

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DIFICLIR 200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 200 mg of fidaxomicin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Capsule shaped tablets of 14 mm, white to off-white in colour, debossed with “FDX” on one side and “200” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DIFICLIR is indicated in adults for the treatment of *Clostridium difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD) (see section 5.1).

Consideration should be given to official guidelines on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Adults and elderly (≥65 years of age)

The recommended dose is 200 mg (one tablet) administered twice daily (once every 12 hours) for 10 days.

Special populations

Renal impairment

No dose adjustment is considered necessary. Due to the limited clinical data in this population, DIFICLIR should be used with caution in patients with severe renal impairment (see sections 4.4 and 5.2).

Hepatic impairment

No dose adjustment is considered necessary. Due to the limited clinical data in this population, DIFICLIR should be used with caution in patients with moderate to severe hepatic impairment (see sections 4.4 and 5.2).

Paediatric population

The safety and efficacy of fidaxomicin in children aged below 18 years has not yet been established. No data are available.

Method of administration

DIFICLIR is intended for oral use.

DIFICLIR can be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hypersensitivity reactions including severe angioedema have been reported (see section 4.8). If a severe allergic reaction occurs during treatment with DIFICLIR, the medicinal product should be discontinued and appropriate measures taken.

Some patients with hypersensitivity reactions reported a history of allergy to macrolides. Fidaxomicin should be used with caution in patients with a known macrolides allergy.

Due to limited clinical data, fidaxomicin should be used with caution in patients with severe renal impairment or moderate to severe hepatic impairment (see section 5.2).

Due to limited clinical data, fidaxomicin should be used with caution in patients with pseudomembranous colitis, fulminant or life threatening CDI.

There are no data in patients with concomitant inflammatory bowel disease. Fidaxomicin should be used with caution in these patients due to the risk of enhanced absorption and potential risk of systemic adverse reactions.

Co-administration of potent P-glycoprotein inhibitors such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone is not recommended (see sections 4.5 and 5.2).

4.5 Interaction with other medicinal products and other forms of interaction

Effect of P-gp inhibitors on fidaxomicin

Fidaxomicin is a substrate of P-gp. Co-administration of single doses of the P-gp inhibitor cyclosporine A and fidaxomicin in healthy volunteers, resulted in a 4- and 2-fold increase in fidaxomicin C_{max} and AUC, respectively and in a 9.5 and 4-fold increase in C_{max} and AUC, respectively, of the main active metabolite OP-1118. As the clinical relevance of this increase in exposure is unclear, co-administration of potent inhibitors of P-gp, such as cyclosporine, ketoconazole, erythromycin, clarithromycin, verapamil, dronedarone and amiodarone is not recommended (see section 4.4 and 5.2).

Effect of fidaxomicin on P-gp substrates

Fidaxomicin may be a mild to moderate inhibitor of intestinal P-gp.

Fidaxomicin (200 mg twice daily) had a small but not clinically relevant effect on digoxin exposure. However, a larger effect on P-gp substrates with lower bioavailability more sensitive to intestinal P-gp inhibition such as dabigatran etexilat cannot be excluded.

Effect of fidaxomicin on other transporters

Fidaxomicin does not have a clinically significant effect on the exposure of rosuvastatin, a substrate for the transporters OATP2B1 and BCRP. Co-administration of 200 mg fidaxomicin twice daily with a single dose of 10 mg rosuvastatin to healthy subjects did not have a clinically significant effect on the AUC_{inf} of rosuvastatin.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data available from the use of fidaxomicin in pregnant women. Animal studies did not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of DIFICLIR during pregnancy.

Breast-feeding

It is unknown whether fidaxomicin and its metabolites are excreted in human milk. Although no effects on the breastfed newborns/infants are anticipated since the systemic exposure to fidaxomicin is low, a risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from DIFICLIR therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

Fidaxomicin had no effects on fertility when evaluated in rats (see section 5.3).

4.7 Effects on ability to drive and use machines

DIFICLIR has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions are vomiting, nausea and constipation.

Tabulated summary of adverse reactions

Table 1 displays adverse reactions associated with twice daily administration of fidaxomicin in the treatment of *C. difficile* infection, reported in at least two patients, presented by system organ class.

