Approval Package for:

APPLICATION NUMBER:
ANDA 078374Orig1s004

Name: Metoclopramide Tablets USP
5 mg and 10 mg

Sponsor: Northstar Healthcare Holdings Limited

Approval Date: February 28, 2011
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APPLICATION NUMBER:
ANDA 078374Orig1s004

APPROVAL LETTER
Northstar Healthcare Holdings Limited
Attention: Joseph Mastronardy
501 Ivy Lake Drive
Forest, Virginia, 24551

Dear Sir:

This is in reference to your supplemental new drug application dated May 26, 2010, submitted pursuant to 21 CFR 314.70(c)(6) [Supplement – Changes Being Effected] regarding your abbreviated new drug application for Metoclopramide Tablets USP, 5 mg and 10 mg.

The supplemental application provides for revisions to the Medication Guide and Container labels in response to the Agency’s written communication dated March 30, 2010.

We have completed the review of this supplemental application and it is approved. However, this supplement is superseded by ANDA 078374/S-005.

We note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The materials submitted are being retained in our files.

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Reference ID: 2910854
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KOUNG U LEE
02/28/2011
For Wm. Peter Rickman
Medication Guide
Metoclopramide Tablets, USP

Read the Medication Guide that comes with metoclopramide tablets before you start taking them and each time you get a refill. There may be new information about the tablets.

Do not take metoclopramide tablets if:

- you have a blood in your stools

If you are not sure whether you are taking this medicine, ask your doctor or pharmacist for a label that lists the ingredients in metoclopramide tablets.

Before you start taking metoclopramide tablets, tell your doctor

- If you are taking any other medicines, including prescription or nonprescription medicines (such as aspirin), and herbal products

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Metoclopramide tablet and some other medicines may interact with each other and may not work as well, or may have serious side effects. Do not start any new medicines while taking metoclopramide tablet until you talk with your doctor.

Tell your doctor or pharmacist if you are taking any of the following:

- alcohol

Do not drink alcohol while taking metoclopramide tablets. Alcohol may make some side effects of metoclopramide tablets worse, such as feeling sleepy.

Do not drive or operate machinery, or do dangerous tasks until you know how metoclopramide tablets affect you.

What is the possible side effects of metoclopramide tablets?

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are severe:

- nervousness

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store metoclopramide tablets?

Keep metoclopramide tablets at room temperature between 68°F to 77°F (20°C to 25°C).

Keep metoclopramide tablets in the bottle it comes in. Keep the bottle closed tightly.

Keep metoclopramide tablets and all medicines out of the reach of children.

General information about metoclopramide tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use metoclopramide tablets for a condition for which it was not prescribed. Do not give metoclopramide tablets to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about metoclopramide tablets. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about metoclopramide tablets that is written for health professionals.

What are the ingredients in Metoclopramide Tablets, USP?

Active ingredient: metoclopramide

Inactive ingredients:

- Polysorbate 80

- Edetate disodium

- Sodium hydroxide or hydrochloric acid to adjust the pH

- Water for injection

- Sodium chloride

- Boric acid

- Methylparaben

- Propylparaben

Manufactured for:
Northstar Rx LLC, Memphis, TN 38141

Revised April 2010

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Medication Guide
Metoclopramide Tablets, USP

Read the Medication Guide that comes with metoclopramide tablets before you start taking it and each time you get a refill. There may be new information. If you take another product that contains metoclopramide (such as metoclopramide injection, metoclopramide orally disintegrating tablets, or metoclopramide oral solution), you should read the Medication Guide that comes with that product. Some of the information may be different. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about Metoclopramide Tablets?
Metoclopramide Tablets can cause serious side effects, including:

Abnormal muscle movements called tardive dyskinesia (TD). These movements happen mostly in the face muscles. You can not control these movements. They may not go away even after stopping metoclopramide tablets. There is no treatment for TD, but symptoms may lessen or go away over time after you stop taking metoclopramide tablets.

Your chances for getting TD go up:
• the longer you take metoclopramide tablets and the more metoclopramide tablets you take. You should not take metoclopramide tablets for more than 12 weeks.
• if you are older, especially if you are a woman
• if you have diabetes

It is not possible for your doctor to know if you will get TD if you take metoclopramide tablets.

