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Changes to Formulary

Additions

All formulary changes and policy/procedure updates have been approved by the Medical & Academic Advisory Council (MAAC) (May-June 1998)

1. Topiramate (Topamax®)

- antiepileptic drug indicated as adjunctive therapy in patients with refractory partial seizures, with or without secondary generalization
- restricted to neurology service
- see page 2 for review

2. Ofloxacin 0.3% eye drops (Ocuflox®)

- fluoroquinolone ophthalmic antibiotic drops
- cost: \$5.95/5mL; comparison gentamicin 0.3% eye drops \$1.90/5mL

Deletions

1. Sodium Hypochlorite solution (Hygeol®, Dakin's solution)

- discontinued by manufacturer alternatives: refer to Patient Care Guidelines S-135 (Wound Management) or contact the wound care consult team at 875-5788.

Updated Policies/Procedures

RETURN OF SPACER DEVICE BACK TO AEROCHAMBER®

In Sept 1997, the Pharmacy switched the spacer device used with metered dose inhalers to the ACE® (Aerosol Cloud Enhancer). However, due to the following reasons, we have switched back to the Aerochamber®:

- 1) Several patients found the ACE® spacer device hard to use. Specifically, they had difficulties removing the MDI canister from the outer shell and placing it into the device. As well, the ACE® is not readily available in community pharmacies.
- 2) One of the advantages of the ACE® was that it could be cleaned and recycled. However, over the past year, very few devices had been returned for recycling.
- 3) The cost difference between the ACE® and Aerochamber® is minimal. The cost to VHHSC for the ACE® is \$7.65 compared to \$10.95 for the Aerochamber®.
- 4) The Aerochamber® is now available with a mask so can be used in patients who require high flow oxygen.

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New Drugs/Drug Products

Topiramate (Topamax®)

Karen Shalansky, Pharm.D., Saira Alladina, B.Sc. (Pharm)
Reviewed by Dr. M. Jones, Director, Epilepsy Clinic

While most patients with epilepsy have good seizure control with a single antiepileptic drug (AED), up to 30% develop refractory epilepsy requiring combinations of AEDs.¹ Topiramate represents one of four AEDs released in the 1990's indicated as adjunctive therapy in the treatment of refractory partial seizures, with or without secondary generalization. The three other AEDs are gabapentin, lamotrigine and vigabatrin. All four AEDs are on formulary at VHSC and restricted to neurology service. Lamotrigine is also approved as monotherapy for generalized seizures after withdrawal of concomitant AEDs; the other 3 agents are currently under study for this indication. Table 1 compares the mechanism of action of AEDs.

Studies have shown adjunctive therapy

AED	Mechanism of Action
phenytoin, carbamazepine, sodium valproate, lamotrigine, topiramate	Blocks sodium channels
sodium valproate, vigabatrin, gabapentin	Increases GABA ^a levels
phenobarbital, clobazam, topiramate	Enhances GABA ^a receptors

^aGABA = gamma-amino butyric acid

with topiramate reduces seizure frequency by at least one-half in 35-52% of adult patients with resistant partial epilepsy compared to 0-19% of placebo recipients.^{2,3} There have been no head-to-head trials comparing the new AEDs to each another. Marson *et al* performed a meta-analysis of 28 randomised, placebo-controlled trials of supplementary AEDs in patients with refractory partial epilepsy to compare the efficacy (i.e. ability to reduce seizure frequency by at least 50%) of the newer agents.¹ The authors found all four AEDs were significantly better than placebo at preventing seizures, but none were

significantly different from the other, though the confidence intervals were wide. Odds ratios for subjects with at least 50% response relative to placebo were: topiramate 4.22 (95% confidence interval 2.80-6.35), vigabatrin 3.68 (95% CI 2.45-5.51), lamotrigine 2.32 (95% CI 1.47-3.68) and gabapentin 2.29 (95% CI 1.53-3.43). The authors suggested that topiramate and vigabatrin may be the best choices in patients with refractory epilepsy due to their apparent higher efficacy. Gabapentin and lamotrigine may be the best options in patients with a history of drug intolerance but adequate seizure control.

Other factors to consider when choosing between the newer AEDs include mechanism of action, route of elimination, drug interactions, adverse effect profile, dosage frequency and cost.

Table 2. Comparison of newer AEDs

Drug	Topiramate (Topamax)	Gabapentin (Neurontin)	Lamotrigine (Lamictal)	Vigabatrin (Sabril)
Route of Elimination	Renal	Renal	Hepatic	Renal
AED Interactions	Yes ^a	-	Yes ^b	not significant
Major Adverse Effects	cognitive disturbance; psychiatric	-	potentially life-threatening skin rashes	visual field constriction (rare); psychiatric
Dose	200-600mg/day divided in 2 doses	900-3600 mg/day divided in	200-400mg/day given in 1-2 doses	2-3g/day as a single dose
Cost/day ^c	\$3.00-10.00	\$3.00-10.00	\$3.00-6.00	\$4.00-6.00

^a Carbamazepine, phenytoin increase clearance of topiramate; topiramate may increase phenytoin levels by 20%

^b Valproate decreases clearance of lamotrigine; carbamazepine, phenytoin, phenobarbital increase clearance of lamotrigine

^c based on VHSC acquisition costs

References

1. Marson AG, Kadir ZA, Chadwick DW. New antiepileptic drugs: a systematic review of their efficacy and tolerability. *Br Med J* 1996;313:1169-74.
2. Langtry HD, Gillis JC, David R. Topiramate. *Drugs* 1997;54:752-71.
3. Privitera MD. Topiramate: a new antiepileptic drug. *Ann Pharmacother* 1997;31:1164-73.