The frequency of adverse reactions is defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Summary of adverse reactions by MedDRA system organ class

MedDRA system organ class	Common	Uncommon	Frequency not known
Immune system disorders		rash, pruritus	hypersensitivity reactions (angioedema, dyspnea)
Metabolism and nutrition disorders		decreased appetite	
Nervous system disorders		dizziness, headache, dysgeusia	
Gastrointestinal disorders	vomiting, nausea, constipation	abdominal distention, flatulence, dry mouth	
Hepatobiliary disorders		alanine aminotransferase increased	

Description of selected adverse reactions

Acute hypersensitivity reactions, such as angioedema and dyspnea, have been reported during post-marketing (see section 4.3 and 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9 Overdose

No adverse reactions for acute overdose have been reported during clinical studies or from post-marketing data. However, the potential for adverse reactions cannot be ruled out and general supportive measures are recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidiarrheals, intestinal antiinflammatory/antiinfective agents, antibiotics, ATC code: A07AA12

Mechanism of action

Fidaxomicin is an antibiotic belonging to the macrocyclic class of antibacterials. Fidaxomicin is bactericidal and inhibits RNA synthesis by bacterial RNA polymerase. It interferes with RNA polymerase at a distinct site from that of rifamycins. Inhibition of the Clostridial RNA polymerase occurs at a concentration 20-fold lower than that for the *E. coli* enzyme (1 µM vs. 20 µM), partly explaining the significant specificity of fidaxomicin activity. Fidaxomicin has been shown to inhibit *C. difficile* sporulation *in vitro*.

Pharmacokinetic/Pharmacodynamic (PK/PD) relationship

Fidaxomicin is a locally acting drug. As a topical agent, systemic PK/PD relationships cannot be established, however *in vitro* data show fidaxomicin to have time-dependent bactericidal activity and suggest time over MIC may be the parameter most predicative of clinical efficacy.

Breakpoints

Fidaxomicin is a topically acting drug that cannot be used to treat systemic infections; therefore the establishment of a clinical breakpoint is not relevant. The epidemiological cut-off value for fidaxomicin and *C. difficile*, distinguishing the wild-type population from isolates with acquired resistance traits, is ≥ 1.0 mg/L.

Antimicrobial spectrum

Fidaxomicin is a narrow spectrum antimicrobial drug with bactericidal activity against *C. difficile*. Fidaxomicin has an MIC₉₀ of 0.25 mg/L versus *C. difficile*, and its main metabolite, OP-1118, has an MIC₉₀ of 8 mg/L. Gram negative organisms are intrinsically not susceptible to fidaxomicin.

Effect on the intestinal flora

Studies have demonstrated that fidaxomicin treatment did not affect *Bacteroides* concentrations or other major components of the microbiota in the faeces of CDI patients.

Mechanism of resistance

There are no known transferable elements that confer resistance to fidaxomicin. Also no cross-resistance has been discovered with any other antibiotic class including β -lactams, macrolides, metronidazole, quinolones, rifampin, and vancomycin. Specific mutations of RNA polymerase are associated with reduced susceptibility to fidaxomicin.

Clinical efficacy

In the pivotal clinical trials the rate of recurrence in the 30 days following treatment was assessed as a secondary endpoint. The rate of recurrence (including relapses) was significantly lower with

fidaxomicin (14.1% versus 26.0% with a 95% CI of [-16.8%, -6.8%]), however these trials were not prospectively designed to prove prevention of reinfection with a new strain.

Description of the patient population in clinical trials

In the two clinical trials of patients with CDI, 47.9% (479/999) of patients (per protocol population) were ≥ 65 years of age and 27.5% (275/999) of patients were treated with concomitant antibiotics during the study period. Twenty-four percent of patients met at least one of the following three criteria at baseline for scoring severity: body temperature $>38.5^{\circ}\text{C}$, leukocyte count $>15,000$, or creatinine value ≥ 1.5 mg/dl. Patients with fulminant colitis and patients with multiple episodes (defined as more than one prior episode within the previous 3 months) of CDI were excluded in the studies.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with fidaxomicin in one or more subsets of the paediatric population in enterocolitis caused by *C. difficile* (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The bioavailability in humans is unknown. In healthy adults, C_{max} is approximately 9.88 ng/ml and AUC_{0-t} is 69.5 ng•hr/ml following administration of 200 mg fidaxomicin, with a T_{max} of 1.75 hours. In CDI patients, average peak plasma levels of fidaxomicin and its main metabolite OP-1118 tend to be 2- to 6-fold higher than in healthy adults. There was very limited accumulation of fidaxomicin or OP-1118 in plasma following administration of 200 mg fidaxomicin every 12 hours for 10 days.

C_{max} for fidaxomicin and OP-1118 in plasma were 22% and 33% lower following a high fat meal vs fasting, but the extent of exposure (AUC_{0-t}) was equivalent.

Fidaxomicin and the metabolite OP-1118 are substrates of P-gp.

In vitro studies showed that fidaxomicin and the metabolite OP-1118 are inhibitors of the transporters BCRP, MRP2 and OATP2B1, but were not found to be substrates. Under conditions of clinical use, fidaxomicin has no clinically relevant effect on the exposure of rosuvastatin, a substrate for OATP2B1 and BCRP (see section 4.5). The clinical relevance of MRP2 inhibition is not yet known.

