



Dedicated to

My deepest gratitude goes to my family who has provided me support throughout my whole life and guided me to reach my objective of life.

Thanks Mom & Dad.

Supervisor: Zakir Rahman

A handwritten signature in black ink, appearing to be "Zakir Rahman".

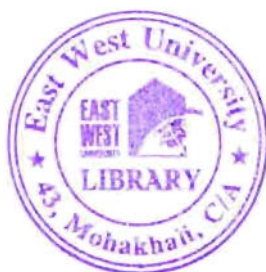


ACKNOWLEDGEMENT

At the outset, I would like to recall the pity & kindness of Almighty Allah & thank Him for showing me the right path of securing special knowledge in science & has made me keen to undertake research work on the topic.

Later, I want to express my heartfelt gratitude to the learned guide & supervisor, lecturer Zakiur Rahman, East West University, whose sincere, active, enthusiastic, outstanding guidance & competent supervision during the tenure of research has enabled me to reach the end.

I express special thanks to Masudur Rahman, product manager, Renata Pharmaceuticals, Dhaka, for extending the facilities to work. Finally, I am thankful to all of them who caused even too a little to my effort as well wishers. May Allah bless and help us all to render something for the cause of the mankind.



Abstract

Doripenem is a novel carbapenem drug. It is broad spectrum antibiotic. Effort was given to find about the characteristics of the drug and whether it is suitable to launch in the Bangladesh market. Information was gathered from website, journal and books. For market feasibility study IMS, MIMS and QUIMP was observed. It was found that doripenem is noninferior to meropenem, imipenem and ertapenem. It can be used in the complicated urinary tract infections and complicated intra abdominal infections. Doripenem is not in Bangladesh yet. If it is launched doripenem market size would be 10,00,000 taka and its growth would be 10% first year, 25% second year, 15% in third year. From the information from market feasibility study, swot analysis and product positioning it may be profitable to launch doripenem in Bangladesh.

Table of content

Background	1
1. Doripenem	1
1.1 History	2
1.2 Mechanism of action	2
1.3 Pharmacokinetics	2
1.4 Time action profile (blood level)	3
2. Doripenem can not used if be	3
3. Before using Doripenem	3
4. How to use Doripenem	4
5. Important safety information	5
6. Possible side effects of Doripenem	6
7. Broad-spectrum antibacterial activity	6
8. Pivotal phase III trials	7
9. Complicated intra-abdominal infections	7
10. Complicated urinary tract infections	8
11. How is doripenem given?	8
12. Recommended dosage	9
13. What is complicated UTIs	11
14. Evaluation of recurrent UTIs	11
15. When to evaluate for complicated infection	11
16. Management of recurrent UTIs	12
17. Relapsing UTIs	12
18. Reinfection in women	12
19. Literature review	13
Objective	16
Hypothesis	17
Method	18
Result and discussion	19
1. Comparison of activity	19
2. Market size of competitor's of doripenem	24
4. Product positioning	27
5. SWOT analysis of doripenem	32
Conclusion	34
Limitations	35
References	36



Background:

1. Doripenem:

Doripenem is an injectable antibiotic having ultra broad spectrum. It is a lactam and belongs to the subgroup of carbapenem. It has coverage against gram positive, gram negative and anaerobic pathogens. Doripenem gives better activity than meropenem against some strains of pseudomonas aeruginosa (U.S. Food and Drug Administration, 2007)

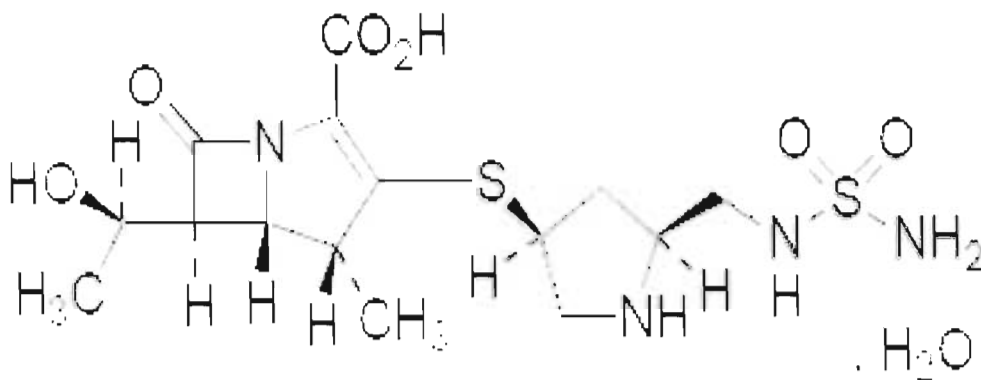


Fig:1 Structure of Doripenem

Chemical formula: C₁₅H₂₄N₄O₆S₂

Mol. Mass: 420.50426g/mol

Systemic IUPAC name: (4*R*,5*S*,6*S*)-6-(1-hydroxyethyl)-4-methyl-7-oxo-3-[(3*S*,5*S*)-5-[(sulfamoyl-amino)methyl]pyrrolidin-3-yl]sulfanyl-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid (U.S. Food and Drug Administration, 2007).

1.1 History:

Shionogy Co of Japan launched Doripenem under the brand name of Finibax in 2005. United Food and Drug administration approved doripenem on October 12, 2007, to be sold under the tradename of doribax (U.S. Food and Drug Administration, 2007).

1.2 Mechanism of action:

Doripenem belongs to the carbapenem class of antimicrobials. Doripenem inhibit bacterial cell wall biosynthesis thus it shows its bactericidal action. Cell death occurs when doripenem inactivates multiple essential penicillin binding proteins. In *E. coli* and *P. aeruginosa* doripenem bind to PBP2, which is involved in the maintenance of cell shape as well as to PBPs 3 and 4 (Fritsche TR, Stilwell MG, Jones RN. 2005).

Doripenem is indicated as a single agent in adults (>18 years of age) for the treatment of:

- Complicated intra-abdominal infections caused by susceptible strains of *E coli*, *K pneumoniae*, *P aeruginosa*, *B caccae*, *B fragilis*, *B thetaiotaomicron*, *B uniformis*, *B vulgatus*, *S intermedius*, *S constellatus*, or *P micros*;
- Complicated urinary tract infections, including pyelonephritis caused by susceptible strains of *E coli*, including cases with concurrent bacteremia, *K pneumoniae*, *P mirabilis*, *P aeruginosa*, or *A baumannii*(same).

1.3 Pharmacokinetics:

The pharmacokinetic profile of doripenem is similar to meropenem and imipenem/cilastatin.

Distribution: penetrates renal and peritoneal and retroperitoneal tissues and fluids.

Absorption: IV administration results in complete bioavailability.

