Donepezil IR switch to Galantamine SA: using published literature and real world data

Veterans Affairs San Diego Healthcare System
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Synopsis

• Discuss the conversion process at the VA.
• Provide an example of a drug to drug conversion at the VA.
• Demonstrate how RCTs and Real world data were used to make a decision to convert a drug to another drug.
• Report the data collected from the conversion.
• Actions taken due to the results.
• Lessons learned and future planning.
VA San Diego Healthcare System

- Provides healthcare to 267,000 veterans in the San Diego and Imperial Valley counties.
- 232 hospital beds, including skilled nursing beds and several regional referral programs such as cardiovascular surgery, and spinal cord injury (SCI).
- Operating budget of $346 million (FY 2007)
- Pharmacy and Therapeutics Committee.
  - Approves/Denies conversions based on efficacy, safety and cost-effectiveness.
- Autoconversion process.
  - Powerful process that allows us to convert a large number of patients overnight.
Alzheimer’s disease treatment

• Acetylcholinesterase inhibitors (AChEIs)
  – Donepezil (Aricept®)
    • Released in 1996
  – Rivastigmine (Exelon®)
    • Released in 2000
  – Galantamine (Razadyne®)
    • Released in 2001
    • Unique MOA: acts as an AChEI and a positive allosteric modulator at nicotinic acetylcholine receptors
    • Good alternative
Conversion opportunity

Donepezil → Galantamine SA
Rationale for conversion

• Donepezil was the preferred AChEI.
• Galantamine accountants offered to reduce prices for their SA products if market share increased to 35%.
• Cost savings estimated to total $560,000.
• Price per day between galantamine IR and SA were roughly the same.
Rationale for conversion

• Concerns regarding destabilizing patients due to the switch were raised; however, current literature showed that patients tolerated the switch.
Literature supports switch from donepezil and galantamine.

– Maelicke (2001) dev. a theoretical model
  • showed that a washout period was not required for switching patients from donepezil to galantamine

  • Patients tolerated switch from donepezil to galantamine with no washout period; 24% GI ADR but none D/C

  • No difference in clinical efficacy, but an increased washout period can lead to more GI ADRs
Real world data

• Data from another VA was available.
• 1113 patients were converted from donepezil to galantamine
• 20 patients experienced ADRs
  – Most common ADR: dizziness.
• 5.8% (N=65) switch backed due to decreased cognitive function.
• Average switch back rate for normal conversion is 10% at the VA.
Conversion at our site

- Conversions are always reviewed and voted on by the Pharmacy and Therapeutics Committee.
- Providers in their respective fields review the procedures and provide feedback.
- Based on their feedback, we amend the process.
- Therefore, the conversion process was reviewed by experts and voted on by the members of P&T before initiation.
- During initiation, patients and providers were provided a letter informing them of the conversion and what to expect.
Conversion at our site

• Once the conversion process began, we monitored the data to find any patients who were missed in the conversion process and integrate them into the system.

• After a couple of months, we analyzed the data to see what the switch back rate was.
Donepezil to Galantamine ER Conversion Timeline

**VASDHS**

**VISN 22 FSC: 12/12/07**
VFL recommended making Razadyne the preferred AchE for new starts. Razadyne BPA is market share based; need > 35%.

**P&T: 1/30/08**
Approved Galantamine ER as preferred AchE for new starts. No new starts for donepezil.

**Dave Gray: 2/29/08**
Notified sites for the need to target market share requirements to capture the galan BPA and potential cost-impact of not meeting goal.

**VASD: 3/1/08**
Form Group sends email to Drs. Galasko, Atkinson, and Thomas for feedback.

**VISN 22 FSC: 3/12/08**
No autoconversion required at this time. Local sites to determine conversion process.

**P&T: 3/26/08**
Autoconversion of donepezil to galantamer approved.

**VASD: 4/21/08**
Conversion initiated. Patient letters sent.

- **P&T: 11/28/07**
  Discussed the recent Galantamine BPA the VHA accepted, effective 1/1/08. P&T asked VISN for clarification of galantamine ER as preferred AchE for new starts.

- **VISN 22 FSC: 1/9/08**
  Galantamine ER selected as preferred AchE for new starts.

- **VASD: 3/6/08**
  Received feedback from Galasko and Thomas approving conversion.

- **VASD: 3/8/08**
  Pharm meets with Dr. Thomas. Agrees with autoconversion process. In-clinic conversion will ↑ workload.

- **VASD: 4/2/08**
  Provider notification letter sent out describing conversion process.
Conversion results

- In the initial analysis, we identified 297 patients who were on donepezil that could be converted to galantamine SA.
- We initially switched 168 patients.
- 26 (15.5%) patients switched back to donepezil.
- This was ~3 times the switchback rate at the other VA and 50% more than the average.
Actions taken

• As a result of the current findings, it was decided that the conversion be halted.
• We voted to limit the conversion to the clinics where providers are able to assess the patients face to face.
• In addition, rather than have patients who were currently stabilized on donepezil switch to galantamine, we required new patients on an AChEI to start on galantamine SA instead.
In retrospect

- Past clinical trials and data from another VA did not evaluate or measure patient reported outcomes.
  - Burden is not only to the patient, but to the care giver.
  - Patient/caregiver perspectives should have been measured.
  - Satisfaction with the conversion and its process would have provided valuable information.

- More resources were probably consumed during the conversion than the benefits attained.
Conclusion

• Despite RW data published literature showing safety and efficacy, our site did not reflect those findings.

• Perspectives of the patient/caregiver needs to be measured.

• Perhaps an initial conversion with a small group of patients, rather than a large group.
  – Identify low risk patients for GI intolerance or destabilization
References