Distribution

The volume of distribution in humans is unknown, due to very limited absorption of fidaxomicin.

Biotransformation

No extensive analysis of metabolites in plasma has been performed, due to low levels of systemic absorption of fidaxomicin. A main metabolite, OP-1118, is formed through hydrolysis of the isobutyryl ester. *In vitro* metabolism studies showed that the formation of OP-1118 is not dependent on CYP450 enzymes. This metabolite also shows antimicrobial activity (see section 5.1).

Fidaxomicin does not induce or inhibit CYP450 enzymes *in vitro*.

Elimination

Following a single dose of 200 mg fidaxomicin, the majority of the administered dose (over 92%) was recovered in the stool as fidaxomicin or its metabolite OP-1118 (66%). The main elimination pathways of systemically available fidaxomicin have not been characterized. Elimination through urine is negligible ($<1\%$). Only very low levels of OP-1118 and no fidaxomicin was detectable in human urine. The half life of fidaxomicin is approximately 8-10 h.

Special populations

Plasma levels appear to be elevated in the elderly (age ≥ 65 years). Fidaxomicin and OP-1118 levels were approximately 2 times higher in patients ≥ 65 years compared to patients < 65 years. This difference is not considered clinically relevant.

Limited data from patients with an active history of chronic hepatic cirrhosis in the Phase 3 studies showed that median plasma levels of fidaxomicin and OP-1118 may be approximately 2- and 3-fold higher, respectively, than in non-cirrhotic patients.

Limited data suggest that there is no major difference in plasma concentration of fidaxomicin or OP-1118 between patients with reduced renal function (creatinine clearance < 50 ml/min) and patients with normal renal function (creatinine clearance ≥ 50 ml/min).

Limited data suggest that gender, weight and race do not have any major influence on the plasma concentration of fidaxomicin or OP-1118.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeat dose toxicity, genotoxicity, and reproductive toxicity.

Reproductive and fertility parameters showed no statistically significant differences in rats treated with fidaxomicin at doses up to 6.3 mg/kg/day (intravenous).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablets:

Microcrystalline cellulose
Pregelatinised starch (maize)
Hydroxypropyl cellulose
Butylated hydroxytoluene
Sodium starch glycolate
Magnesium stearate

Coating:

Polyvinyl alcohol
Titanium dioxide (E171)
Talc
Polyethylene glycol
Lecithin (soy)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

100 x 1 film-coated tablet in alu/alu perforated unit dose blisters.

20 x 1 film-coated tablet in alu/alu perforated unit dose blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Astellas Pharma Europe B.V.

Sylviusweg 62

2333 BE Leiden

The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/11/733/003-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5 December 2011

Date of latest renewal: 22 August 2016

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Astellas Pharma Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency.
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

DIFICLIR 200 mg film-coated tablets
fidaxomicin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 200 mg of fidaxomicin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

100 x 1 film-coated tablet.
20 x 1 film-coated tablet.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Astellas Pharma Europe B.V.

Sylviusweg 62
2333 BE Leiden
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/11/733/003 100 x 1 film-coated tablet

EU/1/11/733/004 20 x 1 film-coated tablet

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

dificlir

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

DIFICLIR 200 mg film-coated tablets
fidaxomicin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Astellas

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

DIFICLIR 200 mg film-coated tablets

Fidaxomicin

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What DIFICLIR is and what it is used for
2. What you need to know before you take DIFICLIR
3. How to take DIFICLIR
4. Possible side effects
5. How to store DIFICLIR
6. Contents of the pack and other information

1. What DIFICLIR is and what it is used for

DIFICLIR is an antibiotic which contains the active substance fidaxomicin.

DIFICLIR is used in adults to treat infections of the lining of the colon (large intestine) with certain bacteria called *Clostridium difficile*. This serious illness can result in painful, severe diarrhoea. DIFICLIR works by killing the bacteria that cause the infection and helps to reduce the associated diarrhoea.

2. What you need to know before you take DIFICLIR

Do not take DIFICLIR

- If you are allergic to fidaxomicin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking DIFICLIR.

If you feel that you might have a severe allergic reaction such as trouble breathing (dyspnea), swelling of the face or throat (angioedema), severe rash or severe itching (pruritus), stop taking DIFICLIR and seek medical advice urgently from your doctor, pharmacist or at your local hospital emergency department (see section 4).

If you are allergic to macrolides (a class of antibiotics), ask your doctor for advice before using this medicine. Your doctor will tell you whether this medicine is suitable for you.

