ECALTA®: IT IS NOT JUST ANOTHER ECHINOCANDIN
MEET THE PATIENTS
Ecalta®: Who is it for?

Ecalta® is indicated for the treatment of invasive candidiasis\(^1\) in different patient populations including:

- **Hepatically-impaired patients**
- **Deep-tissue infections**
- **Neutropenic patients**

- No dose adjustment required in hepatic or renal impairment\(^1\)
- No known drug interactions\(^{1,2}\)
- A favourable pharmacokinetic profile compared to other echinocandins\(^3\)
- Better efficacy and significantly higher global success rate versus the gold standard fluconazole in the treatment of candidaemia\(^4\)
- Ecalta® patent expiry is in March 2018. Following patent expiry cost, savings may be available\(^5\)

The following pages provide an overview of a select range of patient profiles for which Ecalta® would be a suitable treatment option, and the reasons for this.

**References**
Meet the patients with invasive candidiasis

Find out more information by selecting one of the patients below

- **JENNY**
  - Female | Age: 27
  - Patient with hepatic failure who develops renal impairment

- **PETER**
  - Male | Age: 31
  - Patient with a central venous catheter

- **ROSE**
  - Female | Age: 56
  - Patient with oesophageal ulcer and moderate hepatic impairment

- **PHILIP**
  - Male | Age: 54
  - Post-surgical sepsis

- **ANNIE**
  - Female | Age: 40
  - Oncology patient with neutropenia

- **CLIVE**
  - Male | Age: 49
  - Critically ill post-abdominal surgery patient

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
Patient No. 1 with invasive candidiasis
Hepatic failure and renal impairment

Jenny
(Age: 27)

CURRENT SITUATION
AND TEST RESULTS

CO-MORBIDITIES

RELEVANT PHYSICAL AND LAB FINDINGS

WHY ECALTA®?
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Jenny (Age: 27)

Patient No. 1 with invasive candidiasis
Hepatic failure and renal impairment

About Jenny

- Brought into the emergency room after being found disoriented
- Had a **headache, blurred vision, right-sided flank pain, nausea** and **vomiting**
- A toxicology screen tested positive for **opiate use**
- Admitted to **heroin abuse** to cope with painful episodes from **lupus** and frequently **shared needles** with friends
Current situation and test results

- On physical exam, ‘track marks’ along both arms, multiple nodular erythematous lesions with pus drainage on her back and enlarged liver were noted.

- Scan of her back showed multiple lytic lesions in the cartilage of her rib cage which tested positive for Candida albicans.

- Blood tests were positive for hepatitis C.

- Fine needle biopsy of the kidney showed focal segmental glomerulonephritis.
Jenny (Age: 27)

Patient No. 1 with invasive candidiasis
Hepatic failure and renal impairment

Co-morbidities

- Systemic lupus erythematosus
- Active hepatitis C infection
- Focal segmental glomerulonephritis
- Heroin abuse
Jenny (Age: 27)

Patient No. 1 with invasive candidiasis
Hepatic failure and renal impairment

Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Urinalysis</th>
<th>Serum/Blood</th>
<th>Liver Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>++</td>
<td>Alanine transaminase (ALT) ↑↑</td>
</tr>
<tr>
<td>RBC casts</td>
<td>++</td>
<td>Aspartate transaminase (AST) ↑</td>
</tr>
<tr>
<td>eGFR</td>
<td>↓↓</td>
<td>Gamma glutamyl-transferase (GGT) ↑↑</td>
</tr>
<tr>
<td></td>
<td>Albumin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>Alkaline phosphatase (ALP) ↑</td>
</tr>
<tr>
<td></td>
<td>Urea/BUN</td>
<td>Total bilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lactate dehydrogenase ↑↑</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; RBC, red blood cell
Jenny (Age: 27)

Patient No. 1 with invasive candidiasis
Hepatic failure and renal impairment

Why Ecalta®?

With Jenny’s complicated history and extensive liver and kidney damage, choosing the right therapy for her candidiasis will be vital to her potential survival.