Metabolism and excretion: mostly excreted unchanged in urine, minimal metabolism

(Iolanda Cirillo, MBS, Nicole Vaccaro, BS, Kenneth Turner, PhD, Bhavna Solanki, MS, Jaya Natarajan, PhD and Rebecca Redman, MD)

1.4 Time action profile (blood level):

Doripenem is given in IV route. The onset of doripenem is unknown. At the end of infusion peak occurs. Duration or frequency of giving doripenem is after every 8 hours for one-hour infusion. (www.drugguide.com)

Doripenem binds 8% to plasma and meropenem and imipenem bind 2 and 20 respectively. However ertapenem is highly protein. It is a bad aspect of the drug. Because suppose a drug is 99 proteins bound that means 1% is free drug. If the drug loses another 1% its concentration increases by 100%. This can show toxicity. Higher and lower protein binding does not indicate good or bad drug. For example paracetamol is 0% protein binding. (Jones RN, Huynh HK, Biedenbach DJ. 2004)

2. Doripenem can not be used if:

- If patient is allergic to any ingredient in Doripenem or to any other carbapenem or beta-lactam antibiotic (eg, meropenem)(www.drugs.com).
- While taking doripenem patient is taking probenecid(www.drugs.com).

3. Before using Doripenem :

Some medical conditions may interact with Doripenem. Doctors need to be consulted if any of the following apply to patient (www.drugs.com):

- If patient is pregnant, planning to become pregnant, or are breast-feeding.
- If patient is taking any prescription or nonprescription medicine, herbal preparation, or dietary supplement.
- If patient have allergies to medicines, foods, or other substances.
- If patient has had a severe allergic reaction (eg, severe rash, hives, difficulty breathing, and dizziness) to a penicillin antibiotic (eg, amoxicillin) or a cephalosporin antibiotic (eg, cephalexin).

- If patient has a history of seizures.
- If patient has kidney problems or are on dialysis (www.drugs.com).

Some medicine may interact with Doripenem. Doctors need to be consulted especially any of the following medicine is taken with doripenem:

- Probenecid because it may increase the risk of Doripenem's side effects.
- Valproic acid because its effectiveness may be decreased by Doripenem.

This may not be a complete list of all interactions that may occur.

4. How to use Doripenem

Doripenem is used as directed by doctors. For exact dosing instructions the label on the medicine is checked (www.drugs.com).

- Doripenem is usually administered as an injection at doctor's office, hospital, or clinic. If patient is using Doripenem at home, patient should carefully follow the injection procedures taught to the patient by health care provider.
- Doripenem can not be used if it contains particles, is cloudy or discolored, or if the vial is cracked or damaged.
- To clear infection completely, Doripenem is used for the full course of treatment. Patient should keep using it even if he feels good.
- The syringes, needle and doripenem should be kept out of reach of children. Syringes, needle should not be used again. there is instruction about how to dispose syringes, needle. All local rules for disposal should be followed.
- If a dose of doripenem is missed doripenem should be used as soon as possible. If it is almost time for next dose, the missed dose should be skipped and regular dosing schedule should be followed. 2 doses at once should not be used.

5. Important safety information:

Important safety information is given below (www.drugs.com)

- Doripenem only works against bacteria; it does not treat viral infections (eg, the common cold).
- One needs to use Doripenem for the full course of treatment. If someone does not, the medicine may not clear up infection completely. The bacteria could also become less sensitive to this or other medicines. This could make the infection harder to treat in the future.
- Long-term or repeated use of Doripenem may cause a second infection. Doctors need to be consulted if signs of second infection occur. Medicine may need to be changed to treat this.
- If severe diarrhea or stomach pain or cramping develop during treatment or within several months after treatment with Doripenem , doctors need to be consulted immediately.
- Mild diarrhea is common with antibiotic use. However, a more serious form of diarrhea (pseudomembranous colitis) may rarely occur. This may develop while patient use the antibiotic or within several months after patient stop using it. Doctor need to be consulted right away if stomach pain or cramps, severe diarrhea, or bloody stools occur. Should not be treated diarrhea without first checking with doctor.
- Doripenem should be used with caution in the elderly; they may be more sensitive to its effects.
- Doripenem should be used with extreme caution in children; safety and effectiveness in children have not been confirmed.
- Pregnancy and breast feeding: doripenem has pregnancy category B. it is some way better than other medicine. If the patient is breast feeding she need to consult with the doctor about the effect in her baby.(www.fda.gov)

6. Possible side effects of Doripenem:

All medicines cause side effects, but a lot of people have no, or minor, side effects. Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); bloody stools; chest pain; pain, swelling, or redness at the injection site; red, swollen, blistered, or peeling skin; seizures; severe diarrhea; severe stomach cramps or pain; shortness of breath; unusual tiredness or weakness; unusual vaginal odor, itching, or discharge may be seen.

This is not a complete list of all side effects that may occur. (Jones RN, Huynh HK, Biedenbach DJ. 2004)

7. Broad-spectrum antibacterial activity:

It was first introduced into clinical practice about 20 years ago; to the β -lactam class of antibiotics the carbapenems are the most recent addition, one of the largest classes of antibiotics that also include penicillins and cephalosporins (Pappas G, Saplaoura K, Falagas ME. 2009).

Carbapenems occupy the broad-spectrum activity of the β -lactam class but essentially differ from earlier class members in possessing stability to most clinically important bacterial β -lactamases. In first-line treatment of serious bacterial infections and as reserved therapy for defined resistant pathogens this makes them useful (Pappas G, Saplaoura K, Falagas ME. 2009).

Doripenem, a 1- β -methyl carbapenem, has a lot of features that suggest it could be a useful addition to the current range of carbapenems:

- Enhanced activity against non-fermentative gram-negative bacilli
- Bactericidal activity against most pathogens
- Stability to human renal dehydropeptidases
- Stability to common bacterial β -lactamases, including extended-spectrum β -lactamases (ESBLs)
- Post-antibiotic effects against *Pseudomonas aeruginosa*
- Potent activity against penicillin-resistant streptococci
- Effective at low doses



8. Pivotal phase III trials:

Doripenem entered phase III trial in the US after successful completion of phase II trial by Peninsula Pharmaceuticals. On the basis of four phases III trials, which enrolled patients with, complicated intra-abdominal and urinary tract infections regulatory approval was secured. Doripenem emerged non-inferior to both meropenem and intravenous levofloxacin in complicated intra-abdominal and urinary tract infections across the four trials. It was also well tolerated (www.drugdevelopment-technology.com).

Doripenem was proved superior compared to meropenem in pseudomonal eradication. Doripenem cured 95% and 76% of patients respectively while meropenem cured only 79% and 69% respectively in two cIAI clinical studies conducted (www.drugdevelopment-technology.com).

Nosocomial pneumonia is among the most common infections in intensive care units accounting for about 15% of all hospital-acquired infections. IV doripenem is also being evaluated in nosocomial pneumonia. Mortality exceeds 30% and is highest among mechanically ventilated patients. An important determinant of clinical outcome is selecting the right antibiotic in such cases (www.drugdevelopment-technology.com).