Call your doctor right away if you get movements you can not stop or control, such as:
• lip smacking, chewing, or puckering up your mouth
• frowning or scowling
• sticking out your tongue
• blinking and moving your eyes
• shaking of your arms and legs

See the section “What are the possible side effects of metoclopramide tablets?” for more information about side effects.

What is metoclopramide tablet?
Metoclopramide tablets are a prescription medicine used:
• in adults for 4 to 12 weeks to relieve heartburn symptoms with gastroesophageal reflux disease (GERD) when certain other treatments do not work. Metoclopramide tablets relieves daytime heartburn and heartburn after meals. It also helps ulcers in the esophagus to heal.
• to relieve symptoms of slow stomach emptying in people with diabetes. Metoclopramide tablet helps treat symptoms such as nausea, vomiting, heartburn, feeling full long after a meal, and loss of appetite. Not all symptoms may improve at the same time.

It is not known if metoclopramide tablets are safe and works in children.

Who should not take Metoclopramide tablets?
Do not take metoclopramide tablet if you:
• have stomach or intestine problems that could get worse with metoclopramide tablets, such as bleeding, blockage or a tear in the stomach or bowel wall
• have an adrenal gland tumor called a pheochromocytoma
• are allergic to metoclopramide tablets or anything in it. See the end of this Medication Guide for a list of ingredients in metoclopramide tablets.
• take medicines that can cause uncontrolled movements, such as medicines for mental illness
• have seizures

What should I tell my doctor before taking Metoclopramide tablets?
Tell your doctor about all your medical conditions, including if you have:
• depression
• Parkinson’s disease
• high blood pressure
• kidney problems. Your doctor may start with a lower dose.
• liver problems or heart failure. Metoclopramide tablets may cause your body to hold fluids.
• diabetes. Your dose of insulin may need to be changed.
• breast cancer
• you are pregnant or plan to become pregnant. It is not known if metoclopramide tablets will harm your unborn baby.
• you are breast-feeding. Metoclopramide tablets can pass into breast milk and may harm your baby. Talk with your doctor about the best way to feed your baby if you take metoclopramide tablets.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Metoclopramide tablet and some other medicines may interact with each other and may not work as well, or cause possible side effects. Do not start any new medicines while taking metoclopramide tablet until you talk with your doctor.

Especially tell your doctor if you take:
• another medicine that contains metoclopramide, such as metoclopramide orally disintegrating tablets or metoclopramide oral solution
• a blood pressure medicine
• a medicine for depression, especially an Monoamine Oxidase Inhibitor (MAOI)
• insulin
• a medicine that can make you sleepy, such as an anti-anxiety medicine, sleep medicines, and narcotics.

If you are not sure if your medicine is one listed above, ask your doctor or pharmacist.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.
How should I take metoclopramide tablets?
- Metoclopramide Tablets, USP comes as a tablet you take by mouth.
- Take metoclopramide tablets exactly as your doctor tells you. Do not change your dose unless your doctor tells you.
- You should not take metoclopramide tablets for more than 12 weeks.
- If you take too much metoclopramide tablets, call your doctor or Poison Control Center right away.

What should I avoid while taking metoclopramide tablets?
- Do not drink alcohol while taking metoclopramide tablets. Alcohol may make some side effects of metoclopramide tablets worse, such as feeling sleepy.
- Do not drive, work with machines, or do dangerous tasks until you know how metoclopramide tablets affects you. Metoclopramide tablets may cause sleepiness.

