Sunday General Session

**Migraine Prophylaxis and Treatment**

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Department of Neurology
Baylor Scott & White Health
Temple, Texas

**Educational Objectives**
By the end of this activity, the participant should be better able to:
1. Increase awareness and interest of headache in primary care.
2. Provide a clinical framework for the diagnosis, prophylaxis, and treatment of migraine.
3. Identify risk factors for migraine progression and develop a plan for headache treatment based upon migraine staging.

**Speaker Disclosure**
Dr. Ready has disclosed that he is on the speaker’s bureau for Anavir and on the advisory board for Alder.
Migraine: Prophylaxis and Treatment

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Disclosures & Shameless Plug

• Family Physician
• Speaker Bureau for Avanir Pharmaceuticals
• Advisory Board for Alder Biopharmaceuticals
• UCNS Certified in Headache Medicine
• Certified in Pain Management – AAPM
• Just one blind man at the elephant
• You can learn a lot at a Headache meeting

B.O.L.O.

When we wish to perfect our senses, neuroplasticity is a blessing; when it works in service of pain, plasticity can be a curse.

Norman Doidge, MD – Canadian psychiatrist

AHS Choosing Wisely

• Don’t perform neuroimaging studies in patients with stable headaches that meet criteria for migraine
• Don’t perform CT imaging for headache when MRI is available, except in emergency settings
• Don’t recommend surgical deactivation of migraine trigger points outside of a clinical trial
• Don’t prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders
• Don’t recommend prolonged or frequent use of over-the-counter pain medications for headache

Problem Solving

Everything that happens, happens as it should

Marcus Aurelius

“At some point, everything is going to go South on you. You’re going to say, ‘This is it. This is how I end.’ Now, you can either accept that or you can get to work. That’s all it is. You just begin.

You do the math. You solve one problem, and then you solve the next problem, and then solve the next problem, and if you solve enough problems, you get to come home.”

Andy Weir, The Martian

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Brain Basics

- Wired for Action not thought
  - If you have to think about running away from the tiger you are already lunch
  - Can’t think when you’re acting
- Doesn’t like distress
  - When distressed, the Brain wants to distract
  - Only understands pain as a threat to survival
  - Doesn’t distinguish among pain types
  - This focus reinforces pain as “What you pay attention to grows”
- Won’t reflexively “see” when it doesn’t have to respond
  - No automatic appreciation

Pain Basics

- Event → Experience
  - An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

Pain Basics: Sensory Discriminative → Vols. (Sensory signal information/spatial & temporal) → Sensory/somatosensory cortex. It is the Signal.

Pain Basics: Affective Motivational → Amps. (Thalamus, anterior cingulate cortex, prefrontal cortex, amygdala, hippocampus, insula & limbic system) throughout the cortex. Provides the Meaning of the Signal.

Limbic Influences in Pain

- All Pain has meaning
- The Sorrow that hath no vent in tears may make organs weep— Henry Maudsley
- (When) the mind is hurt the body cries out Italian Proverb
- The body remembers what the mind forgets— J.L. Moreno

Not All Pain is Nociceptive

- San Francisco Spine Study 1992
- Five childhood traumas: Loss of parent, emotional neglect, substance abuse, physical abuse, sexual abuse
- No risk factors = 95% chance surgical cure
- 1-2 risk factors = 73% chance surgical cure
- 3 or more risk factors = 15% chance of a surgical cure
- Increased incidence of Chronic Migraine in victims of Sexual Abuse

Headaches in Primary Care

- Primary → Nervous system you are born with or acquire (trauma) and the environment you are in
  - Migraine, Cluster, Tension Type
- Secondary → Headaches that are caused by something else
  - Infection, Mass, Vascular, Trauma
SNOOP4: Ruling Out Secondary Causes of Headache in Migraine