Japanese phase III trials formed the basis of regulatory submissions to the Japanese Ministry of Health, Labor and Welfare; IV doripenem was evaluated in pneumonia, chronic respiratory tract infections, and UTI

In the Japanese phase III trials, which formed the basis of regulatory submissions to the Japanese Ministry of Health, Labor and Welfare, IV doripenem was evaluated in pneumonia, chronic respiratory tract infections, and UTI (www.drugdevelopment-technology.com)

9. Complicated intra-abdominal infections:

Two similar studies enrolled a total of 946 adult subjects. Doripenem was given to subjects (500mg administered over 1 hour every 8 hours) or meropenem was given (1g

administered over 3-5 minutes every 8 hours) in both treatment arms subject was given the option to switch to oral amoxicillin/ clavulnate (875mg/125mg twice daily) after a minimum of 3 days of intravenous therapy for a total of 5-14 days of intravenous and oral treatment. In post treatment doripenem was noninferior to meropenem in clinical cure rates 25-45 days. (Jones RN, Huynh HK, Biedenbach DJ. 2004)

In study where microbiologically evaluable population was enrolled doripenem clinical cure rate was 82.8% and in the meropenem arm the clinical cure rate was 85.9% a -3.1 treatment difference. In study 2 where microbiologically evaluable population was enrolled doripenem clinical cure rate was 81% and meropenem clinical cure rate was 82.1%, a treatment difference of -1.1% (Fritsche TR, Stilwell MG, Jones RN. 2005)

10. Complicated urinary tract infections:

1171 subjects were enrolled in two-multi center, multinational studies. One was double blind study and compared doripenem (500mg administered over 1 hour every 8 hours) to IV levofloxacin (250mg administered every 24 hours. The second study was noncomparative study but design was same. In both trial subjects could switch to oral levofloxacin (250 mg every q24hour) after a minimum of 3 days of IV therapy for a total treatment of 10 days. Subjects were allowed to receive 500mg of IV levofloxacin who had confirmed concurrent bacterimia for a total of 10-14 days of treatment. With regard to the microbiological eradication rates in microbiologically evaluable subjects 5-11 days post treatment doripenem was noninferior to levofloxacin (Hori T, Nakano M, Kimura Y, Murakami K 2006).

The eradication rate for doripenem was 82.1% and levofloxacin was 83.4% a -1.3 treatment difference in the microbiological evaluable population (Bhavnani SM, Hammel JP. 2005)

11. How is doripenem given?

Through a needle placed into a vein doripenem is given as an injection. In hospital or clinic patient is given this medication. The medicine must be given slowly through an IV infusion, and can take at least 1 hour to complete (health.yahoo.com)

Depending on the condition being treated, doripenem is usually given for 5 days to 2 weeks. Patient may be switched to an oral (pill form) antibiotic after the first few days of receiving doripenem by injection. (health.yahoo.com)

At home patient may be shown how to inject the medicine. If he does not understand the mixing process, after giving the injection and properly dispose of needles, IV tubing, and other items used in giving the medicine, patient should not self inject it (health.yahoo.com).

Doripenem is a powder that must be mixed with a liquid (diluent) (health.yahoo.com).

After mixing doripenem with the diluents, keep it in a refrigerator. Keep from freezing, and use the mixture within 24 hours (health.yahoo.com)

12. Recommended dosage:

In-patient greater than 18 doripenem has to be given 500mg after every 8hrs over one hrs

Dosage of doripenem:

Disease name	Dose	Frequency	Duration of treatment
Complicated intra-abdominal infection	500 mg	q8h	5–14 days*
Complicated UTI, including pyelonephritis	500 mg	q8h	10 days*†

* Duration includes a possible switch to an appropriate oral therapy, after at least 3 days of parenteral therapy, once clinical improvement has been demonstrated.

† Duration can be extended up to 14 days for patients with concurrent bacteremia. (www.rxlist.com)

Dosage of doripenem in Patients with Renal Impairment

> 50	No dosage adjustment necessary
≥ 30 to ≤ 50	250 mg intravenously (over 1 hour) every 8 hours
> 10 to < 30	250 mg intravenously (over 1 hour) every 12 hours

The following formula may be used to estimate CrCl. The serum creatinine used in the formula should represent a steady state of renal function.

Males: Creatinine clearance (mL/min) = weight (kg) × (140 - age in years) / 72 × serum creatinine (mg/dL).

Females: Creatinine clearance (mL/min) = 0.85 × value calculated for males doripenem is hemodialyzable; however, there is insufficient information to make dose adjustment recommendations in patients on hemodialysis (www.rxlist.com).

Preparation of solution:

Doripenem drug contain bacteriostatic preservative so aseptic technique is used.

Preparation of 500mg dose:

1. The vial is constituted by 10ml sterile water or .9% sodium chloride injection and gently shaken. The resultant solution is 50mg/ml. This is not for direct injection.
2. Withdraw the suspension using a syringe with a 21 gauge needle and add it to an infusion bag containing 100 mL of normal saline or 5% dextrose; gently shake until clear. The final infusion solution concentration is 4.5 mg/mL
3. Constitute the vial with 10 mL of sterile water for injection or 0.9% sodium chloride injection (normal saline). Then gently shake to form a suspension. The resultant concentration is 50 mg/mL. This is not for direct injection.
4. Withdraw the suspension using a syringe with a 21 gauge needle and add it to an infusion bag containing 100 mL of normal saline or 5% dextrose; gently shake until clear. Remove 55 mL of this solution from the bag and discard. Infuse the remaining solution, which contains 250 mg (4.5 mg/mL) (www.rxlist.com).

13. What is complicated UTIs:

Complicated UTI are found in some young women, most elderly women and mostly men. It occurs when the urinary tract is functionally and structurally abnormal, the host is more resistance against antimicrobial therapy. The symptoms of complicated UTIs include simple cystitis (characterized by frequent, urgent and painful urination) to severe kidney or prostate infection (fever, chills, flank pain, or irritative, obstructive voiding) and life threatening bloodstream infection. These symptoms may not show up initially so a high index of suspicion and careful assessment of outcomes is required. Complicated UTIs are caused by a broad range of bacteria including *E. coli*, other gram negative bacteria (including proteus, klebsiella and pseudomonas species), and gram positive bacteria (enterococci and staphylococci). Since these strains originate from hospital or nursing care environment they appear to be more resistant.

Before starting therapy urine culture must be obtained to identify the pathogen and antimicrobial susceptibility. During treatment culture should be obtained to determine the efficacy (Raz R, Stamm WE. 1993)

14. Evaluation of recurrent UTIs:

In most women with symptoms of UTIs and in many men with symptoms of prostatitis or chronic pelvic pain syndrome, antimicrobial therapy is used without obtaining culture. In recurrent symptoms, it is mandatory that to document that the symptoms are due to bacterial infections. If culture show no infection other causes of symptoms should be evaluated (Hooton TM 2001).

15. When to evaluate for complicated infection:

The women with recurrent UTIs usually have normal urinary tract they do not have structural or functional abnormality. So referral to a urologist is unnecessary.

