UPDATE to Prescribing Information for MINOCIN® (minocycline) for Injection

Subject: Prescribing Information Updated for New Formulation of MINOCIN® (minocycline) for Injection. Updates to Precautions, Changes to the Dosage and Administration instructions and important information regarding the addition of inactive excipient, magnesium sulfate, to the formulation.

Dear Pharmacy:

The purpose of this letter is to inform you of important updates to the Prescribing Information for MINOCIN®, a tetracycline indicated for the treatment of infections due to the susceptible strains of designated organisms, including Acinetobacter species bacteria. These updates to the Prescribing Information are based on the approval of a new formulation of MINOCIN® which is now available on the market.

The new formulation of MINOCIN® (minocycline) for Injection contains magnesium sulfate as an inactive excipient, which results in a higher pH of 4.5–6.0 following dilution. This change allows for a wider range of infusion volumes (100 mL to 1000 mL) than the current formulation. Therefore it is important to distinguish between the two formulations as they have different administration instructions.

Additionally, important new information has been added, including important information regarding the addition of inactive excipient, magnesium sulfate, to the following sections of the Prescribing Information:

• Description
• Precautions
• Drug Interactions
• Adverse Reactions
• Dosage and Administration
• Incompatibilities

Specifically the following language is from the Prescribing Information:

DESCRIPTION

MINOCIN® is supplied as a sterile yellow to amber lyophilized powder for intravenous infusion. Each vial contains minocycline HCl equivalent to 100 mg minocycline, 269 mg magnesium sulfate.
heptahydrate (2.2 mEq of magnesium) (an inactive ingredient) and sodium hydroxide (to adjust pH). When reconstituted with 5 mL of Sterile Water for Injection USP the pH ranges from 4.5 to 5.0.

**PRECAUTIONS**

MINOCIN® (minocycline) for Injection contains magnesium sulfate heptahydrate (see DESCRIPTION). Because magnesium is excreted primarily by the kidney, serum levels of magnesium should be monitored in patients with renal impairment (see DOSAGE AND ADMINISTRATION).

Because MINOCIN® (minocycline) for Injection contains magnesium (see DESCRIPTION), close monitoring is recommended in patients with heart block or myocardial damage.

**DRUG INTERACTIONS**

MINOCIN® (minocycline) for Injection contains magnesium sulfate heptahydrate (see DESCRIPTION). Potentially serious drug interactions may occur when intravenous magnesium sulfate heptahydrate is given concomitantly with CNS depressants, neuromuscular blocking agents and cardiac glycosides.

**ADVERSE REACTIONS**

MINOCIN® (minocycline) for Injection contains magnesium sulfate heptahydrate (see DESCRIPTION). Adverse effects that may be associated with magnesium intoxication include flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and CNS depression proceeding to respiratory paralysis (see PRECAUTIONS).

**DOSAGE AND ADMINISTRATION**

For Pediatric Patients above 8 year of age
Usual pediatric dose: Initial dose of 4 mg/kg, then 2 mg/kg administered over 60 minutes every 12 hours, not to exceed the usual adult dose.

Adults
Usual adult dose: Initial dose of 200 mg, then 100 mg administered over 60 minutes every 12 hours and should not exceed 400 mg in 24 hours.

The lyophilized powder should be reconstituted with 5 mL Sterile Water for Injection USP and immediately further diluted in 100 mL to 1,000 mL with Sodium Chloride Injection USP, Dextrose Injection USP, or Dextrose and Sodium Chloride Injection USP, or in 250 mL to 1,000 mL Lactated Ringer's Injection USP, but not with other solutions containing calcium because a precipitate may form especially in neutral and alkaline solutions.

When diluted in compatible solutions, the pH usually ranges from 4.5 to 6.0.

Once diluted into an intravenous bag, MINOCIN® for Injection may be stored either at room temperature for up to 4 hours or refrigerated
at 2 to 8°C (36 to 46°F) for up to 24 hours. Any unused portions must be discarded after that period.

The pharmacokinetics of minocycline in patients with renal impairment (CLCR < 80 mL/min) have not been fully characterized. Current data are insufficient to determine if a dosage adjustment is warranted. The total daily dosage should not exceed 200 mg in 24 hours in patients with renal impairment. However, due to the anti-anabolic effect of tetracyclines, BUN and creatinine should be monitored (See WARNINGS). Because MINOCIN® (minocycline) for Injection contains magnesium sulfate heptahydrate, serum levels of magnesium should be monitored in patients with renal impairment (See DESCRIPTION, PRECAUTIONS).

INCOMPATABILITIES
Additives or other medications should not be added to MINOCIN® single-use vials or infused simultaneously through the same intravenous line including Y-connectors. If the same intravenous line is used for sequential infusion of additional medications, the line should be flushed before and after infusion of MINOCIN® with Sodium Chloride Injection USP, Dextrose Injection USP, Dextrose and Sodium Chloride Injection USP, or Lactated Ringer's Injection USP.

Reporting Adverse Events
Health care providers and patients are encouraged to report adverse events in patients taking MINOCIN® to The Medicines Company at 1-877-488-6835. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

This letter is not intended to provide a complete description of the Prescribing Information including the benefits and risks related to the use of MINOCIN®. Please refer to the enclosed full prescribing information. You may also contact our medical information department at 1-877-488-6835 if you have any questions about the information contained in this letter or the safe and effective use of MINOCIN®.

Sincerely,

Loretta M Itri, MD., F.A.C.P.
Executive Vice President, Global Health Science & Regulatory Affairs
The Medicines Company

Enclosure(s): MINOCIN® Full Prescribing Information