- Ecalta® is an antifungal that does not get metabolised by the liver, nor excreted via the kidneys\(^1\)
- Ecalta® requires no dosing adjustments for adult patients with renal or hepatic impairment\(^1\)

Peter (Age: 31)

Patient No. 2 with invasive candidiasis
Central venous catheter
Peter (Age: 31)

Patient No. 2 with invasive candidiasis

Central venous catheter

About Peter

- Admitted to the hospital after being found **unconscious**
- Known **type I diabetic** with recurrent bouts of **diabetic ketoacidosis**
- Extended period of unconsciousness led to **hypotensive state** and **acute tubular necrosis**
- **Central venous catheter** was placed three days ago for haemodialysis while waiting for an AV fistula replacement
- Received **prophylactic antibiotics** and **fluconazole**
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

**Current situation and test results**

- Recurrent bouts of **vomiting, nausea, loss of appetite, fever and chills**
- Blood cultures tested positive for *Candida krusei* resistant to fluconazole

**Patient No. 2 with invasive candidiasis**

- Central venous catheter

**Peter (Age: 31)**
Co-morbidities

- Type I diabetes
- Diabetic ketoacidosis
- Acute tubular necrosis
- Obesity
Peter (Age: 31)

Patient No. 2 with invasive candidiasis
Central venous catheter

Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Physical findings</th>
<th>Blood</th>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>100/70 mmHg</td>
<td>Glucose</td>
</tr>
<tr>
<td>HR</td>
<td>80 bpm</td>
<td>Serum creatinine</td>
</tr>
<tr>
<td>BMI</td>
<td>30 kg/m²</td>
<td>Urine output</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proteinuria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Microalbumin</td>
</tr>
</tbody>
</table>

BMI, body mass index; BP, blood pressure; bpm, beats per minute; HR, heart rate

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Why Ecalta®?

With Peter’s complicated history, many considerations must be taken in choosing the right treatment course. Ensuring therapies are not renally excreted will reduce potential stress on his impaired kidneys. As he is infected with a fluconazole resistant strain of Candida krusei, initiating effective antifungal therapy as soon as possible is essential.

- As Ecalta® is not renally excreted, it poses little threat to already damaged kidneys¹
- Ecalta® has no known drug interactions¹,²
- Regardless of weight and liver status, the consistent dosing regimen of Ecalta® allows ease of management¹

References:
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

**Rose (Age: 56)**

**Patient No. 3 with invasive candidiasis**

*Oesophageal ulcer and moderate hepatic impairment*
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

**About Rose**

- Hospitalised after **vomiting** copious amounts of **blood** and subsequently experienced **delirium** and **syncope**
- Had a blood alcohol level of 0.24 g/dL and was both hyponatraemic and hypokalaemic leading to **severe metabolic alkalosis**
- **Febrile** with persistent temperature of 39.0°C
- Has an extensive history of **alcohol abuse** and **smoking**
- Strongly advised to stop all **alcohol consumption** and **smoking** on multiple occasions in the past ten years
- Previously diagnosed with low-grade **Barrett’s oesophagus** and prescribed a PPI

---

**CURRENT SITUATION AND TEST RESULTS**

**CO-MORBIDITIES**

**RELEVANT PHYSICAL AND LAB FINDINGS**

**WHY ECALTA®?**

---

**Patient No. 3 with invasive candidiasis**

Oesophageal ulcer and moderate hepatic impairment
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Rose (Age: 56)

Patient No. 3 with invasive candidiasis
Oesophageal ulcer and moderate hepatic impairment

Current situation and test results

- Found to be **malnourished** with **thiamine deficiency** secondary to years of alcohol abuse and retching

- Stabilised after two units of blood and IV fluids with thiamine due to **severe dehydration, malnutrition** and **anaemia**

- Oral examination showed **pustular nodules** which were later positive for candidiasis

- Multiple **pus-draining lesions** were noted all over her torso and back, **nodular exudate** and **blood cultures** were positive for **candidaemia**

- Endoscopic exam noted a **large ulcer** at the **lower oesophageal lining**

- CT scan of the abdomen confirmed **hepatic steatosis**

CT, computerised tomography; IV, intravenous
Rose (Age: 56)

Patient No. 3 with invasive candidiasis
Oesophageal ulcer and moderate hepatic impairment