However, if the woman has history of childhood UTI or a pattern of recurring infections with the same bacterial strain more evaluation is necessary. This is important if the infection occurs at close intervals.

In older men UTIs are complicated. So imaging a urologic evaluation is necessary. However in young men the response to therapy is assessed and if recur does not occur then urologic evaluation is not necessary (Hooton TM 2001).

16. Management of recurrent UTIs:

If relapse occur than surgery is performed to remove infection focus and if reinfection occurs having no urologic abnormalities long term medical management is given (Hooton TM 2001)

17. Relapsing UTIs:

Rapid recurrence is an indication of relapsing infection. It should be evaluated if the infection is due to same bacteria. CT scan may reveal abnormality in the urinary tract (such as stone) or a congenital or acquired obstruction that impedes flow of urine (such as ureteral pelvic junction obstruction or enlargement of the prostate gland) these findings warrant urologic evaluation. Chronic bacterial prostatitis should be considered in men. If bacterial persistence is observed than surgery can prevent the relapse. For example, ureteral catheters can be placed in the kidney to collect urine and establish the relationship between a stone in the kidney and bacterial persistence. Similarly a prostate localization culture can determine if a patient has chronic bacterial prostatitis. *Proteus mirabilis* forms a stone that leads to high urinary pH, precipitation of crystals and formation of an infection stone that incorporates bacteria within, in this occur surgical removal prevent relapse. (Fihn SD 2003)

18. Reinfection in women:

If two or more symptomatic UTIs in six months or three or more episodes within 12 months occur then it is called reinfection. Prior history of infection, medical comorbidities, use of antimicrobials, sexual history and use of spermicides should be

reviewed. The possibility of communication between the bladder, bowel or vagina is rare condition. For example air in urine (peumaturia), stool in urine (fecaluria) etc is found then urologic referral is necessary.

(Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. 1999)

19. Literature review:

Doripenem is indicated as a single agent in adults (>18 years of age) for the treatment of:

- Complicated intra-abdominal infections caused by susceptible strains of *E coli*, *K pneumoniae*, *P aeruginosa*, *B caccae*, *B fragilis*, *B thetaiotaomicron*, *B uniformis*, *B vulgatus*, *S intermedius*, *S constellatus*, or *P micros*;
- Complicated urinary tract infections, including pyelonephritis caused by susceptible strains of *E coli*, including cases with concurrent bacteremia, *K pneumoniae*, *P mirabilis*, *P aeruginosa*, or *A baumannii* (www.doribax.com).

Very high affinity for penicillin binding proteins:

Doripenem is a highly protein bound drug. Unlike penicillin and cephalosporins, doripenem binds with the highest affinity for the penicillin-binding proteins resulting lyses of bacterial cell wall.

Excellent pharmacokinetic profile:

- Excellent rate of absorption
- No tendency to accumulate in the body
- Rapid distribution through out the body
- Effective concentration in bone
- Good half life

Favorable safety profile:

- Less likely cause inflammation at IV site
- Pregnancy category B no infant harm has been found
- Excellent efficacy in elderly patient
- Effective across a broad range of pathogens, disease severities, and patient types

- An important advance because of the excellent efficacy, antimicrobial spectrum, tolerability, and once-daily dosing

UTIs are treated by doripenem, Gentamicin, Ciprofloxacin.

Gentamicin vs. doripenem:

Ototoxicity is largely irreversible and results from progressive destruction of vestibular or cochlear sensory cells, which are highly sensitive to damage by aminoglycoside. When sensory cells are once damaged regeneration does not occur. (Hardman, Limbird, Gilman2001).

Cochlear damage: it starts from the base and spreads to the apex; hearing loss affects the high frequency sound first, and then progressively encompasses the lower frequencies. No regeneration of the sensory cells occurs; auditory nerve fibers degenerate in a retrograde manner- deafness is permanent (Tripathi KD 2008).

Vestibular damage: headache is usually first to appear, followed by nausea, vomiting, dizziness, nystagmus, vertigo and ataxia. When the drug is stopped at this stage, it passes into a chronic phase lasting 6 to 10 weeks in which the patient is a symptomatic while in bed and has difficulty only during walking. Compensation by visual and proprioceptive positioning and recovery occurs over 1-2 years. (Tripathi KD 2008).

Nephrotoxicity: approximately 8% to 26% of patients who receive an aminoglycoside for more than several days will develop mild renal impairment that is almost always reversible. The toxicity results from accumulation and retention of aminoglycoside in the proximal tubular cells. The initial manifestation of damage at this stage is excretion of enzymes of the renal tubular brush border. After several days, there is a defect in renal concentrating ability; mild proteinuria and the appearance of hyaline granular casts. The glomerular filtration rate is reduced after 5 several additional days (Hardman, Limbird, Gilman2001).

Neuromuscular blockade: all aminoglycoside reduce Ach release from the motor nerve endings. Interfere with mobilization of centrally located synaptic vesicles to fuse with the terminal membrane (probably by antagonizing Ca^{2+}) as well as decrease the sensitivity of the muscle endplates to Ach (Tripathi KD 2008).

ciprofloxacin vs. doripenem:

If **ciprofloxacin** is taken it shows palpitation, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis, phlebitis, tachycardia, migraine, and hypotension. Whereas doripenem has no effect on heart patient. (www.rxlist.com)

Ciprofloxacin may cause interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis, breast pain. Doripenem has to be given in modified doses. (www.rxlist.com)

Ciprofloxacin has pregnancy category C: However doripenem has pregnancy category B. (www.fda.gov)

Ciprofloxacin cause CNS side effects. Doripenem only cause seizure. (www.rxlist.com)

Ciprofloxacin may cause lymphadenopathy, petechia. Doripenem does not cause these side effects. (www.rxlist.com)

Ciprofloxacin may cause amylase increase, lipase increase. However these side effects are not present in doripenem. (www.rxlist.com)

Ciprofloxacin may cause arthralgia or back pain, joint stiffness, achiness, neck or chest pain, and flare up of gout. However these side effects are not present in doripenem. (www.rxlist.com)

Ciprofloxacin may cause dyspnea, epistaxis, laryngeal or pulmonary edema, hiccough, hemoptysis, bronchospasm, pulmonary embolism. However these side effects are not present in doripenem. (www.rxlist.com)

Objective:

My objective was to find the characteristics of doripenem in the treatment of complicated intra abdominal infections and complicated urinary tract infection. I tried to find whether doripenem is superior or inferior to meropenem, imipenem and ertapenem in treating infection. Doripenem is yet not launched in Bangladesh. So to launch it in Bangladesh whom are going to be its competitors, how it will capture the market, what will be the market size, I tried to analyze them. I tried to find whether doripenem is comparatively better than other antibiotics. I tried to gather information about doripenem. I did product positioning, made literature and SWOT analysis.