Infusion Program Updates

Welcome to the new Infusion Program (IP) column! We will be taking advantage of this publication to routinely provide you with program updates, notification of upcoming events, policy changes, tips for practice improvement and other topics of interest.

The IP was formed in January 1998 and is operated by CSU Pharmaceutical Sciences. Originally staffed by two nurse educators, Lynn Chase and Ruth Nicol, the program has recently expanded with the addition of a third educator, Barbara Ferreira and a merger with the I.V. resource nurses (Chris Dela Cuesta, Kay Janzen, Carole Leong and Eileen Plunkett). Together, these individuals are working to provide parenteral therapy-related clinical, educational and research support to the hospital under the direction of Dr. Peter Jewesson and Frances Legault, PPL, Nursing. Working closely with the IP team is Amy Wai, our Home IV Antibiotic Program clinical pharmacist. To ensure good communication with the balance of the hospital, a 13-member advisory committee was formed in April 1998 with representation from nursing, pharmacy, radiology, vascular surgery, microbiology/infection control, infectious diseases and business unit administration.

In addition to the well-known and essential clinical services provided by our I.V. resource nurses, a number of specialized functions are also being provided by the IP educators. These include: central venous catheter (CVC) patient teaching (via referrals from Vascular Surgery and Radiology); CVC device-related complication support; peripherally inserted central catheter (PICC) insertions, teaching

and hospital/community nursing support for select patients and other activities. With the addition of our 3rd educator, the Home IV Antibiotic Program patient enrollment cap and associated PICC line insertion restrictions have been lifted. Starting this month, the IP team launched the first 7-part series of internal continuing nursing education sessions. The team is also busy reviewing hospital-wide parenteral therapy patient care guidelines and practical methods to reduce sharps-related injuries.

The IP office and learning lab is located on CP-3 and the educators can be reached at 875-4706 (answering machine) or pager.

Weekday pager 0800-1700 hrs:

L. Chase 872-9847

B. Ferreira 877-5528

R. Nicol 871-3198

Week-end pager

872-9847

In upcoming issues:

- A review of the activities of the Home IV Antibiotic Program celebrating its 3rd anniversary and over 6000 days of home therapy
- Tips to further improve our response to your requests for I.V. resource nurse support
- New catheter technology...what's available and an algorithm to help you select the best infusion device for your patients
- Tips and tricks to reduce problems with infusion devices

Please provide suggestions for future topics to any member of the IP team. We look forward to continuing to work with you toward optimizing the care of our patients.

Study Recruitment

Outpatient Self-Management of Warfarin

Self-management represents a novel strategy in anticoagulation care. A prospective, randomized trial comparing outpatient self-adjusted versus physician-managed warfarin is being conducted by CSU Pharmaceutical Sciences in collaboration with the Departments of Cardiology, Hematology and Nursing. Our hypothesis is that outpatient self-management of warfarin provides superior anticoagulation compared to physician-managed care.

Eligible patients who are randomized to self-management will test their own INRs using a home INR monitor (ProTime®) and adjust their warfarin dosage according to an individualized protocol. Control patients will continue to be managed in the traditional fashion which involves INR testing at the laboratory and follow-up of results and warfarin dosage adjustments by the physician. A total of 140 patients will be enrolled for a study duration of 8 months.

ARE YOUR PATIENTS ELIGIBLE?

Inclusion Criteria:

- 18 years or older
- anticoagulation to achieve a target INR 2.0-3.0 or 2.5-3.5
- mentally competent
- planned anticoagulation for greater than one year

Exclusion Criteria:

The investigators have recently completed a 3 month pilot study involving 10 patients who managed their own anticoagulation. Patients maintained 76.5% of INRs within the target range with a low error rate in dosage adjustment decisions of 2.5%. All patients expressed a high level of satisfaction and a desire to continue with self-management given the opportunity.

The study is currently underway and we are inviting participation from eligible patients. Please notify Drs. Rubina Sunderji or Karen Shalansky (CSU Pharmaceutical Sciences) at 875-4077 if you have potential candidates or questions.

Abstract

(Formulary 1998;33:54-63)

Use of Cefixime in an IV to Oral Stepdown Program to Reduce Antimicrobial Costs

Dean Elbe, Luciana Frighetto, Donna Nickoloff, Peter Jewesson

Objective: To add cefixime to our existing parenteral to oral (IV-PO) stepdown program and characterize its use and potential cost avoidance under the influence of this intervention.

Design: Single centre retrospective health record review.

Setting: Tertiary care teaching hospital

Patients: Fifty cefixime and 60 ceftriaxone treatment courses during a six month study period.

Intervention: Cefixime was added to an existing IV-PO stepdown program as an oral alternative to ceftriaxone in select patients.

Outcome: Cefixime treatment course characteristics and stepdown associated cost-avoidance was determined. In addition, ceftriaxone treatment courses were stratified by stepdown attributes and compared.

Results: Cefixime was prescribed primarily by respiratory, family practice and general medicine services. Pleuropulmonary and bronchial infections comprised the most common indications. Cefixime was employed as a stepdown agent in 78% of courses reviewed. Stepdown usually occurred on the sixth day of therapy. Clinical cure or improvement was observed in 93% of patients. Gastrointestinal side effects were common. An average cost-avoidance of \$347 per stepdown course was realized. A projected savings of \$27,000 per year was estimated. Ceftriaxone was stepped down to cefixime as often as all other oral agents combined. Stepdown was usually appropriate and most commonly occurred for respiratory tract infections.

Conclusion: Cefixime has a potential role as a stepdown agent for ceftriaxone. Costs can be avoided without apparent negative impact on patient care.