Co-morbidities

- Oesophageal ulcer
- Barrett’s oesophagus
- Alcoholic hepatic steatosis
- Anaemia
- Thiamine deficiency
- Chronic alcohol abuse
- Smoking
### Patient No. 3 with invasive candidiasis

Oesophageal ulcer and moderate hepatic impairment

### Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Physical</th>
<th>Liver panel</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea breath test</td>
<td>Alanine transaminase (ALT)</td>
<td>↑</td>
</tr>
<tr>
<td>BP</td>
<td>Aspartate transaminase (AST)</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Gamma glutamyl-transferase (GGT)</td>
<td>↑↑</td>
</tr>
<tr>
<td></td>
<td>Total bilirubin</td>
<td>↑</td>
</tr>
<tr>
<td>BP</td>
<td>Hgb</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>WBC</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Electrolytes</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Glucose</td>
<td>↓</td>
</tr>
</tbody>
</table>

**BP, blood pressure; Hgb, haemoglobin; WBC, white blood cell count**
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Rose (Age: 56)

Patient No. 3 with invasive candidiasis
Oesophageal ulcer and moderate hepatic impairment

Why Ecalta®?

Initiating antifungal therapy as soon as possible will be essential to Rose’s health. Her history and gastric complications put her in a critical state. Some of her current medications are metabolised by the liver. This along with her moderate hepatic impairment are factors to consider in choosing therapies.

- Ecalta® is not metabolised hepatically, has a large volume of distribution and achieves steady state quickly
- Ecalta® has no known drug interactions

References:
Philip (Age: 54)

Patient No. 4 with invasive candidiasis

Post-surgical sepsis

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
Philip (Age: 54)

Patient No. 4 with invasive candidiasis
Post-surgical sepsis

About Philip

- Admitted to hospital because of a **heart attack**
- Angiogram results showed >90% major artery stenosis leading to **lack of perfusion** to the left side of the heart
- **Cardiac bypass surgery** was advised and scheduled
- Has a **history of hypertension, type II diabetes** and **hypercholesterolemia** but has been **non-compliant with his medications**
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Patient No. 4 with invasive candidiasis
Post-surgical sepsis

Current situation and test results

- Underwent coronary bypass graft surgery
- **Prophylactic antibiotic and fluconazole** administered prior to surgery
- Developed **tachycardia and confusion** on the post-surgical ward
- Given IV fluids with no improvement to status
- Spiked a **temperature of 39.4°C** and had a **blood pressure of 85/55 mmHg**
- Blood cultures confirmed **candidal septicemia**
- Transferred to post-surgical ICU as patient was in **septic shock**
Philip (Age: 54)

Patient No. 4 with invasive candidiasis
Post-surgical sepsis

Co-morbidities
- Coronary artery disease
- Hypertension
- Type II diabetes
- Hypercholesterolemia
## Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Physical Exam</th>
<th>Blood</th>
<th>Cholesterol panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP 95/60 mmHg</td>
<td>WBC ↑↑</td>
<td>LDL ↑↑</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>↑↑</td>
<td>HDL ↓</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>↑</td>
<td>Triglycerides ↑</td>
</tr>
<tr>
<td>Glucose</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>Cardiac enzymes</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PT-INR</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PTT</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>

**BP**, blood pressure; **HDL**, high-density lipoprotein; **LDL**, low-density lipoprotein; **PT-INR**, prothrombin time-international normalised ratio; **PTT**, partial thromboplastin time; **WBC**, white blood cell count.
Why Ecalta®?

Peter is in a critical state and initiating antifungal therapy quickly whilst stabilising his sepsis will be crucial.