Hypothesis:

It is assumed that doripenem is supposed to be active against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides caccae*, *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Streptococcus intermedius*, *Streptococcus constellatus* and *Peptostreptococcus micros*. It is also assumed that doripenem is supposed to treat complicated UTI infection, complicated intra abdominal infections, systemic infections, complicated SSSI, septicemia, nosocomial & community acquired pneumonia, mixed infections –RTIs, meningitis and pelvic inflammatory disease.

It is assumed that it would be profitable to launch doripenem in Bangladesh.

Method:

Information was gathered from website, journal, books, and dictionary. Information was produced in own sentences. For market fusibility study IMS, MIMS and QUIMP were studied. For this purpose Reneta pharmaceutical ltd was visited. For product positioning it was observed what are the antibiotics are used in complicated IAIs and complicated UTIs. Then all other drugs side effect was compared with doripenem. In every case it was found doripenem had fewer side effects. SWOT analysis was made. Ms excel was used for analysis of IMS data.

Result and discussion

1. Comparison of activity

Doripenem is an active drug against a number of bacteria. It is active against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* etc. It can be used in the treatment of complicated intra-abdominal infections and complicated urinary tract infections, including pyelonephritis.

Table 1.1 comparison based on indication of doripenem and its competitors.

Criteria	Imipenem	Meropenem	Doripenem	Ertapenem
Indication	<p>Lower respiratory tract infections- pneumonia and bronchitis as an exacerbation of COPD (chronic obstructive pulmonary disease) caused by <i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae</i></p> <p>Intra-abdominal infections- <i>Enterococcus faecalis</i>; <i>Streptococcus viridans group</i>; <i>Escherichia coli</i>; <i>Klebsiella pneumoniae</i></p> <p>Skin and skin structure infections- <i>Staphylococcus, penicillinase-producing strains; Streptococcus pyogenes, Escherichia coli; Enterobacter cloacae; Klebsiella pneumoniae</i></p>	<p>Skin and Skin Structure Infections- <i>Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli Bacteroides fragili,</i></p> <p>Intra-abdominal Infections- <i>streptococci, Escherichia coli, klebsiella pneumoniae, Pseudomonas aeruginosa</i></p> <p>Bacterial Meningitis- <i>Streptococcus pneumoniae</i>[†], <i>Haemophilus influenzae</i> (β-lactamase and non-β-lactamase-producing isolates), and <i>Neisseria meningitides.</i></p> <p>Mixed infections (RTI,UTI, Septicemia)- <i>E.coli, Staphylococcus pyrogens, Klebsiella pneumoniae , Proteus mirabilis, Clostridium</i></p>	<p>Complicated Intra-abdominal Infections- <i>Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides caccae, Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Streptococcus intermedius, Streptococcus constellatus and Peptostreptococcus micros</i></p> <p>Complicated Urinary Tract Infections, Including Pyelonephritis</p> <p>Doripenem (doripenem for injection) is indicated as a single agent for the treatment of complicated urinary tract infections, including pyelonephritis caused by <i>Escherichia coli.</i></p>	<p>Complicated Intra-abdominal Infections- <i>Escherichia coli, Clostridium clostridioforme, Eubacterium lentum, Peptostreptococcus species, Bacteroides fragilis</i></p> <p>Complicated Skin and Skin Structure Infections, including diabetic foot infections without osteomyelitis- <i>Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Bacteroides fragilis, Peptostreptococcus species.</i></p> <p>Community Acquired Pneumonia- <i>Streptococcus pneumoniae, Haemophilus influenzae</i></p> <p>Complicated Urinary Tract Infections- <i>Escherichia coli, including cases with concurrent bacteremia, or Klebsiella pneumoniae.</i></p> <p>Acute Pelvic Infections including postpartum endomyometritis, septic abortion and post surgical gynecologic infections due to <i>Streptococcus agalactiae, Escherichia coli, Bacteroides fragilis, Porphyromonas asaccharolytica, Peptostreptococcus species, or Prevotella bivia</i></p>

Doripenem bioavailability is not known it is a disadvantage. Doripenem half life is 1 hour. Doripenem protein binding is 8%. Doripenem shelf life is not known it is a disadvantage.

Table 1.2 following comparison is made of pharmacokinetic data of competitors of doripenem.

Criteria	Doripenem	Meropenem	Ertapenem	Imipenem
Bioavailability	Not known	100%	90%	Not known
Half life	1hr	1hr	4 hr	60min
Excretion	70%by kidney. Where 15% ring open metabolite (inactive form) & 10% by faces	Renal (70% unchanged form)	80% by kidney & 10% by faces. Of 80% recovered in urine 38% excreted in unchanged form.	Not known
Metabolism	Doripenem is not a substrate for hepatic CYP-450enzyme.	Unknown	By liver(minor hydrolysis of beta lactum ring , CYP not involved)	Renal
Protein binding	8%	2%	85-95%	Unknown
Penetration to cerebrospinal fluid	No	yes	Yes	Unknown
Distribution	1608 liter	Unknown	In adults- 8 lit Pediatric patient- 0.2lit/kg	Unknown
Shelf life	Unknown	Unknown	2 years	Unknown

Doripenem does not accumulate in the body, it has prophylaxis activity, it has pregnancy category these are the advantage of doripenem. Imipenem has pregnancy category C. so doripenem is a better drug in pregnant woman. Doripenem has FDA approval. Doripenem can be given IV/IM.

Table 1.3 according to prophylaxis activity, pregnancy category, accumulation, route and FDA Approval a comparison is made of doripenem and its competitors.

Criteria	Doripenem	Meropenem	Ertapenem	Imipenem
Accumulation	No	No	no	Unknown
Prophylaxis activity	Yes	Yes	Yes	Yes
Pregnancy category	B	B	B	C
Route	Iv /Im	Iv	Iv /Im	Iv /Im
FDA Approval	Yes	Yes	Yes	Yes

enem is active against complicated UTI infection, complicated intra abdominal infections, meningitis, nosocomial & community acquired pneumonia and mixed infections –RTIs. Unfortunately doripenem is not active against meningitis and pelvic inflammatory disease. It is a disadvantage of doripenem.

Table 1.4 comparison was made based on coverage of doripenem and its competitors.

Disease	Doripenem	Meropenem	Ertapenem	Imipenem
Meningitis	No	Yes	Yes	Yes
Complicated UTI infection	Yes	Yes	Yes	Yes
Complicated intra abdominal infections	Yes	Yes	Yes	Yes
Nosocomial infections	No	Yes	Yes	Yes
Complicated SSSI	Yes	Yes	Yes	Yes
Septicemia	Yes	No	Yes	Yes
Pelvic inflammatory disease	No	Yes	Yes	Yes
Nosocomial & community acquired pneumonia	Yes	Yes	Yes	Yes
Mixed infections –RTIs	Yes	Yes	Yes	Yes

Dosing: In all disease state doripenem has to be given 500mg 3 times a day. So doripenem's dose is same in all disease. It has to be given three times so it is a disadvantage.

Table 1.5 comparison dosing and frequency of doripenem and its competitors.