What are the possible side effects of metoclopramide tablets?
Metoclopramide tablets can cause serious side effects, including:
- Abnormal muscle movements. See “What is the most important information I need to know about metoclopramide tablets?”
- Uncontrolled spasms of your face and neck muscles, or muscles of your body, arms, and legs (dystonia). These muscle spasms can cause abnormal movements and body positions. These spasms usually start within the first 2 days of treatment. These spasms happen more often in children and adults under age 30.
- Depression, thoughts about suicide, and suicide. Some people who take metoclopramide tablets become depressed. You may have thoughts about hurting or killing yourself. Some people who take metoclopramide tablets have ended their own lives (suicide).
- Neuroleptic Malignant Syndrome (NMS). NMS is a very rare but very serious condition that can happen with metoclopramide tablet. NMS can cause death and must be treated in a hospital. Symptoms of NMS include: high fever, stiff muscles, problems thinking, very fast or uneven heartbeat, and increased sweating.
- Parkinsonism. Symptoms include slight shaking, body stiffness, trouble moving or keeping your balance. If you already have Parkinson’s disease, your symptoms may become worse while you are receiving metoclopramide tablets.

Call your doctor and get medical help right away if you:
- feel depressed or have thoughts about hurting or killing yourself
- have high fever, stiff muscles, problems thinking, very fast or uneven heartbeat, and increased sweating
- have muscle movements you cannot stop or control
- have muscle movements that are new or unusual

Common side effects of metoclopramide tablets include:
- feeling restless, sleepy, tired, dizzy, or exhausted
- headache
- confusion
- trouble sleeping

You may have more side effects the longer you take metoclopramide tablets and the more metoclopramide tablets you take.
You may still have side effects after stopping metoclopramide tablets. You may have symptoms from stopping (withdrawal) metoclopramide tablets such as headaches, and feeling dizzy or nervous.
Tell your doctor about any side effects that bother you or do not go away. These are not all the possible side effects of metoclopramide tablets.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA-1088.

How should I store metoclopramide tablets?
- Keep metoclopramide tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep metoclopramide tablets in the bottle it comes in. Keep the bottle closed tightly.

Keep metoclopramide tablets and all medicines out of the reach of children.

General information about metoclopramide tablets
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.
Do not use metoclopramide tablets for a condition for which it was not prescribed. Do not give metoclopramide tablets to other people, even if they have the same symptoms that you have. It may harm them.
This Medication Guide summarizes the most important information about metoclopramide tablets. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about metoclopramide tablets that is written for health professionals.

What are the ingredients in Metoclopramide Tablets, USP?
Active ingredient: metoclopramide
Inactive ingredients:
**Metoclopramide Tablets, USP 10 mg:** Colloidal silicon dioxide, Corn starch, Pregelatinized starch, Magnesium stearate, Mannitol, Microcrystalline cellulose.
**Metoclopramide Tablets, USP 5 mg:** Colloidal silicon dioxide, Corn starch, D&C yellow # 10 (15 –20) aluminium lake, FD&C blue # 1 (11 –13) aluminium lake, Pregelatinized starch, Magnesium stearate, Mannitol, Microcrystalline cellulose.

Manufactured for
Northstar Rx LLC, Memphis, TN 38141

Revised April 2010

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Each tablet contains 5 mg of metoclopramide base as the monohydrochloride monohydrate.

Usual dosage: See accompanying descriptive literature.

Dispense in tight, light-resistant container as defined in the USP.

Storage: Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

PHARMACIST: Dispense the enclosed Medication Guide to each patient.

Manufactured for: Northstar Rx LLC
Memphis, TN 38141

Manufactured by: Piramal Healthcare Limited
Pithampur, Madhya Pradesh 454775, INDIA

Mfg Lic No.: 26/10/92
Each tablet contains 10 mg of metoclopramide base as the monohydrochloride monohydrate.

Usual dosage: See accompanying descriptive literature.

Dispense in tight, light-resistant container as defined in the USP.

Storage: Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

PHARMACIST: Dispense the enclosed Medication Guide to each patient.

Manufactured for: Northstar Rx LLC
Memphis, TN 38141

Manufactured by: Piramal Healthcare Limited
Pithampur, Madhya Pradesh 454775, INDIA

Mfg Lic No.: 25/10/52

Reference ID: 2910853
APPLICATION NUMBER:
ANDA 078374Orig1s004

LABELING REVIEW
Labeling Supplement Review

Application Number: 078374/S-004

Name of Drug: Metoclopramide Tablets USP, 5 mg and 10 mg

Applicant: Northstar Healthcare Holdings Limited

Material Reviewed: (specify labeling pieces)

Submission Date(s):
May 26, 2010

CBE Supplement:
INSERT with attached Medication Guide, Separate Medication Guide, Container labels

Background and Summary

1. Background: Safety labeling changes [under Section 505(o)(4) of the FDCA] pertaining to the risk of tardive dyskinesia and Risk Evaluation and Mitigation Strategy (REMS) was approved March 30, 2010.