- Ecalta® is more effective than fluconazole in severely ill patients

- In comparison to micafungin and caspofungin, Ecalta® reaches steady state much faster

References:
Annie (Age: 40)

Patient No. 5 with invasive candidiasis
Oncology patient with neutropenia

CO-MORBIDITIES
RELEVANT PHYSICAL AND LAB FINDINGS
WHY ECALTA®?
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Annie (Age: 40)

**Patient No. 5 with invasive candidiasis**
Oncology patient with neutropenia

### About Annie

- Diagnosed with **acute myeloid leukaemia (AML)**
- Received standard **leukaemia therapy** leading to successful remission
- **Relapsed** and was admitted to hospital for **severe weakness**
- Disclosed to recently experiencing frequent **weak episodes** and **syncope**
- Lives a **sedentary lifestyle**
Current situation and test results

- Receiving a regular dose of intensive chemotherapy
- Found to be febrile on Day 7 of haematopoietic stem cell therapy (HSCT)
- Patient is neutropenic and immunocompromised
- Cultures came back positive for candidaemia with Candida glabrata resistant to fluconazole
- Despite treatment, patient condition is deteriorating with further dissemination of the candidiasis
These case studies are hypothetical. Symptoms and therapies described are not based on real patients.

Co-morbidities

- Acute myeloid leukaemia
- Neutropenia

Annie (Age: 40)

Patient No. 5 with invasive candidiasis
Oncology patient with neutropenia
Annie (Age: 40)

Patient No. 5 with invasive candidiasis
Oncology patient with neutropenia

Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Blood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>↓↓</td>
</tr>
<tr>
<td>Monocytes</td>
<td>↑</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>↑</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>↓↓↓</td>
</tr>
<tr>
<td>Hgb</td>
<td>↓</td>
</tr>
</tbody>
</table>

Hgb, haemoglobin; WBC, white blood cell count

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
Annie (Age: 40)

Patient No. 5 with invasive candidiasis
Oncology patient with neutropenia

Why Ecalta®?

Strains of *Candida glabrata* have shown to be resistant to fluconazole.¹ In such cases proceeding carefully is vital to a patient’s survival. Nosocomial infections are hard to treat especially in the neutropenic patient population.

- Ecalta® has been approved for the treatment of candidiasis in neutropenic patients²

References:
Date accessed: May 2017.
Clive (Age: 49)

Patient No. 6 with invasive candidiasis
Critically ill post-abdominal surgery

ABOUT CLIVE

CURRENT SITUATION AND TEST RESULTS

CO-MORBIDITIES

RELEVANT PHYSICAL AND LAB FINDINGS

WHY ECALTA®?
Clive (Age: 49)

Patient No. 6 with invasive candidiasis
Critically ill post-abdominal surgery

About Clive

• **History of colon cancer** with removal of cancerous polyps performed six years ago leading to remission

• **Poor eating habits** and **low fibre diet** leading to a **50 kg weight gain** over the past four years

• Against medical advice has **not had a colonoscopy** since post-surgery

• Recently admitted with **loss of appetite, 10 kg weight loss, skin paleness** and **weakness**

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
Current situation and test results

- Disclosed seeing bright red blood with bowel movements
- Experienced varied episodes of diarrhoea and constipation in the past month
- Due to low haemoglobin, transfused with blood until stable
- Colonoscopy showed multiple cancerous polyps, surgical resection was scheduled
- Post-surgery, deep tissue infection was suspected, cultures were positive for Candida albicans
Clive (Age: 49)

Patient No. 6 with invasive candidiasis
Critically ill post-abdominal surgery

Co-morbidities

- Colon cancer
- Obesity
- Anaemia
- Hypertension
Patient No. 6 with invasive candidiasis
Critically ill post-abdominal surgery

Relevant physical and lab findings

<table>
<thead>
<tr>
<th>Physical Exam</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>Hgb</td>
</tr>
<tr>
<td>110/75 mmHg</td>
<td>↓</td>
</tr>
<tr>
<td>BMI</td>
<td>WBC</td>
</tr>
<tr>
<td>32.0 kg/m²</td>
<td>↑</td>
</tr>
<tr>
<td>Bowel sounds</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>+</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Neutrophils</td>
</tr>
<tr>
<td></td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Eosinophils</td>
</tr>
<tr>
<td></td>
<td>↑</td>
</tr>
<tr>
<td>PT-INR</td>
<td>Normal</td>
</tr>
<tr>
<td>PTT</td>
<td>Normal</td>
</tr>
</tbody>
</table>

BMI, body mass index; BP, blood pressure; Hgb, haemoglobin; PT-INR, prothrombin time-international normalised ratio; PTT, partial thromboplastin time; WBC, white blood cell count

These case studies are hypothetical. Symptoms and therapies described are not based on real patients.
Clive (Age: 49)

Patient No. 6 with invasive candidiasis
Critically ill post-abdominal surgery

Why Ecalta®?

