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Date: 01/14/2004 12:55:32 PM
From: CN=Jerry D Clewell/OU=AM/O=LLY
Subject: Re: Annals of Pharmacotherapy Recent articles of interest 2004
Attachments: Liu cost comparison review OLZ vs RIS Ann Pharma 1-04.pdf; Sprague Selection of APDs Ann Pharm 2-04.pdf

Ginny et. al.

I too would like to offer a couple of observations from the Payer world relative to these studies and the environment.

It can not be understated that the Annals (as well as AJHP) are very widely read pharmacy journals that influence clinical pharmacists and their recommendations at the patient, and P&T Committee levels.

These reviews, especially in addition to this month's publication of the Consensus Guidelines for Schizophrenia (published in AJHP), can provide powerful arguments for P&T committee members to restrict access to olanzapine on the basis of (1) perceived parity or near parity in efficacy in light of (2) the perceived 2X cost differential between olanzapine and risperidone.

1. Selection of atypical antipsychotics for the management of schizophrenia- Denise Sprague

Payers have already expressed to me (just yesterday) that they view this information as confirming their interpretation of the data that there is very little clinical difference between olanzapine and risperidone. Never mind the author's comments that drug therapy should be individualized.

What can/should we do in reaction to these perceptions?

I believe this means that we have to step up all publication and communication efforts to educate decision makers and their consultants (Thought Leaders, PBM's, etc) on the long-term effectiveness (relapse prevention, and medication persistence) of olanzapine. We were specifically criticized yesterday by a large Medicaid payer consultant for not being able to provide more peer-reviewed publications supporting an argument for long-term effectiveness.

As a company, we all need to do a much better job of proactively listening to payers (and other customers) concerns, and proactively communicating important information such as adverse effect label changes without a tone of minimizing their importance (e.g. wt gain, diabetes, CVA). Payers and clinicians have clearly articulated that this is an area where Lilly has lost its scientific integrity and therefore exposed us to great scepticism when we need to communicate the positive benefits of our products.

Best Regards,

Jerry D. Clewell, Pharm.D., MBA BCPS
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01/12/2004 01:29 PM

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Toalson/AM/LLY@Lilly, David L Van Brunt/AM/LLY@Lilly, David L Van Brunt/AM/LLY@Lilly
Subject: Re: Annals of Pharmacotherapy Recent articles of interest 2004

Vicki et al,

Thanks for forwarding out the abstract of the review on the selection of atypical antipsychotics in the treatment of schizophrenia. Attached is the PDF of this paper as well as a cost comparison review on olz vs ris that was published in the Jan issue of this journal. I think both of these reviews are worthy of our attention and it is important for us to know that while Annals of Pharmacotherapy is not a widely distributed psych journal it is a respected, peer reviewed journal that does have a wide distribution to practicing clinical pharmacists and others involved with clinical pharmacotherapy decision making and formulary decisions. With that being said, let me make a few comment regarding the papers below:

Selection of atypical antipsychotics for the management of schizophrenia- Denise Sprague, the authors are not from the US, they did do a comprehensive review of the current literature and only came up with head to head comparisons of olz vs ris, as we know there are now other atypical head to head papers published but did not make this paper do to a timing issue. In addition to the head to head comparisons of olz and ris the meta analysis papers are reviewed. I think it is important to point out that their review of the literature is consistent with what we know, "There are trends toward lower withdrawal rates, greater magnitude of improvement in PANSS scores, and greater improvement in negative symptoms with OLZ compared to RIS." I think this statement will likely be stronger when other long-term head to head comparisons with olanzapine and other atypicals are available. Also, observational data was not included in this literature review. Please look at the conclusions in the actual paper, very much based on the current state of the published literature and does not clearly make the statement of selecting the APD based on side effects.

Cost comparisons of olanzapine and risperidone in treating schizophrenia- Gordon Liu- This review was funded by a grant from Lilly (not sure from who) but is a comprehensive review of randomized and retrospective studies in the literature. Also reviews the literature for each of these agents vs conventionals which is very useful. I have made the HGFI core team aware of this paper and we briefly discussed at our last meeting.

Thanks and let me know if you have any comments or questions.



Sprague Selection of APDs Ann Pharm 2-0Liu cost comparison review OLZ vs RIS Ann Pharma 1-04.pdf

Vicki Poole Hoffmann

01/12/2004 08:57 AM

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cc:

Subject: Ann Pharmacotherapy Table of Contents for 1 February 2004; Vol. 38, No. 2

Below is an abstract from *The Annals of Pharmacotherapy* February Issue. It appears to say that all antipsychotics have equal efficacy, so drug selection should be based on side effect profile.

If anyone has the pdf, please forward.

Thank you,

Vicki

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DRUG SELECTION PERSPECTIVES

Selection of Atypical Antipsychotics for the Management of Schizophrenia

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OBJECTIVE: To review the evidence for selecting one atypical antipsychotic agent over another for management of schizophrenia.

DATA SOURCES: A literature search of MEDLINE (1966–June 2003), EMBASE (1998–June 2003), and the Cochrane Library was conducted using the following terms: schizophrenia, quetiapine, ziprasidone, olanzapine, aripiprazole, and risperidone. Bibliographies of relevant articles were hand-searched for additional references.

STUDY SELECTION AND DATA EXTRACTION: Prospective, randomized, blinded trials and meta-analyses that directly or indirectly compared 2 atypical antipsychotic agents in the management of schizophrenia are included in this review. Studies comparing an atypical agent with clozapine are not included.

DATA SYNTHESIS: A small number of prospective, randomized, blinded trials that compare efficacy and tolerability of olanzapine and risperidone have been published. These trials did not reveal clinically meaningful differences in efficacy but did confirm that their adverse effect profiles are slightly different (more weight gain with olanzapine and more extrapyramidal reactions with risperidone). Direct comparisons between other atypical antipsychotics are not available. Systematic reviews (indirect comparisons) of placebo-controlled or traditional antipsychotic-controlled trials suggest similar efficacy for quetiapine, olanzapine, and risperidone when placebo is the comparator and inferior efficacy of quetiapine compared to olanzapine and risperidone when haloperidol is the comparator. The few available economic analyses are difficult to interpret in light of current practice.

CONCLUSIONS: Additional randomized, blinded clinical trials directly comparing efficacy, tolerability, and cost-effectiveness are needed to

confirm the proposed differences among atypical antipsychotic agents before recommendations can be made with confidence.

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