Cost analysis of a provincial drug program to guide the treatment of upper gastrointestinal disorders

Ford Bursey, Mary Crowley, Colleen Janes, Christopher J. Turner

Abstract

Background: Concerned with the rising costs of its drug programs for seniors and social-assistance recipients, the government of Newfoundland and Labrador requested physicians and pharmacists at the Memorial University of Newfoundland and the Newfoundland and Labrador Medical Association and the Newfoundland Pharmaceutical Association to provide guidance to the health care community for the use of drugs to treat upper gastrointestinal disorders.

Methods: Algorithms for the management of dyspepsia and gastrointestinal reflux disease were created and distributed to all physicians and pharmacists in the province in June 1996. On July 1, 1996, the provincial government implemented a program to restrict payment for proton-pump inhibitors through its drug programs to situations defined by the algorithms. Restrictions were not applied to the prescribing of cimetidine, ranitidine and prokinetic agents. The status of famotidine and nizatidine was changed from “open benefit” to “special consideration,” which requires prescribers to request authorization of their use on a case-by-case basis.

Results: Between July 1 and Dec. 31, 1996, 973 of 1078 requests for a proton-pump inhibitor were approved (679 for gastroesophageal reflux, 186 for Helicobacter pylori eradication, 55 for ulcer treatment and 53 for other reasons). The program resulted in a sustained reduction in drug expenditures. Total drug expenditures, which had risen from $39.0 million in 1992/93 to $50.8 million in 1995/96, fell after implementation of the program to $46.4 million in 1996/97 because of a decrease of more than 80% in the use of proton-pump inhibitors. Expenditures on proton-pump inhibitors, which had increased from $0.7 million for the 6 months ending March 1993 to $1.6 million for the 6 months ending March 1996, decreased to $0.3 million for the 6 months ending March 1997. The use of H2-antagonists, but not prokinetic agents, increased concomitantly with the decline in proton-pump inhibitor use. Compared with the year preceding implementation of the program, annual combined expenditures in the subsequent 3 years for H2-antagonists, prokinetic drugs and proton-pump inhibitors were reduced by $1.6 million, $1.7 million and $1.0 million, respectively. Feedback from physicians and pharmacists was supportive for the clinical information and prescribing guidelines. Concerns were mostly limited to process issues.

Interpretation: The program, designed by health care professionals, approved by health care associations and implemented by the province of Newfoundland and Labrador to guide the treatment of upper gastrointestinal disorders, has achieved a substantial reduction in drug expenditures.

The Department of Health and Community Services (DHCS) of the Government of Newfoundland and Labrador provides the Senior Citizen’s Drug Subsidy Program to residents of the province aged 65 years and older who receive the federal guaranteed income supplement and provides the Income Support Drug Program to recipients of social assistance. In 1996, 1997 and 1998 these programs provided coverage to 117 637, 114 035 and 109 792 individuals, respectively. In 1995 the provincial government, concerned with the rising costs of its drug programs (Fig. 1), approached members of the Faculty of Medicine and the School of Pharmacy at Memorial University of Newfoundland, the New-
foundland and Labrador Medical Association (NLMA) and the Newfoundland Pharmaceutical Association (NPhA) to assist in the development of a program to reduce expenditures and still provide appropriate drug coverage. The government chose drugs for upper gastrointestinal disorders for the program because of the high annual expenditures for such drugs ($6.6 million) and because of experiences of other provinces with similar programs.

The government requested help to define the appropriate use of H2-antagonists, prokinetic agents, proton-pump inhibitors and other drugs for the management of dyspepsia and gastroesophageal reflux disease. The program’s purpose was to change the status of proton-pump inhibitors, which accounted for about 50% of gastrointestinal drug costs, and of famotidine and nizatidine from “open benefit” to “special consideration” (requiring prescribers to request authorization for their use on a case-by-case basis) and to define the circumstances in which approval for a proton-pump inhibitor would be granted. This paper presents the algorithms that were created and a financial analysis of total drug expenditures and drug use in the province before and after implementation of the program.

