
Pfizer Hospital
SHOULDN'T AN ANTIFUNGAL OFFER MORE THAN JUST SURVIVAL?
CRESEMBA® is indicated in adults for the treatment of:[1]
• Invasive aspergillosis
• Mucormycosis in patients for whom amphotericin B is inappropriate
Consideration should be given to official guidance on the appropriate use of antifungal agents.[1]
Prescribing information can be accessed at the end of this document.
CRESEMBA®
(ISAVUCONAZOLE)

Invasive aspergillosis and mucormycosis can be life threatening, difficult to identify and are increasingly common

Mortality with invasive mould infections can vary depending on the underlying condition, but rates are generally very high if not diagnosed and treated[2]

- Invasive aspergillosis: up to 87%[2,3]
- Mucormycosis: up to 88%[4]

Identifying invasive species in time is often very challenging

- Only 50% of invasive fungal infections are diagnosed before death[5]
- Diagnostic challenges and a complicated clinical picture often lead to detrimental delays[6,7]
- Discriminating between invasive aspergillosis and mucormycosis in a timely fashion can prove to be difficult[7]

Incidence of invasive aspergillosis and other mould infections has increased in recent years[8–10]

- Estimated annual global cases of invasive aspergillosis: >300,000[11]
- Estimated annual global cases of invasive mucormycosis: >10,000[11]

HOW MIGHT A FLEXIBLE ANTIFUNGAL AGENT WITH BROAD-SPECTRUM EFFICACY HELP OPTIMISE PATIENT OUTCOMES?

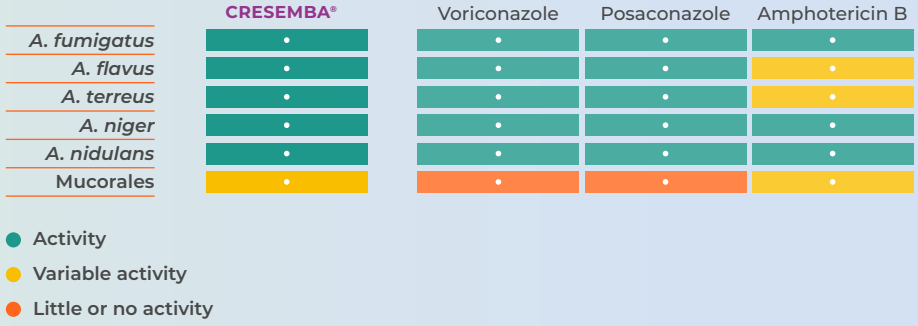
CRESEMBA® is licensed for both invasive aspergillosis and mucormycosis[1]

CRESEMBA® is indicated in adults for the treatment of:[1]

- Invasive aspergillosis
- Mucormycosis in patients for whom amphotericin B is inappropriate

CRESEMBA® is a latest-generation azole with extended anti-mould activity across *Aspergillus* species and Mucorales[1,12,13]

CRESEMBA® activity *in vitro*[1,14–16]

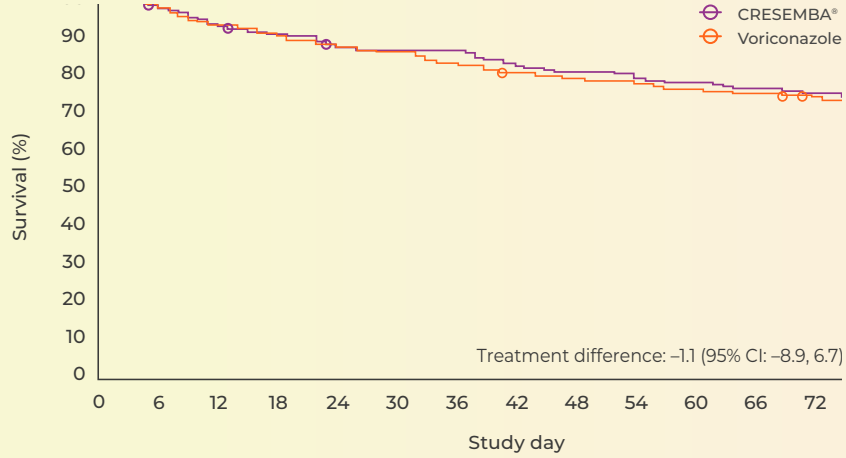


Adapted from references 1, 14–16.

CRESEMBA® is as effective as the standard of care in invasive aspergillosis

In invasive aspergillosis, CRESEMBA® offers survival rates comparable with the standard of care, voriconazole[17]

- In the SECURE Phase 3 pivotal trial, survival rates were comparable between CRESEMBA® and voriconazole throughout the study[17,a]



Number at risk													
CRESEMBA®	258	252	240	232	224	220	220	211	206	204	199	195	192

Survival from baseline to day 84 with CRESEMBA® and voriconazole in the SECURE trial (ITT population; results were similar in the mITT population). Patients were censored on the day of their last known survival status (circles). Adapted from reference 17.