Clive is in need of effective antifungal therapy quickly to stabilise his deep tissue infection.

• Ecalta® is indicated for invasive candidiasis in patients with deep tissue wounds¹

• Ecalta® has a more favourable pharmacokinetic profile than the other echinocandins²

PREScribing INFORMATION
ECALTA® (Anidulafungin) PRESCRIBING INFORMATION – UK
Please refer to the SPC before prescribing Ecalta. Presentation: Each vial of Ecalta powder for concentrate for solution for infusion contains 100 mg anidulafungin. The reconstituted solution contains 3.33 mg/mL anidulafungin and the diluted solution contains 0.77 mg/mL anidulafungin. Indications: Treatment of invasive candidiasis in adult patients. Administration & dosage: Treatment should be initiated by a physician experienced in the management of invasive fungal infections. Ecalta should be reconstituted with water for injections and subsequently diluted before use. Give a single 200 mg loading dose by intravenous infusion on Day 1, followed by 100 mg daily thereafter. Duration of treatment should be based on the patient’s clinical response. In general, antifungal therapy should continue for at least 14 days after the last positive culture. There are insufficient data to support the 100 mg dose for longer than 35 days of treatment. The IV infusion rate should not exceed 1.1 mg/minute (equivalent to 1.4 ml/min) to minimise infusion associated reactions. Ecalta must not be administered as a bolus injection. Patients with renal impairment: No dose adjustment required. Ecalta is not dialysable and can be given without regard to the timing of haemodialysis. Patients with hepatic impairment: No dose adjustment required. Children and adolescents (under 18 years of age): Not recommended. Contra-indications: Hypersensitivity to anidulafungin, another echinocandin or to any of the excipients. Warnings and precautions: ECALTA has not been studied in patients with Candida endocarditis, osteomyelitis or meningitis. The efficacy of ECALTA has only been evaluated in a limited number of neutropenic patients. Isolated cases of significant hepatic dysfunction, hepatitis or worsening hepatic failure have been reported. Monitor patients with increased hepatic enzymes for evidence of worsening hepatic function and evaluate the risk/benefit of continuing anidulafungin therapy. Anaphylactic reactions, including shock, were reported with the use of anidulafungin. If these reactions occur, anidulafungin should be discontinued and appropriate treatment administered. Infusion-related adverse events have been reported with anidulafungin, including rash, urticaria, flushing, pruritus, dyspnoea, bronchospasm and hypotension. Infusion-related adverse events are infrequent when the rate of anidulafungin infusion does not exceed 1.1 mg/minute. Care should be taken when co-administering anidulafungin and anaesthetic agents since exacerbation of infusion-related reactions by co-administration of anaesthetics has been seen in a non-clinical (rat) study. Patients with fructose intolerance should not take Ecalta. Drug Interactions: Drug interaction studies were performed with anidulafungin and other medicinal products likely to be co-administered. No dosage adjustment of either medicinal product is recommended when anidulafungin is co-administered with ciclosporin, voriconazole or tacrolimus and no dosage adjustment for anidulafungin is recommended when co-administered with amphotericin B or rifampicin. Also see precautions above. Pregnancy and lactation: Ecalta is not recommended in pregnancy. Animal studies have shown excretion in breast milk. Not known whether excreted in human breast milk. A risk/benefit assessment should be carried out before deciding to use in breast feeding women. Side-effects: Very Common (incidence ≥1/10): hypokalaemia, nausea, diarrhoea. Common (incidence ≥1/100 to <1/10): hyperglycaemia, convulsion, headache, hypotension, hypertension, bronchospasm, dyspnoea, vomiting, blood creatinine increased, rash, pruritus, increased levels of alanine aminotransferase, blood alkaline phosphatase, aspartate aminotransferase, blood bilirubin and cholestasis. See SPC for other side effects. Legal category: POM. Marketing Authorisation Number: EU/1/07/416/002. Basic NHS cost: £299.99 per pack containing 1 vial of 100 mg anidulafungin powder. Marketing Authorisation Holder: Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom. Further information is available on request from: Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS. Date of Preparation: April 2017
Ref: ECW 5_0