- Systemic symptoms and signs
- Neurologic symptoms or signs
- Onset: peak at onset or <1 minute
- Older: after age 50 years
- Previous headache: pattern change
- Postural, positional aggravation
- Precipitated by valsalva, exertion, etc.
- Papilledema

Imaging

- Pattern recognition
  - Abnormal neurological exam
- When to get a CT – Suspect a bleed
- When to get an MRI
  - Mass/Aneurysm
  - Pressure HA – High or Low (low must have contrast)
- Remember a radiologist is talking
  - WMLUS

What is Migraine?
Patient Preferred Explanation

- You are genetically predisposed to migraine because of abnormal hyper-excitability of neurons in certain regions of the brain.
- We believe that this hyper-excitability is caused by in part mutations in channels on the surface of neurons that, when triggered, allow for the abnormal flow of sodium, calcium, and other brain chemicals in and out of the cell.

More than a Headache

- TTH & Migraine 2nd & 3rd most prevalent medical disorder worldwide
- Migraine accounts 30% of global burden of disability & 50% of all Neuro disability
- 4th leading cause of disability in women & 7th overall
  Lancet 2012

Severe Migraine is Ranked in the Highest Disability* Class by WHO

<table>
<thead>
<tr>
<th>Disability Class</th>
<th>Disability Weight</th>
<th>Indicator Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00-0.02</td>
<td>Vomiting, face, weight for height less 2 SDs</td>
</tr>
<tr>
<td>2</td>
<td>0.02-0.32</td>
<td>Watery diarrhea, severe sore throat, severe anemia</td>
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<tr>
<td>3</td>
<td>0.12-0.24</td>
<td>Radius fracture in a stiff cast, incontinence, dysesthesia, rheumatoid arthritis, angina</td>
</tr>
<tr>
<td>4</td>
<td>0.24-0.38</td>
<td>Below the knee amputation, deafness</td>
</tr>
<tr>
<td>5</td>
<td>0.30-0.50</td>
<td>Rectoscopic fistula, mild mental retardation, Down syndrome</td>
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<tr>
<td>6</td>
<td>0.50-0.70</td>
<td>Unipolar major depression, blindness, paraplegia</td>
</tr>
<tr>
<td>7</td>
<td>0.70-1.00</td>
<td>Active psychosis, dementia, severe migraine, quadriplegia</td>
</tr>
</tbody>
</table>

*Assessment of disease severity determined by Global Burden of Disease researchers using the porous trade-off method, which includes judgments about the trade-off between quality and quantity of life. Spectrum ranges from 0 (perfect health) to 1 (death).

Migraine – Most Common Headache in Clinical Practice

- Patients seen in primary care
- IHS diagnosis based on diary review

- Migraine-type
- Episodic Tension-type
- Unclassifiable
**Why Migraine?**
Why Should I Care?

- 6%♂, 18%♀, 33-37% reproductive♀, 4% CDH
- Returning armed forces 38%♂, 58%♀, 20% CDH
- Most common 25 – 55 yr (most productive years)

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**Why Should I Care?**

- Developed by Lipton, Cady, Farmer, & Bigal
- 1st doctor/patient book
- Based on frequency not severity of HA
- www.managingmigraine.org

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**Staging Migraine**

- **Stage 1 – Infrequent Episodic**
  - ≤ 1 Migraine/month
- **Stage 2 – Frequent Episodic**
  - 2-6 Headache days/month
- **Stage 3 – Transforming Migraine**
  - 7-14 Headache days/month
- **Stage 4 – Chronic Migraine**
  - ≥ 15 Headache days/month

  - Education plus effective acute treatment
  - Education plus effective acute treatment with back up; medications limits; preventive measures
  - Education; preventive pharmacology; acute pharmacology with back up & rescue; behavioral
  - Education; preventive pharmacology; judicial acute pharmacology with back up and rescue; behavioral interventions

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**Risk Factors for Progression**

**Modifiable**

- Attack frequency
- Poorly treated acute HA
- Obesity
- Snoring/OSA
- Stressful life events
- Medication overuse
- Caffeine overuse

