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.

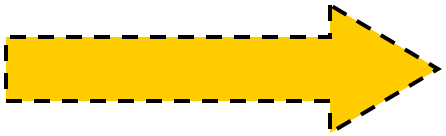
VA San Diego Healthcare System

- 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
- Rasmusen, et al (2001) trial data
  - Patients tolerated switch from donepezil to galantamine with no washout period; 24% GI ADR but none D/C
- Wilkinson, et al (2005) trial data
  - 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.

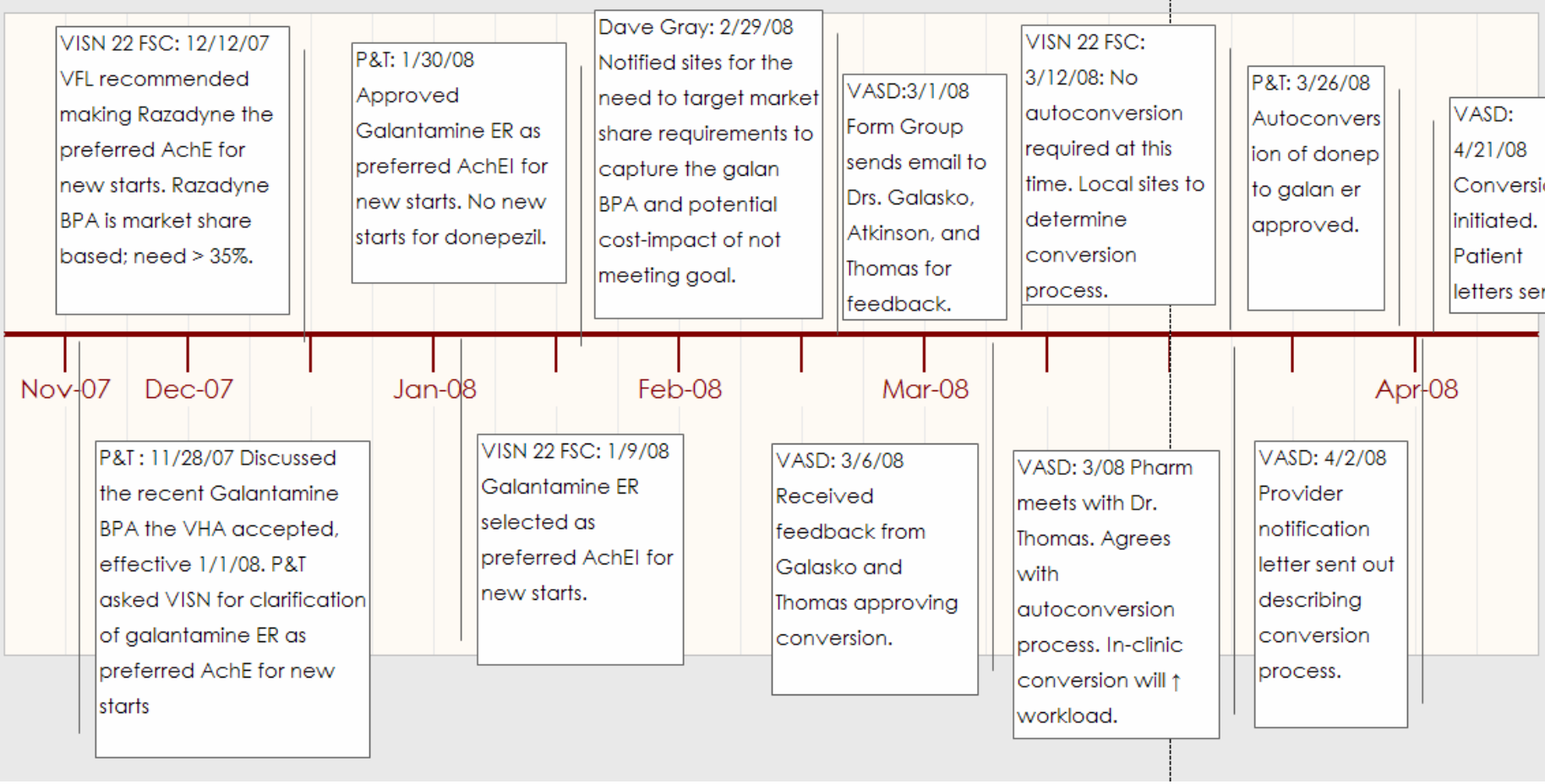
Conversion at our site

- 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



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

- Maelicke A. Pharmacokinetic rationale for switching from donepezil to galantamine. Clin Ther 2001;23 suppl:A8-A12.
- Rasmussen L, Yan B, Robillard A, Dunbar F. Effects of washout and dose-escalation periods on the efficacy, safety, and tolerability of galantamine in patients previously treated with donepezil: ongoing clinical trials. Clin Ther 2001;23 Suppl:A25-A30.
- Wilkinson DG, Howe I, on behalf of the GAL-GBR-1 Study Group. Switching from donepezil to galantamine: a double-blind study of two wash-out periods. Int J Geriatr Psychiatry 2005;20:489-491.