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304 616161
PRESCRIBING INFORMATION

DIFLUCAN® (FLUCONAZOLE) – PRESCRIBING INFORMATION

Summary of Product Characteristics (SmPC) for full details before prescribing. Presentation: Diflucan is supplied as 50mg, 150mg and 200mg hard capsules, 2mg/ml solution for infusion and powder for oral suspension where each ml of reconstituted suspension contains 10mg or 40mg fluconazole. Indications: Diflucan (hard capsules, solution for infusion and powder for oral suspension) is indicated in adults in the treatment of invasive candidiasis (see SmPC section 4.1 for more indications). In term newborns, infants, toddlers, children, and adolescents aged from 0 to 17 years old, Diflucan (hard capsules, solution for infusion and powder for oral suspension) is used for the treatment of invasive candidiasis (see SmPC section 4.1 for more indications). Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly. Consideration should be given to official guidance on the appropriate use of antifungals. Dosage: Adults: Dosage should be adjusted based on the renal function in the elderly See SmPC section 4.2. Invasive Candidiasis: Loading dose of 800mg on Day 1 followed by 400mg daily for 2 weeks after first negative blood culture (see SmPC section 4.2 for dosing recommendations in other indications). Paediatric population: A maximum dose of 400mg daily should not be exceeded in paediatric population. In infants, toddlers and children (from 28 days to 11 years old), for the treatment of invasive candidiasis and cryptocoecal meningitis, 6 to 12mg/kg daily. For maintenance therapy, 6mg/kg daily. Clinical data indicate that children have a higher fluconazole clearance than observed for adults. A dose of 100, 200 and 400mg in adults corresponds to a 3, 6 and 12mg/kg dose in children to obtain a comparable systemic exposure. Safety and efficacy for genitral candidiasis indication in paediatric population has not been established. Current available safety data for other paediatric indications are described in SmPC section 4.8. Contra-indications: Hypersensitivity to the active substance, to related azole substances, or to any of the excipients. Co-administration of terfenadine is contraindicated in patients receiving Diflucan at multiple doses of 400 mg per day or higher based upon results of a multiple dose interaction study. Co-administration of other medicinal products known to prolong the QT interval and which are metabolised via the cytochrome P450 (CYP) 3A4 such as cisapride, astemizole, pimozide, quinidine and erythromycin are contraindicated in patients receiving fluconazole (see Summary of Products Characteristics for full details). Warnings and precautions: Diflucan should not be used for the treatment of tinea capitis as it was shown not to be superior to griseofulvin and the overall success rate was less than 20%. There is only limited evidence for efficacy of fluconazole in the treatment of cryptococcosis of other sites (pulmonary/ cutaneous) as well as in the treatment of other forms of endemic mycoses. Renal system: Diflucan should be administered with caution to patients with renal dysfunction. Adrenal insufficiency: Ketoconazole is known to cause adrenal insufficiency, and this could also, although rarely seen be applicable to fluconazole. Hepatobiliary system: Diflucan should be administered with caution to patients with liver dysfunction. Diflucan has been associated with rare cases of serious hepatic toxicity including fatalities, primarily in patients with serious underlying medical conditions. In cases of fluconazole associated hepatotoxicity, no obvious relationship to total daily dose, duration of therapy, sex or age of patient has been observed. Fluconazole hepatotoxicity has usually been reversible on discontinuation of therapy. Patients who develop abnormal liver function tests during fluconazole therapy must be monitored closely for the development of more serious hepatic injury. The patient should be informed of suggestive symptoms of serious hepatic effect (important asthenia, anorexia, persistent nausea, vomiting and jaundice). Treatment of fluconazole should be immediately discontinued and the patient should consult a physician. Cardiovascular system: Some azoles, including fluconazole, have been associated with prolongation of the QT interval on the electrocardiogram. Fluconazole causes QT prolongation via the inhibition of Rectifier Potassium Channel current (Ikr). The QT prolongation caused by other medicinal products (such as amiodarone) may be amplified via the inhibition of cytochrome P450 (CYP) 3A4. During post-marketing surveillance, there have been very rare cases of QT prolongation and torsades de pointes in patients taking Diflucan. These reports included