**Not Modifiable**

- Age
- Female sex
- Low education or socioeconomic status
- Genetic factors
- Head injury
Migraine Progression Risk Factors

**Attack Frequency**
- Them that gets gets!
- The Brain learns Pain
- Inflection point starts at about 5 attacks a month
- Use a Bridge Therapy to suppress Headaches
  - Naproxen BID X 30 days
  - Steroids burst or taper
  - Repeated Blocks
  - Methylergonovine 0.2mg 1-2 PO TID X 14 – 28 days

**Poor Acute Migraine Treatment**
- Inadequate acute treatment associated with ↑ 1 yr risk migraine progression
  - Good acute txt 1.9%
  - Poor acute txt 4.4%
  - Very poor acute txt 6.8%
- Diary review 888 attacks / 185 patients
  - Not treating @ mild pain
  - Waiting to see if need to treat
  - Medication limits
  - Rapid onset migraine
  - Wake up/throw up headache

**Use Stratified Care**
- Suit the treatment to the attack
  - Mild – Distract, ignore, eat, rest, ice...
  - Moderate – NSAID +/- Triptan
  - Severe – Nasal or Parental; bypass the gut
    Olanzapine 10 or 20mg PO & go to bed
- Augment with Magnesium, Metoclopramide, Prochlorperazine

**Obesity/Dietary**
- Weight loss shown ↓ HA frequency; intensity, disability & acute med usage @ 60 months/c improvement thru 12 months.
- Improvement also seen /p bariatric surgery.
- Calorie restricted diets enhance neuroplasticity affecting pain sensation & cognitive function
  - Believed to stimulate neuroplasticity & increased resistance to oxidative stress
- Chronic Migraine pts randomized to
  - Diet high on Omega 3
  - Diet low in Omega 6
  - Both groups improved but Omega 3 group better 8.8 days vs 4.6 days.
- 30% improvement in HA days/attacks /c IgG elimination diet
- Additional support in small trial in pts /c comorbid migraine & IBS showed improvement with IgG elimination diet was observed antibodies were eliminated.
Migraine Progression Risk Factors
Sleep Disorders

• Poor sleep (not rested most mornings)
  – Worsen additional migraine comorbidities
    • Depression/anxiety/fibromyalgia
• May mean the difference between success & failure
• Simple behavioral instructions provided to chronic female
  migranuers
  – 58% remission to episodic migraine @ 12 weeks
  – No remission in sham group @ 6 weeks, then crossover
  – Crossover 43% remission to episodic migraine @ 6 weeks
  – Improvement correlated /c adherence to instructions

Simple Sleep Hygiene

• Schedule an initial consistent bedtime and awakening that allows for
  eight hours in bed, seven days a week— weekdays & weekends
• The bed is only for sleep and adult intimacies.
• No distractions while in bed. No television, reading, smart phones, pets
  or other children while in bed.
• White noise such as a fan or relaxing music is OK.
• Search www.youtube for “Weightless” by Marconi Union.
  – This song has been shown to help people fall asleep faster.
• Use visualization technique (guided imagery), autogenic phrases, or
  progressive muscle relaxation to start to get to sleep.

Autogenic Training

• My mind is quiet and at peace.
• My shoulders are heavy.
• My jaw is heavy and relaxed.
• It is time to sleep and restore.
• My right arm is heavy.
• My right leg is heavy.
• My left arm is heavy.
• My left leg is heavy.
• I am calm and at peace.
• It is time to sleep and restore.
• I am calm and at peace.

Sleep Restriction Therapy

• Do not nap
• Use bed only for sleep and adult intimacies.
• Go to sleep only you are likely to fall asleep within 10 - 20 minutes.
  Repositioning twice trying to fall asleep is equivalent to 20 minutes.
• Don’t watch the clock. Face clock away from your vision.
• If unable to fall asleep in 20 minutes, leave the bedroom & come
  back only when sleepy again.
• Get up at the same time every day. Do not “snooze”.