Methods

Literature concerning the diagnosis and management of upper gastrointestinal disorders was reviewed to create algorithms for the management of dyspepsia and gastroesophageal reflux disease. These algorithms were reviewed and modified by a committee comprised of representatives from the DHCS, the Faculty of Medicine (Gastroenterology) and the School of Pharmacy at the Memorial University of Newfoundland, the NLMA and the NPhA. The algorithms (Appendices 1 to 3) were endorsed by the NLMA and the NPhA and then distributed in June 1996 to all physicians and pharmacists in the province, together with supporting information to explain the purpose of the program and its operation. The algorithms reflect the realities that dyspepsia and gastroesophageal reflux disease affect large numbers of Canadians, that many cases can be addressed with lifestyle changes and nonprescription drugs, and that human, physical and financial resources for the diagnosis, treatment and monitoring of upper gastrointestinal disorders are limited.

On July 1, 1996, after endorsement of the program, the provincial government removed all proton-pump inhibitors and famotidine and nizatidine from open-benefit status in its drug programs. The decision to limit open formulary status to cimetidine and ranitidine was based on evidence that all H2-antagonists have similar efficacy and safety but that they differ in cost. At the time the program was implemented, the daily ingredient costs paid by the 2 drug programs were $0.28–0.39 for cimetidine, $0.87–0.94 for ranitidine, $1.25–1.38 for famotidine and $1.75–1.94 for nizatidine.

Concomitant with the new restrictions, the government implemented a process by which prescribers and pharmacists could submit (including by fax) written requests on behalf of patients for coverage of a proton-pump inhibitor or of famotidine or nizatidine. The operation of the program was designed on an honour system such that physicians were requested to state information (e.g., “the patient has a radiographically proven duodenal ulcer” or “lifestyle modification has failed”) rather than provide proof. The DHCS required the name of the patient, the diagnosis, a statement of the clinical and diagnostic evidence supporting the use of the medication, the name of the medication, the dose regimen, the expected duration of therapy, the name of the prescriber and, if appropriate, the drug names, dose regimens, durations of treatment and responses to previous pharmacotherapy. The submission of other information including the patient’s benefit plan identification number, home address and telephone number, and pharmacy was encouraged as a means to speed the approval process. To minimize the bureaucratic process and because of the relatively small cost, the DHCS approved requests for first courses of Helicobacter pylori eradication therapy with no requirement for clinical and diagnostic information. To minimize the bureaucratic process further, the DHCS did not require the use of forms.

Written requests were reviewed by staff pharmacists in the DHCS, who consulted staff physicians when necessary, and were automatically approved if the request met the guidelines. Requests were granted for up to 40 mg of omeprazole or 60 mg lansoprazole daily for 3–6 weeks to treat endoscopically or radiographically confirmed duodenal ulcers and for up to 12 weeks for endoscopically or radiographically confirmed gastric ulcers (to allow time for endoscopic proof of healing), for 12 months (renewable) to treat reflux esophagitis refractory to first-line therapy, as defined in the guidelines, and for 7 days as part of H. pylori eradication therapy (the minimum duration of proton-pump inhibitor therapy in combination with clarithromycin and amoxicillin or metronidazole needed

![Fig. 1: Top: Total drug expenditures in Newfoundland and Labrador from 1992/93 to 1998/99. Bottom: Expenditures for drugs to treat upper gastrointestinal disorders, in 6-month intervals from March 1993 to March 1999.](image-url)
to eradicate \textit{H. pylori} was not fully determined in July 1996: requests for 10 days of therapy were approved until the 7-day regimens became standard practice. Requests based on circumstances falling outside the algorithms were evaluated on an individual basis.

The DHCS staff was available by telephone to answer questions and discuss requests. Physicians and pharmacists were informed that most requests would be processed within a few days but that decisions might take up to 2 weeks in high-volume periods or if additional information was required. Requests by the DHCS for additional information were made by telephone or in writing. Patients and pharmacists were informed of approvals by telephone, with a written reply to the physician. Nonapprovals were explained in writing to the physician.

**Results**

The program was implemented July 1, 1996, and statistics on the number and nature of requests for proton-pump inhibitors, nizatidine and famotidine were recorded for the following 6 months. Of 1078 requests for proton-pump inhibitors 973 (90%) were approved, primarily to treat gastroesophageal reflux disease and to eradicate \textit{H. pylori} (Table 1). Approval for their use to treat peptic ulcer disease was sometimes sought once the approval for \textit{H. pylori} eradication therapy had been given; therefore, the 973 approvals do not signify 973 patients. Some patients given \textit{H. pylori} eradication therapy were then prescribed a histamine antagonist to complete a course of peptic ulcer treatment. The number of requests for famotidine and nizatidine was negligible.