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304 616161

Continued on next slide >
PRESCRIBING INFORMATION

DIFLUCAN® (FLUCONAZOLE) – PRESCRIBING INFORMATION

seriously ill patients with multiple confounding risk factors, such as structural heart disease, electrolyte abnormalities and concomitant treatment that may have been contributory. Patients with hypokalemia and advanced cardiac failure are at an increased risk for the occurrence of life threatening ventricular arrhythmias and torsades de pointes. Diffucan should be administered with caution to patients with potentially proarrhythmic conditions. Coadministration of other medicinal products known to prolong the QT interval and which are metabolised via the cytochrome P450 (CYP) 3A4 are contraindicated. Halofantrine: Halofantrine has been shown to prolong QTc interval at the recommended therapeutic dose and is a substrate of CYP3A4. The concomitant use of fluconazole and halofantrine is therefore not recommended. Dermatological reactions: Patients have rarely developed exfoliative cutaneous reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, during treatment with fluconazole. AIDS patients are more prone to the development of severe cutaneous reactions to many medicinal products. If a rash, which is considered attributable to fluconazole, develops in a patient treated for a superficial fungal infection, further therapy with this medicinal product should be discontinued. If patients with invasive/systemic fungal infections develop rashes, they should be monitored closely and fluconazole discontinued if bullous lesions or erythema multiforme develop. Hypersensitivity: In rare cases anaphylaxis has been reported. Cytochrome P450: Fluconazole is a potent CYP2C9 inhibitor and a moderate CYP3A4 inhibitor. Fluconazole is also an inhibitor of CYP2C19. Diffucan treated patients who are concomitantly treated with medicinal products with a narrow therapeutic window metabolised through CYP2C9 and CYP3A4, should be monitored. Excipients: Diffucan solution for infusion contains 0.154 mmol sodium per ml. To be taken into consideration by patients on a controlled sodium diet. Diffucan powder for oral suspension contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose/galactose malabsorption and sucrase-isomaltase insufficiency should not take this medicine. Diffucan Capsules contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. See Summary of Product Characteristics for full details. Ability to drive and use machines: Patients should be warned about the potential for dizziness or seizures and should be advised not to drive or operate machines if any of these symptoms occur. Interactions: Concomitant use of cisapride, astemizole, pimozone, quindine, erythromycin is contraindicated (see SmPC section 4.5). The combined use of fluconazole at doses of 400mg or greater with terfenadine is contraindicated and coadministration at doses lower than 400mg per day should be carefully monitored. Concomitant use of fluconazole and halofantrine has the potential to increase the risk of cardiotoxicity and consequently sudden heart death. Hence this combination should be avoided. Concomitant administration of fluconazole with amiodarone may increase QT prolongation. Caution must be exercised if the concomitant use of fluconazole and amiodarone is necessary, notably with high dose fluconazole (800 mg) (see SmPC section 4.5). Interaction studies have shown that when oral fluconazole is coadministered with food, cimetidine, antacids or following total body irradiation for bone marrow transplantation, no clinically significant impairment of fluconazole absorption occurs. Fluconazole is a potent inhibitor of cytochrome P450 (CYP) isoenzyme 2C9 and a moderate inhibitor of CYP3A4. Fluconazole is also an inhibitor of the isozyme CYP2C19. In addition to the observed/documented interactions mentioned above, there is a risk of increased plasma concentration of other compounds metabolized by CYP2C9 and CYP3A4 coadministered with fluconazole. Therefore caution should be exercised when using these combinations and the patients should be carefully monitored. The enzyme inhibiting effect of fluconazole persists 4-5 days after discontinuation of fluconazole treatment due to the long half-life of fluconazole (see SmPC section 5.2). Dose adjustment of rifampicin, alfentanil, amitriptyline/nortriptyline, warfarin, carbamazepine, celecoxib, benznidazepine, fentanyl, ciclosporin, sirolimus, tacrolimus, methadone, NSAIDs, everolimus, saquinavir, vinca alkaloids, zidovudine and ivacaftor may be necessary. In patients taking concomitant moderate CYP3A inhibitors, such as fluconazole and erythromycin, a

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Pfizer Medical Information on 01304 616161.

