



Summary of investigation results

Metronidazole, Lansoprazole/Amoxicillin hydrate/Metronidazole, Rabeprazole sodium/Amoxicillin hydrate/Metronidazole

Aug 6, 2014

Non-proprietary Name

- a. Metronidazole
- b. Lansoprazole/Amoxicillin hydrate/Metronidazole
- c. Rabeprazole sodium/Amoxicillin hydrate/Metronidazole

Brand Name (Marketing Authorization Holder)

- a. Flagyl tablets 250 mg (Shionogi & Co., Ltd) and the others
- b. LAMPION pack (Takeda Pharmaceutical Company Limited)
- c. Rabefine pack (Eisai Co., Ltd.)

Indications

- a. Flagyl tablets 250 mg (Shionogi & Co., Ltd) and the others
- Trichomoniasis (*Trichomonas vaginalis* infection)
- Bacterial anaerobic infections

Applicable microorganisms:

Metronidazole-susceptible strains of genus *Peptostreptococcus*, genus *Bacteroides*, genus *Prevotella*, genus *Porphyromonas*, genus *Fusobacterium*, genus *Clostridium*, and genus *Eubacterium*

Applicable conditions:

Deep-seated skin infections, secondary infections that are suffered from trauma, thermal burn, and surgical wound, osteomyelitis, pneumonia or pneumonitis, pelvic inflammatory disease, peritonitis or intra-abdominal abscess, liver abscess, and brain abscess



This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

- Enteritis infectious
 - Applicable microorganisms:
 - Metronidazole-susceptible strains of *Clostridium difficile*
 - Applicable conditions:
 - Enteritis infectious (including pseudomembranous colitis)
 - Bacterial vaginosis
 - Applicable microorganisms:
 - Metronidazole-susceptible strains of genus *Peptostreptococcus*, *Bacteroides fragilis*, *Prevotella bivia*, genus *Mobiluncus*, and *Gardnerella vaginalis*
 - Applicable conditions:
 - Bacterial vaginosis
 - *Helicobacter pylori* infection
 - Applicable microorganisms:
 - Metronidazole-susceptible strains of *Helicobacter pylori*
 - Applicable conditions:
 - Helicobacter pylori* infection in stomach and *Helicobacter pylori* gastritis after endoscopic therapy of gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphoid tissue lymphoma, idiopathic thrombocytopenic purpura, or early stage gastric cancer
 - Amoebic dysentery
 - *Giardia lamblia* infection
- b. LAMPION pack (Takeda Pharmaceutical Company Limited) and c. Rabefine pack (Eisai Co., Ltd.)
- Applicable microorganisms:
 - Amoxicillin and metronidazole-susceptible strains of *Helicobacter pylori*
 - Applicable conditions:
 - Helicobacter pylori* infection in stomach and *Helicobacter pylori* gastritis after endoscopic treatment of gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphoid tissue lymphoma, Idiopathic thrombocytopenic purpura, or early stage gastric cancer



Summary of revision

- a. Flagyl tablets 250 mg (Shionogi & Co., Ltd) and the others
'Haemorrhagic colitis' should be added in Clinically significant adverse reactions section.
- b. LAMPION pack (Takeda Pharmaceutical Company Limited) and c. Rabefine pack (Eisai Co., Ltd.)
'Haemorrhagic colitis' should be added in Flagyl subsection of Clinically significant adverse reactions section.

Background of the revision and investigation results

Cases of haemorrhagic colitis have been reported in patients treated with metronidazole-containing products in Japan. Following an investigation result based on opinions of expert advisors and available evidence, the MHLW/PMDA concluded that revision of the package inserts was necessary.

The number of reported adverse reaction and fatal cases in the last 3 fiscal years in Japan

- a. Flagyl tablets 250 mg (Shionogi & Co., Ltd) and the others
A total of 10 cases of haemorrhagic colitis has been reported (including 7 cases in which causality could not be ruled out). Of the 10 cases*, no fatalities have been reported.
- b. LAMPION pack (Takeda Pharmaceutical Company Limited)
A total of 10 cases of haemorrhagic colitis has been reported (including 3 cases in which causality could not be ruled out). Of the 10 cases*, no fatalities have been reported.
- c. Rabefine pack (Eisai Co., Ltd.)
No haemorrhagic colitis cases* have been reported in the last 3 fiscal years in Japan.

NOTE

* Haemorrhagic colitis cases are defined as those cases in which patients are required to be admitted to hospital because of haemorrhagic colitis (including a case in which necessity of admission to hospital was not clear in a patient treated with Flagyl tablets or others).