Disease	Dosage of different drugs			
	Doripenem	Meropenem	Ertapenem	Imipenem
Complicated intra-abdominal infections	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h
Complicated skin /skin structure infection	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h
Community acquired pneumonia	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h
Complicated urinary tract infection	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h
Surgical site infection	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h
Acqute pelvic infection	500mg 3times a day	1 g in every 8 h	1g once daily	500mg- 1g in every 8 h



2. Market size of competitor's of doripenem:

Doripenem is not yet launched in Bangladesh. So an idea about its market size is acquired from analyzing its competitors market size. The market size of different generic is given in the following table.

Table 2.1 yearly market sizes of competitors of doripenem

Generic	Yearly market size of doripenem and competitors of doripenem			
	2Q-2007	2Q-2006	2Q-2005	2Q-2004
CEFTRIAXONE	924,667,050	1,041,445,490	732,510,001	650,099,214
CEFTAZIDIME	44,557,775	52,087,564	43,113,440	60,190,598
CEFPIROME	3,979,484	6,710,434	6,867,647	0
CEFEPIME	16,199,633	19,542,849	7,893,492	5,352,604
MEROPENEM	17,363,729	57,918,600	30,798,741	6,127,679
IMIPENEM	165,900	0	0	0

Growth of doripenem can be assumed from the growth of doripenem's competitors.

Table 2.2 yearly market growths of competitors of doripenem.

Generic	Yearly market growth 2Q-2007	Yearly market growth 2Q-2006	Yearly market growth 2Q-2005
CEFTRIAXONE	-11	42	13
CEFTAZIDIME	-14	21	-28
CEFPIROME	-41	-2	
CEFEPIME	-17	148	47
MEROPENEM	-70	88	403
IMIPENEM			

Growth of Market size of different generic in different year

From table 2.3 it is seen from 2004 to 2005 ceftriaxone growth was 13%. So it had little growth. Probably it took the market of ceftazidime. From table 2.3 it is seen from 2005 to 2006 ceftriaxone growth was 42%. Probably it took the market of cefpirome. From table 2.3 it is seen from 2006 to 2007 growth was - 11%.

Table 2.3 Growth of Market size of different generic in different year

Name of the drug	Growth of Market size of different generic in different year		
	2004-2005	2005-2006	2006-2007
CEFTRIAZONE	13%	42%	-11%
CEFTAZIDIME	-28%	21%	-14%
CEFPIROME	-	-2%	-41%
CEFEPIME	47%	148%	-17%
MEROPENEM	403%	88%	-70%
IMPENEM	-	-	-

Total market size and total market growth:

It happened because of all antibiotic price decreased by 50%. From table 2.3 it is seen from 2004 to 2005 ceftazidime growth was -28%. Growth decreased probably because cefepime and meropenem captured its market. From table 2.3 it is seen from 2005 to 2006 ceftazidime growth was 21%.

Probably it captured the market of cefpirome. From table 2.3 it is seen from 2006 to 2007 growth was - 14%. From 2006 to 2007 price of product decreased by 50%.

Table 2.4 total market size and total market growth.

	2004	2005	2006	2007
Total market size	721,770,095	821,183,321	1,177,704,937	1,006,933,571
Total market growth	-	13.77353075	43.41559392	-14.50035239

There was no growth of cefpirome from 2004 to 2005. Probably cefpirome was first introduced in Bangladesh in 2005. From table 2.3 it is seen from 2005 to 2006 cefpirome growth was -2%. Probably meropenem captured its market and also may be marketing was not good. From table 2.3 it is seen from 2006 to 2007 cefpirome growth was -41%. From 2006 to 2007 price of product decreased by 50%. From table 2.3 it is seen from 2004 to 2005 cefepime growth increased by 47%. It happened probably because cefepime captured ceftazidime's market. From 2005 to 2006 cefepime growth was 148%. It happened probably because it captured cefpirome market. From 2006 to 2007 cefepime growth was -17%. From 2006 to 2007 price of product decreased by 50%. From table 2.3 it is seen from 2004 to 2005 meropenem growth was 403%. It happened because it captured the market of ceftazidime and ceftriaxone. From table 2.3 it is seen from 2005 to 2006 meropenem growth was 88% it happened probably it took the market of cefpirome. From table 2.3 it is seen from 2006 to 2007 meropenem growth decreased by 70%. It happened because from 2006 to 2007 price of product decreased by 50%. Imipenem was launched in market in 2006.

From table 2.3 it is seen from 2004 to 2005 total market growth was 13.77353%. From table 2.3 it is seen from 2005 to 2006 the growth increased by 43.41559%. But from 2006 to 2007 market growth was -14.50035%. It happened because from 2006 to 2007 price of product decreased by 50%.

Doripenem's opportunity: doripenem is a novel carbapenem drug. It can take the market of ceftazidime, cefpirome, cefepime, meropenem; imipenem. From 2004 to 2005 meropenem's growth was 403% and meropenem's market was around 6,127,679. So if doripenem does the marketing well it can make a lot of profit. Doripenem market size would be 10,00,000 taka and its growth would be 10% first year, 25% second year taka.

From the above discussion it is evident that doripenem is highly potential drug. It can take the market of cephalosporin and effectively compete with the carbapenem class. Its safety profile is noninferior to other carbapenem.

3. Product positioning

Definition of product positioning:

Positioning starts with a product. A piece of merchandise, a service, a company, an institution, or even a person..... But positioning is not what you do to a product. Positioning is what you do to the mind of the prospect. That is, you position the product in the mind of the prospect. (Philip Kotler 2003)

Doripenem is a carbapenem drug. It is used in the treatment of complicated UTI, complicated IAIs.

Doripenem, Gentamicin, Ciprofloxacin, Trimethoprim-sulfamethoxazole, and Levofloxacin treat uTIs.

Gentamicin vs. doripenem:

Effect on renal system:

Gentamicin is potentially nephrotoxic. Doripenem does not cause nephrotoxicity. The risk of nephrotoxicity is greater in patients with impaired renal function and in those who receive high dosage or prolonged therapy (www.rxlist.com).

Effect on CNS:

Neurotoxicity manifested by ototoxicity, both vestibular and auditory, can occur in patients treated with gentamicin. Aminoglycoside-induced ototoxicity is usually irreversible. Doripenem does not cause ototoxicity. But seizure can occur (www.rxlist.com).

Pregnancy category:

Gentamicin has pregnancy category D. However doripenem has pregnancy category B.

Gentamicin can be given to cardiac patient. Also there is no problem to give doripenem in cardiac patient (www.rxlist.com).

Blood glucose level:

Gentamicin and doripenem can be given to diabetic patient.

So observing the above doripenem is the drug of choice.

Gentamicin and doripenem does not cause hepatotoxicity (www.rxlist.com).

Ciprofloxacin vs. doripenem:

Effect on cardio vascular patient:

If ciprofloxacin is taken it shows palpitation, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis, phlebitis,

tachycardia, migraine, and hypotension. Whereas doripenem has no effect on heart patient (www.rxlist.com).