Continued on next slide >
**PRESCRIBING INFORMATION**

**DIFLUCAN® (FLUCONAZOLE) – PRESCRIBING INFORMATION**

Reduction of the ivacator dose to 150 mg once daily is recommended. Fluconazole has the potential to increase the systemic exposure of the calcium channel antagonists. Frequent monitoring for adverse events is recommended. Combination therapy with cyclophosphamide and fluconazole results in an increase in serum bilirubin and serum creatinine. If concomitant therapy is necessary with HMGCoA reductase inhibitors, the patient should be observed for symptoms of myopathy and rhabdomyolysis and creatine kinase should be monitored. Fluconazole inhibits the metabolism of losartan to its active metabolite (E-31 74) which is responsible for most of the angiotensin II-receptor antagonism which occurs during treatment with losartan. Patients should have their blood pressure monitored continuously. With coadministration with phenytoin, rifabutin, sulfonylurea or theophylline concentration levels should be monitored in order to avoid toxicity. Patients on long-term treatment with fluconazole and prednisone should be carefully monitored for adrenal cortex insufficiency when fluconazole is discontinued. Combination therapy with all-trans-retinoid acid may be used but the incidence of CNS related undesirable effects should be borne in mind. Monitoring for voriconazole associated adverse events is recommended if voriconazole is used sequentially after fluconazole. Multiple dose use of fluconazole at 50 to 200mg daily is unlikely to have an effect on the efficacy of the combined oral contraceptive. *Fertility, pregnancy and lactation*: An observational study has suggested an increased risk of spontaneous abortion in women treated with fluconazole during the first trimester. There have been reports of multiple congenital abnormalities (including brachycephaly, ears dysplasia, giant anterior fontanelle, femoral bowing and radio-humeral synostosis) in infants whose mothers were treated for at least three or more months with high doses (400 - 800 mg daily) of fluconazole for coccidiodomycosis. The relationship between fluconazole use and these events is unclear. Studies in animals have shown reproductive toxicity (see section 5.3). Fluconazole in standard doses and short-term treatments should not be used in pregnancy unless clearly necessary. Fluconazole in high dose and/or in prolonged regimens should not be used during pregnancy except for potentially life-threatening infections. Fluconazole passes into breast milk to reach concentrations lower than those in plasma. Breast-feeding may be maintained after a single use of a standard dose 200 mg fluconazole or less. Breast-feeding is not recommended after repeated use or after high dose fluconazole. Fluconazole did not affect the fertility of male or female rats (see section 5.3). **Side effects**: The most frequently (‘Very Common’, ≥1/10) reported adverse reactions are headache, abdominal pain, diarrhoea, nausea, vomiting, alanine aminotransferase increased, rash, aspartate aminotransferase increased, blood alkaline phosphatase increased. The pattern and incidence of adverse reactions and laboratory abnormalities recorded during paediatric clinical trials, excluding the genital candidiasis indication, are comparable to those seen in adults. See Summary of Product Characteristics for full details on all other adverse reactions. **Overdose**: There have been reports of overdose with Diflucan and hallucination and paranoid behaviour have been concomitantly reported. **Legal category**: POM. **Package quantities, marketing authorisation numbers and basic NHS price**: Diflucan hard capsules 50mg- £16.61 (PL 00057/0289), 150mg- £7.12 (PL 00057/0290), 200mg-£6.42 (PL 00057/0344). **Marketing Authorisation Holder**: Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK. **Further information** is available on request from Medical Information Department, Pfizer Limited, Walton Oaks, Dorking Road, Walton-on-the-Hill, Surrey. KT20 7NS. Tel: +44 (0) 1304 616161 **Date of revision**: May 2017 **Ref**: DF 4.0 Combined UK

---

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304 616161

---

Continued on next slide >