Total annual drug program expenditures, and 6-month expenditures for prokinetic drugs, \(H_2\)-antagonists and proton-pump inhibitors, are presented in Fig. 1. Total expenditures increased between 6% and 13% per annum, from $39.0 million in 1992/93 to $50.8 million in 1995/96. They then decreased by 9% to $46.4 million in 1996/97, which coincided with the introduction of the program, and thereafter resumed the annual rate increase seen before 1996/97. The decrease in total expenditures was due to a reduction in payments for proton-pump inhibitors. Before the program was implemented, the 6-month expenditures for proton-pump inhibitors increased from $0.7 million for the period ending March 1993 to $1.6 million for the period ending March 1996. After implementation of the program the expenditures for such drugs fell substantially, and the decline for the most part was sustained: for the 6 months ending March 1997 the expenditures were $0.3 million, 82% lower than those before program implementation, and for the 6 months ending March 1999 they were $0.6 million, 62% lower than those before implementation. Expenditures for \(H_2\)-antagonists, which remained at about $1.1 million per 6-month interval up to 1996, increased after the program was implemented, reaching $1.5 million for the 6 months ending March 1999. Expenditures for prokinetic drugs increased gradually, from $0.3 million for the 6 months ending March 1993 to $0.6 million for the 6 months ending March 1999, with no changes temporally correlated with the introduction of the program. The combined 6-month expenditure for the 3 classes of drugs rose from $2.1 million for the period ending March 1993 to $3.2 million for the period ending March 1996. After implementation of the program this figure fell by 36% to $2.0 million for the 6 months ending March 1997. A further 2 years later, for the 6 months ending March 1999, the combined expenditure was $2.7 million, which was still 16% lower than the combined expenditure for the 6 months ending March 1996.

Prescribers expressed positive comments, agreeing with the clinical information and prescribing guidelines. Criticism was mostly directed at process issues: short notification before implementation of the program, no access to toll-free telephone communication and no remuneration for the provision of supporting documentation. A few prescribers informed the DHCS that they would not participate in a process that required them to provide clinical information about their patients.

**Interpretation**

The program implemented by the DHCS to guide in the management of dyspepsia and gastroesophageal reflux disease represents a collaboration between the provincial government and health care professionals and associations and is the first such program to be designed and implemented in Newfoundland and Labrador. Following the program’s introduction, expenditures for gastrointestinal drugs in the 2 drug benefit plans, which had been increasing steadily from 1993 until the implementation of the program, fell substantially. It is reasonable to attribute a large portion of this decrease to the program. The DHCS’s total drug expenditures also increased from 1993 to the implementation of the program but thereafter showed no decrease beyond that attributable to the program. The reduction in expenditures was attributable almost entirely to diminished use of proton-pump inhibitors, particularly for long-term indications. The expenditures for proton-pump inhibitors in the first 6 months of the program were 90% lower than those in the preceding 6 months. This difference waned in the following months for a number of possible reasons, including improved familiarization by physicians and pharmacists with the authorization procedure and increased recognition of the benefit of \textit{H. pylori} eradication

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. (and %)</th>
<th>Duration of approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>679 (70%)</td>
<td>46 wk (average)</td>
</tr>
<tr>
<td>\textit{Helicobacter pylori} eradication therapy</td>
<td>186 (19%)</td>
<td>7–10 d</td>
</tr>
<tr>
<td>Peptic ulcer therapy</td>
<td>55 (6%)</td>
<td>9 wk (average)</td>
</tr>
<tr>
<td>Other</td>
<td>53 (5%)</td>
<td>28 wk (average)</td>
</tr>
<tr>
<td>Total</td>
<td>973 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Approvals for proton-pump inhibitor therapy in Newfoundland and Labrador from July 1 to Dec. 31, 1996
therapy. Nonetheless, a substantial reduction in annual expenditures for gastrointestinal drugs has been sustained since the program’s implementation.