Effect on renal system:

Ciprofloxacin may cause interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis, breast pain. Doripenem has to be given in modified dose (www.rxlist.com).

Pregnancy category:

Ciprofloxacin has pregnancy category C: However doripenem has pregnancy category B (www.fda.gov).

Effect on CNS:

Ciprofloxacin may cause restlessness, dizziness, lightheadedness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor, ataxia, convulsive seizures, lethargy, drowsiness, weakness, malaise, anorexia, phobia, depersonalization, depression, paresthesia, abnormal gait, grand mal convulsion (www.rxlist.com).

Gastrointestinal side effects: ciprofloxacin cause painful oral mucosa, oral candidacies, dysphasia, intestinal perforation, gastrointestinal bleeding, cholestatic jaundice, hepatitis. However these side effects are not present in doripenem (www.rxlist.com).

Hemic\ lymphatic side effects: ciprofloxacin may cause lymphadenopathy, petechia. Doripenem does not cause these side effects (www.rxlist.com).

Metabolic\ nutritional:

Ciprofloxacin may cause amylase increase, lipase increase. However these side effects are not present in doripenem (www.rxlist.com).

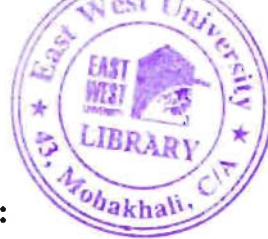
Musculoskeletal side effects:

Ciprofloxacin may cause arthralgia or back pain, joint stiffness, achiness, neck or chest pain, and flare up of gout. However these side effects are not present in doripenem (www.rxlist.com).

Respiratory side effect:

Ciprofloxacin may cause dyspnea, epistaxis, laryngeal or pulmonary edema, hiccough, hemoptysis, bronchospasm, pulmonary embolism. However these side effects are not present in doripenem (www.rxlist.com).

So doripenem is better drug than ciprofloxacin.



Trimethoprim-sulfamethoxazole vs. doripenem:

Trimethoprim-sulfamethoxazole is given a skin rash may be followed by a more severe reaction, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, and serious blood disorders. Clinical signs, such as rash, sore throat, fever, arthralgia, pallor, purpura or jaundice may be early indications of serious reactions. However these side effects are not present in doripenem. Trimethoprim –sulfamethoxazole has pregnancy category C and doripenem has pregnancy category B (www.rxlist.com). So doripenem is better drug than trimethoprim-sulfamethoxazole.

Levofloxacin vs. doripenem:

Hepatotoxicity:

Levofloxacin cause hepatotoxicity but doripenem does not cause hepato toxicity.

Effect on CNS:

Levofloxacin cause increased intracranial pressure and central nervous system stimulation, which may lead to tremors, restlessness, anxiety, lightheadedness, confusion, hallucinations, paranoia, depression, nightmares, insomnia, and, rarely, suicidal thoughts or acts. Doripenem only cause seizure (www.rxlist.com).

Effect on cardio vascular patient:

Some fluoroquinolones, including Levofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. However these side effects are not present in doripenem (www.rxlist.com).

Blood glucose level:

As with other fluoroquinolones, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported with Levofloxacin usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide) or with insulin. Doripenem can be given to diabetic patient (www.rxlist.com).

Hypersensitivity Reactions

Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with fluoroquinolones, including levofloxacin. These reactions often occur following the first dose. Some reactions have been accompanied by cardiovascular collapse, hypotension/shock, seizure, loss of consciousness, tingling, angioedema (including tongue, laryngeal, throat, or facial edema/swelling), airway obstruction (including bronchospasm, shortness of breath, and acute respiratory distress), dyspnea, urticaria, itching, and other serious skin reactions. However these side effects are not present in doripenem (www.rxlist.com).

Pregnancy category:

Levofloxacin has pregnancy category C: However doripenem has pregnancy category B (www.fda.gov).

So doripenem is better drug than levofloxacin.

Complicated IAIs are treated by ceftazidime, tigecycline and doripenem.

Ceftazidime vs. doripenem

Effect on cardio vascular patient: ceftazidime and doripenem has no side effect on heart patient (www.rxlist.com).

Effect on renal system:

In addition, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia have been reported in renally impaired patients treated with unadjusted dosage regimens of ceftazidime. The dose of doripenem is modified in renally impaired patient (www.rxlist.com).

Pregnancy category:

Ceftazidime has pregnancy category B: However doripenem has also pregnancy category B (www.rxlist.com).

Effect on CNS: (less than 1%) included headache, dizziness, and paresthesia. Seizures have been reported ceftazidime. Doripenem may also cause seizure (www.rxlist.com).

Blood glucose level:

Both ceftazidime and Doripenem can be given to diabetic patient.

So doripenem is better drug than ceftazidime (www.rxlist.com).

Tigecycline vs. doripenem:

Effect on cardio vascular patient: both can be given to cardiac patients (www.rxlist.com).

Effect on renal system: the dose of doripenem needs to be changed (www.rxlist.com).

Pregnancy category:

Tigecycline has pregnancy category D: However doripenem has also pregnancy category B (www.rxlist.com).

Effect on CNS: doripenem cause seizure (www.rxlist.com).

Blood glucose level: both have no effect on blood glucose (www.rxlist.com).

Hepatic Effects: Increases in total bilirubin concentration, prothrombin time and transaminases have been seen in patients treated with tigecycline. Isolated cases of significant hepatic dysfunction and hepatic failure have been reported in patients being treated with tigecycline (www.rxlist.com).

Anaphylaxis/Anaphylactoid Reactions:

Anaphylaxis/anaphylactoid reactions have been reported with nearly all-antibacterial agents, including tigecycline, and may be life-threatening (www.rxlist.com).

From the above evidence of pregnancy category, effect on CNS, effect on Cardiovascular patient, effect on renal system it is clearly confirmed that doripenem is better drug than others.

1. SWOT analysis of doripenem

Strength:

1. Active against **pseudomonas ariginosa**.
2. Active against community acquired pneumonia.
3. Active against complicated UTIs.
4. Active against Nosocomial pneumonia and early onset VAP.
5. Active against CAIs.
6. Active against systemic infection.
7. Active against septicima.
8. Active against surgical site infection.
9. Half-life is one hour.
10. Doripenem is not a substrate for cyp450.
11. Pregnancy category B.
12. No company has launched yet. So it will be a pioneer product.
13. Like imipenem, cilastatin is not required.

Weakness:

1. Pioneer product so pricing has to be justified.
2. Expensive than cephalosporin and penicillin.
3. Has to be given 3 times after every 8 hours.
4. Has to be given I.V.
5. Has side effects e.g. Anaphylaxis and serious hypersensitivity reactions, Interaction with sodium valproate, Clostridium difficile-associated diarrhea, Development of drug-resistant bacteria, Pneumonitis with inhalational use.

