

Landscape of OA Drug Development

CDER Regulatory Perspective

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DAAP focuses on drug development for pain of OA

- DAAP regulates drugs and biologics in the therapeutic areas of anesthesiology, addiction medicine, and analgesics.
- We regulate essentially all analgesics excepting a few specific painful conditions (e.g. migraine, endometriosis, interstitial cystitis).
- OA falls within our jurisdiction. However, with the advent of the concept of Disease Modifying Osteoarthritis Drugs (DMOADs), DAAP's role is to regulate drugs for the pain of OA

Products Under Development For Pain Of OA

- NSAIDs
- Glucosamine and analogs
- Anti-Nerve Growth Factor monoclonal antibodies
- Novel agents (e.g. based on targets proposed for symptomatic OA therapy)
- Other nutritional supplements
- Reformulated corticosteroids
- TRPV1 agonists

DAAP regulates drugs for the pain of OA

- Historically, DAAP or its predecessors approved drugs for symptomatic OA with some form of an indication containing, “...signs and symptoms of osteoarthritis”
 - Supported by three co-primary endpoints: WOMAC pain, WOMAC function, patient global assessment
- Because of interest in DMOADs and given that DAAP regulates analgesics, this has been reconsidered:
 - Drugs regulated in DAAP do not affect signs of OA
 - Essentially all drugs under development for OA in DAAP are currently considered for some form of “management/treatment of pain of OA”
 - Clinical trials require a single endpoint based on a fit-for-purpose self-reported measure of pain intensity
- Joint-specific indications may be appropriate for certain products

Typical DAAP OA Selection Criteria

- Adults diagnosed with OA of the hip or knee based on ACR criteria and confirmed with knee x-ray (KL \geq 2)
- WOMAC pain or NPRS \geq 5
- Other causes of index joint pain must be excluded (inflammatory joint disease, crystalline disease, etc.)
- Patients with a planned surgical procedure are excluded
- Patients who have received intra-articular therapies within a certain period of time are excluded

Primary OA Outcome Measure Used in DAAP

- Generally, to support an indication of “pain of OA,” an acceptable primary measurement instrument is a 0-10 point Numerical Pain Rating Scale (NPRS)
- The joint-specific, accepted instrument for knee and hip OA is the WOMAC pain subscale

Secondary Outcome Measures for OA studies (DAAP)

- **WOMAC function**
- **Patient Global Assessment**
- Visual Analog Scale
- Joint-specific assessments of pain and function
- Brief Pain Inventory
- OMERACT-OARSI
- Quality of life instruments



Primary Efficacy Endpoint for OA Studies (DAAP)

- Primary efficacy endpoint is the change in pain intensity from baseline (average PI in week immediately prior to randomization) to end-of-treatment (average PI in last week of treatment)
- Registrational trials must be of at least 12-weeks duration (double-blind)



Thank you



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