Our economic evaluation of the program has limitations because other factors may have contributed to the observed reduction in expenditures for gastrointestinal drugs. For example, the number of subscribers to the 2 drug benefit plans fell by about 6%, from 117,637 in 1996 to 109,792 in 1998. In addition, analysis of the DHCS database showed that some patients who had been long-term users of gastrointestinal drugs stopped taking them after H. pylori eradication therapy. However, the impact would have been slight because there were about 30 such patients in the first 6 months of the program; even if all had been taking a proton-pump inhibitor, the savings would have been no more than $36,000 annually ($100 per patient per month). The first over-the-counter H2-antagonist was licensed for sale in Canada in June 1996; however, it is unlikely that its availability would account for the observed reduction in the use of proton-pump inhibitors, given that prescription-strength H2-antagonists were available and widely used by subscribers to the 2 drug benefit plans long before 1996. Another possible reason for the reduction in expenditures is the change in patient eligibility. Patients can gain, lose and regain eligibility for coverage on a month-to-month (seniors drug plan) and year-to-year (income-support drug plan) basis. However, the eligibility rules for these plans were last changed before 1991, and therefore it is unlikely that any reduction in annual expenditures after July 1996 can be attributed to changes in eligibility. Nonetheless, changes in eligibility mean that the expenditures do not necessarily reflect all treatment received by these patients for upper gastrointestinal disorders, and most nonprescription medications for upper gastrointestinal disorders are not covered by the drug plans.

The sharp decline in the prescribing of proton-pump inhibitors seen immediately after introduction of the program was accompanied by an increase in expenditures for H2-antagonists, despite the fact that the most expensive H2-antagonists were delisted. This suggests that physicians switched their patients’ prescriptions to cimetidine or ranitidine. We found no indication that physicians switched them to prokinetic drugs.

Patients may have continued to use proton-pump inhibitors outside the drug plans, but we believe that this is unlikely in most cases because of the cost, the increased use of H2-antagonists and the lack of complaints about the change in coverage. Comments from physicians indicated that, before implementation of the program, their prescribing decisions were often directed by patient demand for particular proton-pump inhibitors and that, after implementation, they found it easier to prescribe their choice of therapy.

In addition to the economic evaluation, the program itself has limitations. It was not designed to quantify acceptance by the health care community. However, given the lack of complaints to the DHCS and health care associations, it was judged to have been well accepted. In addition, the program was not designed to measure health outcomes. If approval was not sought for continued use of appropriate proton-pump inhibitor therapy after July 1996, some patients may have experienced an adverse health outcome. A small number of patients (estimated at fewer than 5) with a history of esophageal strictures properly treated with proton-pump inhibitors were referred to a gastroenterologist after new strictures developed because approval for continued use of the inhibitors was not requested by their physicians. Such cases illustrate that programs created to address overutilization of proton-pump inhibitors do not necessarily address, and may increase, inappropriate underutilization. Further study is needed to assess the management of upper gastrointestinal disorders in Newfoundland and Labrador.

Conclusions

A program designed by health care professionals, approved by health care associations and implemented by the government to guide the treatment of upper gastrointestinal disorders has been introduced in Newfoundland and Labrador and has achieved a substantial reduction in drug expenditures. The program has been well accepted by the health care community. Research is required to determine the impact of the program on health outcomes.

Competing interests: None declared for Ms. Crowley, Ms. Janes or Dr. Turner. Dr. Bursey has received speaker fees from AstraZeneca, Byk Gulden, Abbott Laboratories Ltd., and Janssen–Ortho Inc.

References


Reprint requests to: Dr. Christopher J. Turner, School of Pharmacy, University of Colorado Health Sciences Center, 4200 East Ninth Ave., Box C238, Denver CO 80262, USA; fax 303 315-8983; christopher.turber@uchsc.edu
Appendix 1: Gastrointestinal Medication Therapeutic Initiative

The Newfoundland and Labrador Prescription Drug Program (NLPDP), which administers the Social Services Drug Program and Senior Citizen’s Drug Subsidy Program, has accepted the therapy guidelines that were developed by the Gastrointestinal Review Ad hoc Committee. This Committee consisted of representatives of the Newfoundland and Labrador Medical Association, the Newfoundland Pharmacy Association, the Department of Health, as well as members of the academic community of School of Pharmacy and Faculty of Medicine. The Committee was established in order to develop therapy guidelines for specific gastrointestinal conditions including appropriate medication therapy as supported by clinical data and taking into account local practice and availability of resources. Its implementation by the Drug Program was intended to continue to provide maximum health benefits while reflecting both cost-effective pharmaceutical care and the appropriate utilization of medication.