Migraine Progression Risk Factors
Stressful Life Events

• Leading Single Migraine Trigger
• Adverse Childhood Experiences increase risk
• What is Stress?
  – Anything that acts on you to provoke a response
• Goal of “Stress Management” is to build resilience
  – Timex watch
Migraine Progression Risk Factors
Stressful life events
- They Can’t Find Anything Wrong – David Clarke MD
  - www.stressillness.com
  - Is Stress Making You Ill? Handout on disk
- Breathe2Relax app
  - No Charge
  - Available in multiple formats
  - ≥ 10min/Day associated with ↓ BP
- DawnBuse.com
  - Relaxation exercises download for free
- Hypnotize Yourself Out of Pain now! – Bruce Eimer Ph.D.
- The Relaxation and Stress Reduction Workbook – M. Davis

Migraine Progression Risk Factors
Symptomatic Medication Overuse
- AKA “Rebound” – not best term
  - Overuse isn’t much better
  - Migraine frequency ↑/↓ increasing acute medication use
- HA that occurs in an individual with a pre-existing 1’ HA when in the presence of MO develops a new type of HA or a marked worsening of their pre-existing HA – ICHD IIβ
- Pts do not understand this condition
  - See usage as a direct response to their headaches
- Incidence in Primary Care Clinic = 21%
  - Much higher in specialty clinic

Migraine Progression Risk Factors
Symptomatic Medication Overuse
- SMO ↑cerebral cortex/trigeminal neuronal excitability
  - Hyper excitability makes the migraine brain more susceptible to cortical spreading depression
  - Shares similarities with addiction
    - Genetic basis
    - Continued use despite harm
    - See use as restoring order/relieving pain

Migraine Progression Risk Factors
Symptomatic Medication Overuse
- Patient must be educated about limits on acute medications.
  - Max 10-12 d/m
- Need to know that HA’s unlikely to get better if continue to overuse
- May need to withdraw in a controlled setting
- Headaches worsen during withdrawal
  - Use a “Bridge” therapy
  - Just say no!
  - If you must...
    - Limit to two servings a day
    - ≤ 200mg/day

Walking ≥ 3 Kilometers a day is associated with positive neuroplastic changes.
Prevention

- Consider when Migraine significantly disrupts ADLs, despite acute treatment
- Attack frequency >1/wk
- Only 5 FDA approved drugs for Migraine
- One FDA approved drug for Chronic Migraine
- Many off-label choices
- Start low and titrate as tolerated

Prevention – Pound of Cure

- Supplements – Mg 500mg, Riboflavin 400mg, CoQ-10 200mg BID, Butterbur (should be PA free - HA docs starting to avoid Butterbur)
- Membrane Stabilizing medications – Valproate, Topiramate, Gabapentin
- Anti-HTN – Beta-Blockers, CCB, ACE, Candesartan 16mg
- TCA (off-label) most data is with amitriptyline – SSRIs not thought to be effective
- OnabotulinumtoxinA – FDA approved for Chronic Migraine Oct 2010

AAN/AHS Preventive Recommendations

**Level A**

- Divalproex Sodium
- Sodium valproate
- Topiramate
- Metoprolol
- Propranolol
- Timolol
- Frovatriptan (MRM)

**Level B**

- Amitriptyline
- Venlafaxine
- Atenolol
- Nadolol
- Naratriptan (MRM)
- Zolmitriptan (MRM)

Migraine Preventive Therapy

Possible reasons for lack of efficacy

- Inadequate duration (<6-8 wk) at suboptimal dose
- Poor Pt. adherence (side effects, half-life, unrealistic expectations)
- Concomitant drug-induced headache – Prevention unlikely to work in MOH
- Newly developed medical condition causing a secondary headache