2. The supplemental application provides for revisions to the Medication Guide and Container labels in response to the Agency’s written communication dated March 30, 2010 (post approval comments from the labeling review of S-003).

3. This supplement is not combined with chemistry.


Review

- INSERT: The insert should be revised to be in accordance with the most recently approved RLD insert, NDA 017854/S-055, approved November 18, 2010 (revisions to the WARNINGS, Tardive Dyskinesia section). See S-005.

- MEDICATION GUIDE: Revisions were made as requested in the March 30, 2010 Agency letter.

- CONTAINER: Medication guide statement has been revised to read “PHARMACIST: Dispense the enclosed Medication Guide to each patient.”
Recommendation

Submitted labels and labeling are acceptable.

INSERT with attached Medication Guide
Satisfactory in final print as submitted in the May 26, 2010 e-submission.

MEDICATION GUIDE
Satisfactory in final print as submitted in the May 26, 2010 e-submission.

CONTAINER (bottles of 30, 60, 90, 100, 500 and 1000)
Satisfactory in final print as submitted in the May 26, 2010 e-submission.

However, this supplement is superseded by ANDA 078374/S-005.

{see appended electronic signature}

Sarah Park
Labeling Reviewer

Supervisory Comment/Concurrence:

{see appended electronic signature}

Koung Lee
Team Leader
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SOOJUNG S PARK
02/27/2011

KOUNG U LEE
02/28/2011
For Wm. Peter Rickman
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 078374Orig1s004

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
SUPPLEMENT - CHANGES BEING EFFECTED (CBE)

Re: ANDA 78-374 for Metoclopramide Tablets, USP 5 mg, 10 mg of Northstar Healthcare Holdings Limited.

Reference is made to our Abbreviated New Drug Application (ANDA 78-374) for Metoclopramide Tablets, USP 5 mg, 10 mg approved on 30th November 2007 and supplement—Changes Being Effectcd approved on 30th March 2010. At this time Northstar Healthcare Holdings Limited is submitting a Supplement—Changes Being Effectcd, in response to the revisions requested to be made in our current labeling by FDA through a written communication dated 30th March 2010.

Form 356h is also included herewith.

1. CONTAINER — Please revise the Medication Guide statement on the principal display panel to one of the following:

 "PHARMACIST: Dispense the enclosed Medication Guide to each patient."

 "PHARMACIST: Dispense the accompanying Medication Guide to each patient." or "PHARMACIST: Dispense the Medication Guide provided separately to each patient."

The Medication Guide statement on the principal display panel of the labels of all the retail packs is revised to "PHARMACIST: Dispense the enclosed Medication Guide to each patient."
2. MEDICATION GUIDE

a. First paragraph - Revise the third sentence as follows:

If you take another product that contains metoclopramide (such as metoclopramide injection, metoclopramide orally disintegrating tablets, or metoclopramide oral solution), you should read the Medication Guide that comes with that product.

As requested, Medication guide has been revised to reflect the above mentioned revision.

b. Under "Especially tell your doctor if you take:”, please revise the first bullet as follows:

another medicine that contains metoclopramide, such as metoclopramide orally disintegrating tablets or metoclopramide oral solution.

As requested, Medication guide has been revised to reflect the above mentioned revision.

The revised labeling (container labels and package inserts with medication guide) shall be implemented for commercial distribution from 10th July 2010 onwards.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

We confirm to comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.
Northstar is confident that the information contained in this labeling amendment will satisfactorily provide the information requested by the agency. The US Agent, Joseph Mastroanardy, will provide any additional information as needed. Please contact him at 434-525-6084.

Sincerely,

Signature:

Collette Rohan  May 20th 2010

Michael Forkan Ph D.
Compliance Manager
Northstar Healthcare Limited
E-Mail: Michael.Forkan@nhl.ie
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