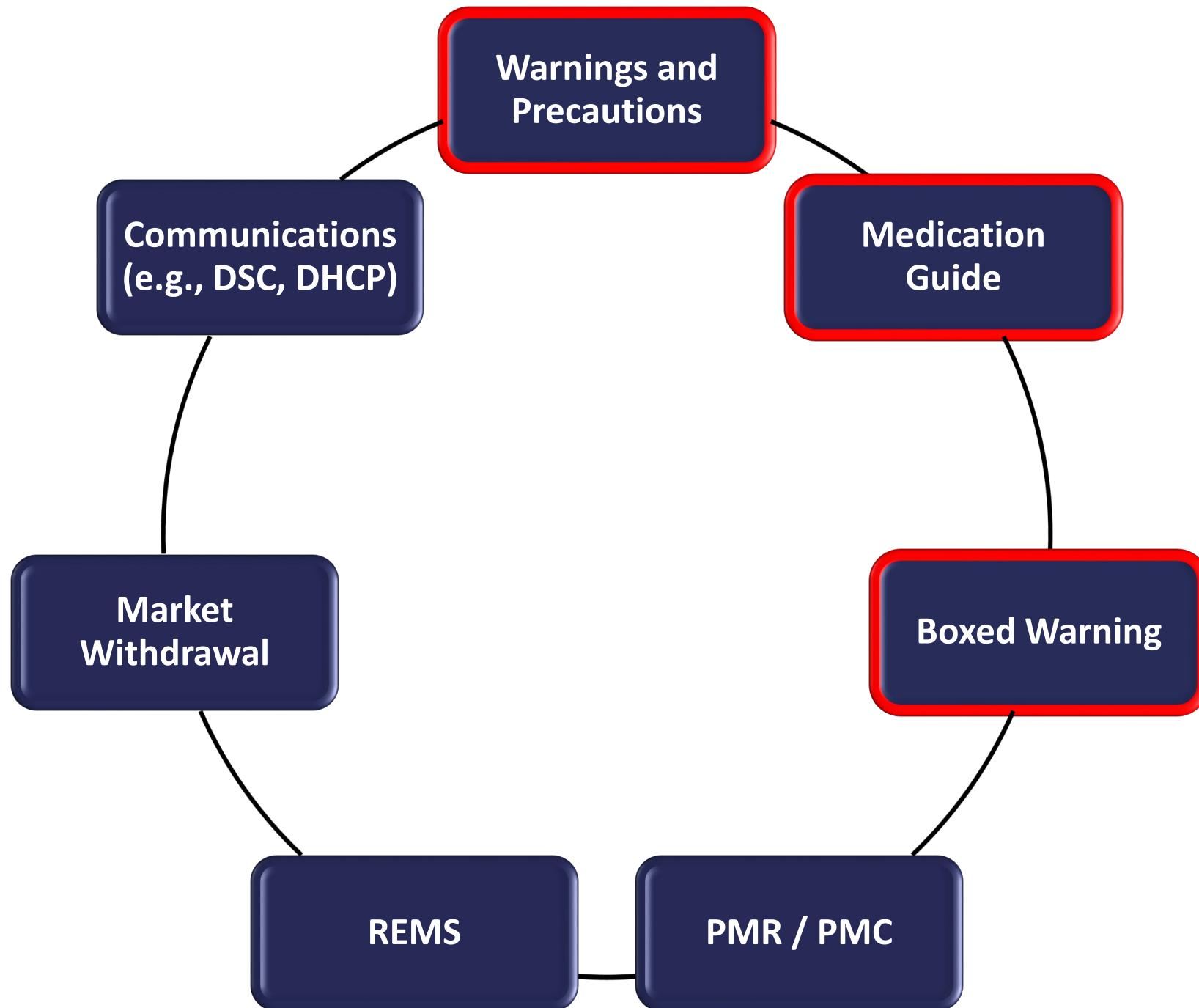












# Warnings and Precautions

- Describes clinically significant adverse reactions or potential safety hazards
- *21 CFR 201.57(c)(6)*
  - *Adverse reactions are serious or otherwise clinically significant and have implications for prescribing decisions or patient management*
  - *Reasonable evidence of causal association*
- Order should reflect relative clinical significance

# Medication Guide

- FDA required patient labeling
- 21 CFR 208.1
  - *Patient labeling could help prevent serious adverse effects*
  - *Serious risks (relative to benefits) of which patients should be made aware because information could affect decision to use the product*
  - *Patient adherence instructions for use is crucial to drug's effectiveness*

# Boxed Warning

- Calls attention to serious or life-threatening risks
- 21 CFR 201.57(c)(1)
  - *Adverse reaction so serious in proportion to benefit that it is essential to consider in assessing risks and benefits of using the drug*
  - *Serious adverse reaction that can be prevented or reduced by appropriate use*
  - *Approved with restrictions to ensure safe use because drug can be safely used only if distribution or use is restricted*

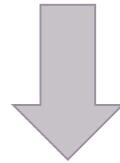


# Previous Communication Efforts

- Labeling updates
- Drug Safety Communications
- Dear Health Care Provider letters
- Medscape interview
- Publication in AAP News
- Discussion at open Advisory Committee meetings

# Communication Strategies

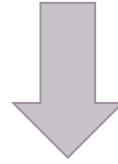
## Target Audience



Patients / Caregivers  
Primary care physicians  
Physician assistants  
Nurse practitioners  
Pediatricians  
Specialists  
Pharmacists  
School nurses

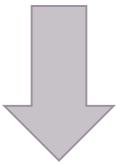
# Communication Strategies

## Target Audience



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## Target Organizations



Professional Societies  
(AAP, AAFP, AAAAI)  
Nursing Associations  
Asthma Networks

# Communication Strategies



# Questions for the Committee

*1) Discuss the neuropsychiatric safety findings presented for montelukast*

# Questions for the Committee

*2) Discuss the current labeling for montelukast, including:*

- *Current Warnings and Precautions*
- *Request for Medication Guide and Boxed Warning*

# Questions for the Committee

*3) Discuss your recommendations for communication strategies*

- *Target audience*
- *Target organizations*
- *Modalities of communication*



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ADMINISTRATION**