Migraine Preventive Therapy Education

- [www.Managingmigraine.com](http://www.Managingmigraine.com)
  - Sign up & receive about 10 emails
  - Refers to The Headache Friendly Lifestyle
  - Download free for Kindle Unlimited
- The Woman’s Migraine Toolkit – Dawn Marcus
- Knock Out Headache – Gary Ruoff

Headache Treatments

- **Preventive** – Reduce frequency, intensity and improve response to acute meds
- **Abortive** – Pain freedom in 2 hours
- **Rescue** – When the stop medicine didn’t
Abortive Therapy

• Goal is pain freedom in 2 hours
• Treat at mild pain (prior to central sensitization)
• May use polypharmacy

Oral Therapies

• Non-triptan
  — NSAIDS
  — Combinations
    • APAP/ASA/caffeine
    • Analgesics
  — Antiemetics
• Triptans
• Ergotamines
• When to consider
  — First-line therapy
  — Adjunctive therapies

What I Do

• Sooooo Off-Label & Remember my patients aren’t yours
• 3 tablets Effervescent ASA + Mg 500mg or
  Ibuprofen 1000-1200mg + Mg
• Naproxen 500mg + Mg
• Augment /c Metoclopramide or Prochlorperazine
• Triptan – Sumatriptan, Rizatriptan, Naratriptan, Almotriptan, Zolmatriptan, Frovatriptan generic.
  — Generic Sumatriptan ≤ $2/pill, GoodRX.com

Headache Treatments

• Preventive – Reduce frequency, intensity and improve response to acute meds
• Abortive – Pain freedom in 2 hours
• Rescue – When the stop medicine didn’t

Why Should I Treat Acute Headaches?

• Have to keep these people out of the ED
• Primary HAs are not an emergency
• Not the best place – too bright, too loud, often ignored
• Can’t risk exposure to opiates
• More likely to V.O.M.I.T. in ED
No Opiates for Headaches

- Major risk factor for medication overuse HA
- Once established it’s a self fulfilling prophesy
- Jakubowsk, et al. 2005 Wolfe Award paper
- 64%-71% Migraine pts pain-free 1’/p ketorolac iv
- Only factor that predicted ketorolac failure: hx of opioid txt in the nonresponders
- Rewires the brain to perpetuate the HA state by inhibiting the breakdown of glutamate

Clinical Headache Rescue

- Assoc. Neurologist of S. CT AHS SA Poster
- Drop in HA Clinic – Prevent ED visits
- 9/05 - 8/07 500 pts
- Time to Present = 104 hours (8-240h)
- VAS pain: Entry 8.5 Discharge 1.5
- Txt: IVF (94%), Ketrorol (84%), Suma sq (78%), Prochlorperazine (52%), Metocloprimide (21%), DHE (8%), Mg (4%)
- Average charge $426, Average payment $272.64

Clinical Headache Rescue

UAB Experience

- 200 pts. Randomized Optimal Self Admin or Optimal Self Admin + Optional in-clinic Headache rescue

<table>
<thead>
<tr>
<th>Optimal Self-Admin</th>
<th>Clinic Rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>423 visits</td>
</tr>
<tr>
<td></td>
<td>33.6k ($80)</td>
</tr>
<tr>
<td>73</td>
<td>ED Visits</td>
</tr>
<tr>
<td>147.9k ($2027)</td>
<td>ED Direct Cost</td>
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<tr>
<td></td>
<td>45.3k ($1609)</td>
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<tr>
<td></td>
<td>79% no d/a &gt; 24'</td>
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</table>

Rescue Headache Interventions

- IV >> IM >> PO
- Sumatriptan 6mg IM/SC
- Dihydroergotamine 1mg IM/SC/IV
- Ketorolac 30mg IV / 60mg IM
- Neuroleptics – Dopamine Antagonists (Droperidol, Metocloprimide, Prochlorperazine)
- Steroids
- Others – Mg++, Valproic Acid, Diphenhydramine
- Procedures – Occipital Nerve Block, Lower Cervical Intramuscular Injections