Opportunity:

1. No company has started production of it so pioneer product.
2. Can do business up to 2016 before patent rule becomes applicable.
3. As bacteria are becoming resistant it can be used vastly.
4. It can take the place of meropenem, imipenem.

Threat:

1. Other companies will start producing it.
2. Doctors who are prescribing meropenem, imipenem may not like to prescribe doripenem
3. Local companies will produce the drug at low price

Ertapenem can take doripenem place

Doripenem is noninferior to meropenem, imipenem, and ertapenem. It can be used forcefully in the treatment of complicated IAIs and complicated UTIs. It had lesser side effects than cephalosporins. Doripenem, Gentamicin, Ciprofloxacin, Trimethoprim-sulfamethoxazole, and Levofloxacin treat UTIs. Doripenem has fewer side effects than Gentamicin, Ciprofloxacin, Trimethoprim-sulfamethoxazole, and Levofloxacin. Complicated IAIs are treated by ceftazidime, tigecycline and doripenem. Doripenem has fewer side effects than ceftazidime, tigecycline. So doripenem is the drug of choice for complicated urinary tract infection and complicated intra abdominal infection. Doripenem is not yet launched in Bangladesh yet. If it is launched it can take the partial market of meropenem, imipenem and other cephalosporins. Meropenem's growth was 403% in 2004-2005. Doripenem initially can make a lot of profit. As it is carbapenem its price is on the higher side. Doripenem market size would be 10,00,000 taka and its growth would be 10% first year, 25% second year and in third year 15%.

Conclusion:

Doripenem is a novel carbapenem drug. Doripenem is used in the treatment of complicated urinary tract infection and complicated intra abdominal infection. Doripenem is non-inferior to meropenem, imipenem and other cephalosporins. It is active against *pseudomonas ariginosa*. Doripenem is also active against community-acquired pneumonia. Doripenem has better cure rate than imipenem and other cephalosporins. Doripenem requires less time to treat than cephalosporins thus it is cost effective than cephalosporins. Doripenem market size would be 10,00,000 taka and its growth would be 10% first year, 25% second year and in third year 15%. So it would be profitable to launch doripenem.

Limitations:

Doripenem is a new drug. Not a lot of journal has been published about doripenem. Lot of clinical trial is not available. Doctors were not consulted because time was constant. Market fisiblity was done of only 6 drugs. By observing only 6 drugs it is not possible to make complete assumption. Doripenem is an expensive drug it is not possible for everyone to buy. SWOT analysis was essentially based on strength and opportunity. In product positioning only side effects were evaluated. A lot journal required money, which was impossible to afford.



References:

- Hardman Limbird Gilman, 2001, Goodman & Gilman's The Pharmacological Basis of Therapeutics, Tenth edition, McGraw Hill companies, p1228, 1229
- KD Tripathi 2008 essentials of medical pharmacology, fifth edition, Jaypee: New Delhi, p721, 686
- Bhavani SM, Hammel JP, Cirincione BB, Wikler MA, Ambrose PG 2005 Use of pharmacokinetic-pharmacodynamic target attainment analyses to support phase 2 and 3 dosing strategies for doripenem. Antimicrobial agents and chemotherapy Sep; 49(9): 3944-7
- Fihn SD. 2003 Clinical practice. Acute uncomplicated urinary tract infection in women. N Engl J Med 349(3): 259-66.
- Fritsche TR, Stilwell MG, Jones RN. 2005 Antimicrobial activity of doripenem (S-4661): a global surveillance report. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases; 11(12): 974-84.
- Gaynes R, Edward JR; 2005 the National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by gram-negative bacilli. Clin Infect Dis.; 41:848-854.
- Hooton TM. Recurrent urinary tract infection in women. 2001 Int J Antimicrob Agents; 17(4): 259-68.
- Hori T, Nakano M, Kimura Y, Murakami K 2006 Pharmacokinetics and tissue penetration of a new carbapenem, doripenem, intravenously administered to laboratory animals. *In vivo* Jan-Feb;20(1):91-6

Iolanda Cirillo, MBS, Nicole Vaccaro, BS, Kenneth Turner, PhD, Bhavna Solanki, MS, Jaya Natarajan, PhD and Rebecca Redman, MD. Pharmacokinetics, Safety, and Tolerability of Doripenem after 0.5-, 1-, and 4-Hour Infusions in Healthy Volunteers

Jones RN, Huynh HK, Biedenbach DJ. 2004 Activities of doripenem (S-4661) against drug-resistant clinical pathogens. *Antimicrobial agents and chemotherapy* Aug;48(8):3136-40

Naber KG, Llorens L, Kaniga K, Kotey P, Hedrich D, Redman R. 2009 Jul 6 Intravenous Doripenem 500 mg Versus Levofloxacin 250 mg With an Option to Switch to Oral Therapy for the Treatment of Complicated Lower Urinary Tract Infection and Pyelonephritis. *Antimicrob Agents Chemother.*

Pappas G, Saplaoura K, Falagas ME. 2009 Current treatment of pseudomonal infections in the elderly. *Drugs Aging.*;26(5):363-79

Philip Kotler. (2003) marketing management. Eleventh edition, Upper Saddle River: New Jersey. p-309

Raz R, Stamm WE. 1993 A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med*; 329(11): 753-6.

Stamm WE. 1982 Recent developments in the diagnosis and treatment of urinary tract infections. *West J Med*; 137(3): 213-20

U.S. Food and Drug Administration (October 17, 2007). FDA Approves New Drug to Treat Complicated Urinary Tract and Intra-Abdominal Infections. Press release. <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01728.html>. Retrieved on 2007-10-25.

Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. 1999
Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis
and acute pyelonephritis in women. Infectious Diseases Society of America
(IDSA). Clin Infect Dis; 29(4): 745-58.

<http://www.drugs.com/cdi/doripenem.html> (6-6-2009)

<http://www.drugdevelopment-technology.com/projects/doripenem/> (6-6-2009)

<http://health.yahoo.com/urinary-medications/doripenem/healthwise--d07049a1.html>(6-6-2009)

<http://www.rxlist.com/doribax-drug.htm> (6-6-2009)

<http://www.who.int/hinari/en/> (6-6-2009)

<http://www.rxlist.com/cipro-drug.htm>(6-6-2009)

<http://www.rxlist.com/genoptic-drug.htm>(6-6-2009)

<http://www.rxlist.com/cipro-drug.htm>(6-6-2009)

<http://www.rxlist.com/zotrim-drug.htm>(6-6-2009)

<http://www.rxlist.com/levaquin-drug.htm>(6-6-2009)

<http://www.rxlist.com/ceptaz-drug.htm>(6-6-2009)

http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022106s002s0051bl.pdf(6-6-2009)

[http://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4399s1-06%20\(Levofloxacin\).pdf](http://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4399s1-06%20(Levofloxacin).pdf)(6-6-2009)

<http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm130712.htm>(6-6-2009)

<http://www.rxlist.com/tygacil-drug.htm>(6-6-2009)

<http://www.rxlist.com/ceptaz-drug.htm>(6-6-2009).