Effective 1 July 1996, NLPDP shall be moving some open-benefit medications to the current restricted access process. Special authorization for coverage of these restricted access medications will be considered on an individual patient basis, and shall require documentation from the physician that provides clinical support in accordance with the guideline. It is recognized that while this places an additional burden on the physician to provide this information for those patients that are eligible recipients of the Program and who wish to have coverage provided, it is also felt that this is the only way in which compliance with the guidelines can be reasonably achieved and measured.

Questions and answers on guidelines and coverage of medication for gastrointestinal conditions

How much money does the program expect to save through the implementation of these guidelines? The Drug Program expended $6.6 million on medications within the gastrointestinal class, for which omeprazole accounted for approximately 50%. Based on the experiences of other provinces who have adopted similar guidelines for coverage of these medications, we would expect that considerable cost reduction can be achieved, while still providing appropriate medication coverage. The changes to medication coverage, from open-benefit to restricted access, for beneficiaries of the Social Services Drug Plan or Senior Citizens Drug Plan, will assist in ensuring that effective, but costly medication is available to those individuals who require it, in accordance with the guidelines.

When will the guidelines start to be enforced for prescriptions for seniors and indigents? The implementation date is 1 July 1996.

What medication coverage changes were made? Changes were made to the H2-antagonist and proton-pump inhibitor class. Of the four currently available H2-antagonists, cimetidine, ranitidine, famotidine and nizatidine, only the first two medications shall be provided as open-benefit medications. Ranitidine capsules, famotidine and nizatidine shall not be covered. Clinical literature supports that these four H2-antagonists have similar efficacy, but have significant therapy cost differences. As such, only the two lower cost medications shall be covered. The majority of prescriptions for H2-antagonists currently use ranitidine tablets.

Omeprazole has moved from open-benefit to restricted access. Consideration for coverage of a proton-pump inhibitor will now apply to all medications within this category (i.e., omeprazole and lansoprazole).

How does a physician go about getting omeprazole or other restricted drugs approved for the individual patient? Can the physician receive approval with a telephone call? Will a specific form be provided? What information will be required? All requests for coverage of restricted-access drugs should be made in writing to the Drug Program. There is no form provided for this request, as the information that would be provided is individually based, and may cover a variety of circumstances. The information should include, but is not limited to, specific diagnosis, clinical and diagnostic evidence supporting the use of the medication, the medication dosage and strength requested, and the expected duration of the therapy. Including information that further identifies the patient, (e.g., drug card identification number, telephone number, pharmacy, etc.) would reduce time to action approvals. As the Drug Program has no access to MCP numbers, the provision of this number would not be helpful. Information should be forwarded to: Newfoundland and Labrador Prescription Drug Program, Department of Health and Community Services, PO Box 8700, St. John’s NF A1B 4J6; fax 709 729-5824, if busy 729-3151.

What happens to patients who are due for renewals soon after the implementation date, but do not require another visit to the physician? Consideration for coverage cannot be given until documentation supporting the request for coverage is received and assessed by the Drug Program. The forwarding of such documentation on behalf of the patient may not necessarily require a medical visit by the patient first. If the support is there, in accordance with the guidelines, then the information can be sent to the Drug Program.

How long will the delay be for approval of a restricted drug for an individual patient? This process is not intended to operate as same-day access, although every effort will be made to process all requests as quickly as possible and to minimize administrative delays. While many requests should be able to be processed within a few days, a two-week turnaround may be expected during high-volume periods and where further information is needed to evaluate the request. Approvals will be actions by telephone to the patient and/or pharmacy, with a written reply to the physician. If further information is required the physician will be contacted by telephone or in writing. Non-approvals will be explained in writing to the physician. It is recognized that while some delay may be unavoidable, it is felt that this is the only way in which compliance with the guidelines can be reasonably achieved and measured. Consideration was also given to the category of medication and the respective disease states that would be affected by these changes. The fact that proton-pump inhibitors and some H2-antagonists will no longer be available or their provision delayed, should not present a life-threatening situation. It is recognized that some patients will be discomforted until approval is given, while in continued on page 822
other cases it is expected that the degree of discomfort experienced by the patient may be alleviated by lifestyle changes or modifications.