If you have kidney or liver problems, ask your doctor for advice before using this medicine. Your doctor will tell you whether this medicine is suitable for you.

If, next to your infection of the large intestine, you also have an inflammation of the intestines (inflammatory bowel disease), ask your doctor for advice before using this medicine. Your doctor will tell you whether this medicine is suitable for you.

There are limited data available on the use of fidaxomicin in severe cases of the disease (e.g. pseudomembranous colitis). Your doctor will know whether your disease falls in the severe categories and will tell you whether this medicine is suitable for you.

Children and adolescents

DIFICLIR should not be used in children or adolescents aged below 18 years as there is no information on this use in this population.

Other medicines and DIFICLIR

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

DIFICLIR blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking DIFICLIR. Examples of such medicines are:

- cyclosporin (a medicine used to dampen down the body's immune reactions, used e.g. after an organ or bone marrow transplant, for psoriasis or eczema, or for rheumatoid arthritis or nephrotic syndrome)
- ketoconazole (a medicine used to treat fungal infections)
- erythromycin (a medicine used to treat ear, nose, throat, chest and skin infections)
- clarithromycin (a medicine used to treat chest infections, throat and sinus infections, skin and tissue infections and *Helicobacter pylori* infections associated with duodenal or stomach ulcer)
- verapamil (a medicine used to treat high blood pressure or to prevent chest pain attacks, or used following a heart attack to prevent another one)
- dronedarone and amiodarone (medicines used to control the heartbeat)
- dabigatran etexilat (a medicine used to prevent the formation of blood clots after hip or knee replacement surgery)

You should not use DIFICLIR in combination with one of these medicines, unless your doctor tells you otherwise. If you use one of these medicines, please ask your doctor for advice before taking this medicine.

Pregnancy and breast-feeding

You should not take DIFICLIR if you are pregnant, unless your doctor tells you otherwise.

This is because it is not known whether fidaxomicin can harm your baby.

If you are pregnant or think you may be pregnant, ask your doctor or pharmacist for advice before taking this medicine.

It is not known whether fidaxomicin passes into breast milk, but it is not expected to do so.

If you are breastfeeding ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

DIFICLIR is not expected to affect your ability to drive, use tools or machines.

3. How to take DIFICLIR

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The recommended dose is one tablet (200 mg) twice daily (one tablet every 12 hours) for 10 days. Swallow the tablets whole with a glass of water. You can take DIFICLIR before, during or after meals.

If you take more DIFICLIR than you should

If you have taken more tablets than you should have, talk to a doctor. Take the medicine pack with you so the doctor knows what you have taken.

If you forget to take DIFICLIR

Take the tablet as soon as you remember, unless it is time for the next dose. In that case, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking DIFICLIR

Do not stop taking DIFICLIR, unless your doctor has advised you to do so.

Keep taking this medicine until the course is finished, even if you feel better.

If you stop taking this medicine too soon, the infection may come back.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

A severe allergic reaction may occur, including trouble breathing (dyspnea), swelling of the face or throat (angioedema), severe rash or severe itching (pruritus) (see section 2). If such reaction occurs, stop taking DIFICLIR and seek medical advice urgently from your doctor, pharmacist or at your local hospital emergency department.

The most **common side effects (may affect up to 1 in 10 people)** are vomiting, nausea and constipation.

Other possible side effects are the following:

Uncommon side effects (may affect up to 1 in 100 people)

- decreased appetite
- dizziness, headache
- dry mouth, altered taste (dysgeusia)
- bloated feeling, wind (flatulence)
- certain blood tests might show changed levels, e.g. increased liver enzymes (alanine aminotransferase)
- rash, itching (pruritus)

Not known side effects (frequency cannot be estimated from the available data)

- swelling of the face and throat (angioedema), trouble breathing (dyspnea)

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system** listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store DIFICLIR

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after “EXP”. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What DIFICLIR contains

- The active substance is fidaxomicin. Each film-coated tablet contains 200 mg of fidaxomicin.
- The other ingredients are:
Tablet core: microcrystalline cellulose, pregelatinised starch, hydroxypropyl cellulose, butylated hydroxytoluene, sodium starch glycolate and magnesium stearate
Coating: polyvinyl alcohol, titanium dioxide (E171), talc, polyethylene glycol and lecithin (soy)

What DIFICLIR looks like and contents of the pack

DIFICLIR 200 mg film-coated tablets are capsule shaped tablets, white to off-white in colour, with “FDX” on one side and “200” on the other side.

DIFICLIR is available in:

100 x 1 film-coated tablet in alu/alu perforated unit dose blisters.

20 x 1 film-coated tablet in alu/alu perforated unit dose blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Manufacturer

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>