Procedures

- Lower Cervical Intramuscular Injections
- Occipital Nerve Block
- Sphenopalatine Ganglion Block
- Pericranial Injections
**Lower Cervical Intramuscular Injections**

- Headache 10/06
- 417 ED Pts / 1 yr
- 65% relief in 15m
- Repeat injection brought additional relief
- Worsened HA in 1%

**Lower Cervical Intramuscular Injections**

- 3mL bupivacaine 0.5%
- 25g 1.5” / 27g 1.25”
- 2-3cm lateral to the spinous processes between C6 & C7
- AE /CI
- Vasovagal, Neck stiffness, usual injection risks

**Occipital Nerve Block**

- Local anesthetic (bupivacaine).5% lidocaine 1% - Duration of anesthesia doesn’t correlate to duration of relief
- Steroid (triamcinolone 40mg/mL) evidence doesn’t support general use
- 3mL total per side
- 25 or 27 gauge needle
- May place as a “ridge” of anesthesia, “trigger points”, or fixed.

**Occipital Nerve Block**

- EEs & CIs
- Prior hx of craniotomy over injection site
- EEs primarily related to steroid- fat atrophy, alopecia, pigment change
- Vagal response – Happened to me X 3 in over 6000 blocks

**Sphenopalatine Ganglion Block**

- Multiple commercial devices now available
- Videos on youtube.com
- Tian TX 360
- Sphenocath
- Allevio
Pericranial Bupivacaine Injections

- 218 Subjects
- 34 sites – 0.25% Bup
- Q.12 weeks
- 87.1% Female
- Age – 40.4 years
- Migraine for 18.5 years
- 21.4/28 days /c HA
- 15.5 Severe HA days
- 18.3 Treatment days

- 55.2 % > 50% reduction
- 35.3% achieved by 4 wk
- ↓ HA days 22.8d to 9d
- ↓ Severe 15.9d to 6.1d
- ↓ Treatment 18.1d to 7.9d
- 11.5% no response/Lost-FU

Pericranial Bupivacaine Injections

Robert Kaniecki, MD
University of Pittsburgh

Pericranial Bupivacaine Injections

Robert Kaniecki, MD
University of Pittsburgh

Migraine in 4 Sentences or less

- It is Neurological
- Its is Genetic
- It is Highly Disabling
- It is infinitely treatable
- And it is by far the most fascinating neurological condition you can treat!

Peter Goadsby, MD

Potpourri

- Migraine Sunglasses FL-41 tint only
  – Indoor /Outdoor tints available
  – May use Flex Spending Account
  – $ 100 –200. Money back guarantee available
- Headache Hat $40 online
- Timoptic % 1 drop OS/OD
  – Eye exam 1st but...
  – Not needed is used sub lingual
  – Clinical trial underway
  – https://clinicaltrials.gov/ct2/show/NCT02630719
  – Articles on the DVD
Hot off the Presses!

- Timoptic % 1 drop OS/OD
  - Eye exam 1st but...
  - Not needed is used sub lingual

- Clinical trial underway
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- Articles on the DVD
The following medications were discussed in this presentation. The table below lists the generic and trade name(s) of these medications.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
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<tbody>
<tr>
<td>Almotriptan</td>
<td>Axert</td>
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<tr>
<td>Atenolol</td>
<td>Tenormin</td>
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<td>Bupivacaine</td>
<td>Marcaine, Exarel</td>
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<td>Dihydroergotamine</td>
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<td>Divalproex</td>
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<td>Naproxen</td>
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<td>Olanzapine</td>
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<td>Propranolol</td>
<td>Hemangeol, Inderal, Innopram XL</td>
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<td>Rizatripan</td>
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<td>Sumatriptan</td>
<td>Imitrex, Onzetra Xsail, Zembrace, SymTouch</td>
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<td>Topiramate</td>
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<td>Venlafaxine</td>
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<td>Zolmitriptan</td>
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