What group of patients are expected to receive authorization?
Requests shall be considered on the following basis:
1. Gastric ulcer/duodenal ulcer*: up to 40 mg omeprazole or 60 mg lansoprazole daily, for a 3–6 week period. Intended for those refractory to H2-antagonist therapy or as a cost-effective measure based on shorter treatment period.
2. Reflux esophagitis*: refractory to first-line therapy as per guideline. Up to 40 mg omeprazole or 60 mg lansoprazole daily, to be reviewed at least annually.
3. Helicobacter pylori eradication: coverage considered for 7-day cost-effective therapy that may include one of the newer antibiotics, such as clarithromycin, and a proton-pump inhibitor. Authorization shall be given for the first course without the need for documentation. The Program may be contacted by the pharmacy, the patient or the physician, and same-day access would be expected. However, further courses may require documentation including diagnostic support.
4. Other exceptional circumstances, including Zollinger–Ellison syndrome, or Barrett's esophagitis, will be evaluated on an individual basis. Some requests may require confirmation by a specialist qualified to diagnose and treat the condition.

It is recognized that there will be patients who will not receive approval for coverage of these restricted medications, and may state that full symptomatic relief is not felt using the medications that are available as open-benefits. However, it is strongly felt that there are patients who would be able to achieve appropriate relief but to do so would have to make significant and consistent lifestyle modifications. For those who do not wish to make such changes, the desired medication will certainly be available to them, but at their own expense.

What if the patient has already had the test indicated by the guideline? Will approval be granted?
It is not the intention of the Drug Program to request duplication of testing. In cases such as gastroesophageal reflux disease, where the diagnosis has been confirmed through appropriate diagnostic procedures, that other conventional therapy has been trialed, and determined to be clinically unsatisfactory, and that appropriate lifestyle changes have been made by the patient, then it is reasonable to expect coverage would be given. In other cases where the condition is acute, or short-term, then appropriate testing may be expected for each occurrence or episode.

Will the guidelines be reviewed regularly?
Yes. It is intended that any adopted guidelines will be reviewed as necessary, and at least annually. Comments, or input by practitioners on guideline content are welcomed and will be passed on to the appropriate committee.

*Diagnosis must be confirmed by endoscopy or radiology report.

Appendix 2: Algorithm for the management of gastroesophageal reflux disease.

*Patients with anemia, weight loss, aspiration and dyspepsia, in addition to symptoms of gastroesophageal reflux disease, should be referred for endoscopy.
†Offending drugs include α- and β-adrenergic agonists, β-blockers, calcium-channel blockers, benzodiazepines and theophylline. These drugs should be discontinued or alternative therapy considered, if possible. Lifestyle modification would include elevation of head of bed (6–8 inches), weight loss, avoidance of "irritating" food/drink, cessation or reduction in smoking.
‡Prescription-strength H₂-antagonists.
Appendix 3: Algorithm for the management of dyspepsia.

*Dyspepsia
Withdraw offending agents (e.g., NSAIIDs) if possible and address lifestyle changes (e.g., smoking and alcohol)

Adequate response
Continue current therapy

Inadequate response
Investigate: upper GI investigation*

*Upper GI investigation refers to procedures of radiography (barium swallow) and/or endoscopy

Duodenal ulcer

Helicobacter pylori eradication therapy†

Adequate response
No further treatment

Inadequate response
Endoscopy

Treatment as prescribed by endoscopist

Gastric ulcer

Endoscopy

Treatment as prescribed by endoscopist

Non-ulcer dyspepsia

Endoscopy if treatment unsatisfactory

Treat with H₂-antagonist and/or prokinetic agent

Maintenance treatment for chronic or recurrent symptoms

†A reasonable 1-week, twice daily therapy regimen for H. pylori eradication:
20 mg omeprazole or 30 mg lansoprazole, 250 mg clarithromycin, and 500 mg metronidazole
or 20 mg omeprazole or 30 mg lansoprazole, 500 mg clarithromycin, and 1000 mg amoxicillin

Treatment to complete the course necessary for the healing of peptic ulcers should be H₂-antagonist...