In the SECURE trial, all-cause mortality was comparable with CRESEMBA® and voriconazole in both the ITT and mITT populations[17,a]

- Day 42 (ITT population): 19% vs 20% (adjusted treatment difference: –1.0%; 95% CI: –7.8, 5.7)[17]
- In the SECURE trial, with CRESEMBA® overall response to treatment, as well as clinical, mycological and radiological responses were all comparable with voriconazole[17,a]

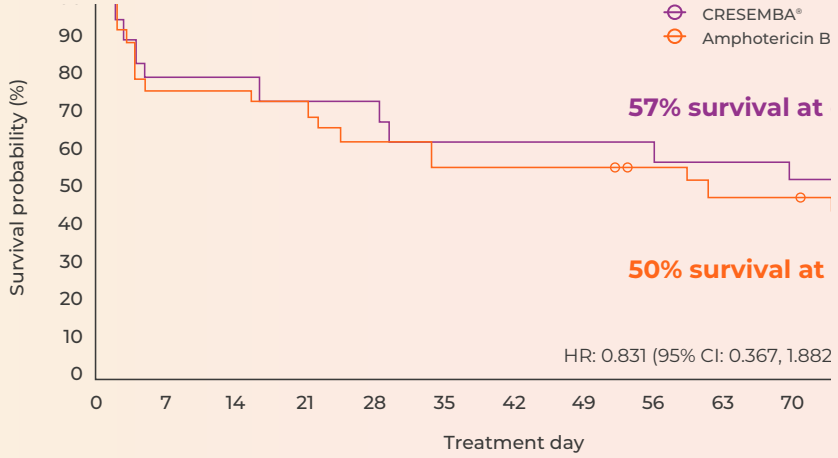
a. The non-inferiority margin was 10% (adjusted treatment differences).

ITT, intention-to-treat; mITT, modified intention-to-treat

CRESEMBA® is effective in mucormycosis

CRESEMBA® has similar survival rates to amphotericin B in mucormycosis[18]

- A case-control analysis matching patients who received primary CRESEMBA® in VITAL with controls from the FungiScope Registry treated with amphotericin B showed similar survival rates for both drugs[18]



Number at risk											
CRESEMBA®	21	17	17	16	16	14	14	14	14	13	12

Survival from baseline to day 84 in patients who received CRESEMBA® as primary treatment in VITAL vs matched controls treated with amphotericin B (FungiScope). Adapted from reference 18.

VITAL was a single-arm, open-label trial of CRESEMBA® in rare invasive mould infections, which included 37 patients with mucormycosis[18]

In the VITAL trial, CRESEMBA® was associated with an overall response of 11% at day 42 (primary endpoint), rising to 31% (complete and partial response) at the end of treatment[18,a]

a. Overall response was based on individual clinical, mycological, and radiological response assessed by the Data Review Committee[18]

HR, hazard ratio; CI, confidence interval

In invasive aspergillosis, CRESEMBA® has enhanced tolerability vs the standard of care

In invasive aspergillosis, CRESEMBA® combines standard-of-care efficacy with improved tolerability vs voriconazole[17]

- In the SECURE trial, the proportion of invasive aspergillosis patients with treatment-emergent AEs was overall similar with CRESEMBA® and voriconazole (96% vs 98%)[17]
- Drug-related AEs were significantly less frequent with CRESEMBA® vs voriconazole[17]
- The frequency of AEs and drug-related AEs leading to discontinuation were considerably lower with CRESEMBA® than with voriconazole[17]

Drug-related AEs and treatment discontinuations in the SECURE trial[17]

	CRESEMBA® (n=257)	Voriconazole (n=259)	p value
Drug-related AEs	42%	60%	<0.001
AEs leading to discontinuation	14%	23%	–
Drug-related AEs leading to discontinuation	8%	14%	–

AEs typical to voriconazole were less common with CRESEMBA®[17]

- Voriconazole is often associated with neurotoxic, hepatic and visual AEs, which can lead to premature treatment discontinuation[17]
- In invasive aspergillosis, CRESEMBA® showed significant reductions vs voriconazole in the frequency of skin and subcutaneous tissue disorders[17]

System organ classes with significantly fewer drug-related AEs with CRESEMBA® vs voriconazole[17]

	CRESEMBA® (n=257)	Voriconazole (n=259)	p value
Skin and subcutaneous tissue disorders	33%	42%	0.037
Eye disorders	15%	27%	0.002
Hepatobiliary disorders	9%	16%	0.016

AE, adverse event

CRESEMBA® has a consistent tolerability profile across clinical trials for invasive aspergillosis and mucormycosis[18]

In the VITAL trial, only 16% of patients discontinued CRESEMBA® due to AEs[18]

The AE profile in VITAL was consistent with observations from the SECURE trial[18]

Most common (≥10%) TEAEs reported for CRESEMBA® in VITAL[18]

TEAE	Incidence® (N=37)
Overall	**95%**
Vomiting	32%
Diarrhoea	27%
Nausea	27%
Pyrexia	27%
Constipation	22%
Decreased appetite	16%
Headache	16%
Oedema, peripheral	16%
Abdominal pain	14%
Dyspnoea	14%
Pneumonia	14%
Back pain	11%
Cough	11%
Hypoglycaemia	11%
Insomnia	11%
Restlessness	11%

Adapted from reference 18.

AE, adverse event; TEAE, treatment-emergent adverse event

CRESEMBA® helps you manage the invasive mould infection while focusing on the underlying condition[6,8,19–25]

CRESEMBA® can be used in patients with renal impairment, without dose adjustments[1,19,20]

- Unlike other IV azoles, CRESEMBA® does not contain cyclodextrin, eliminating the potential for renal toxicity[1,21,26,27]

Unlike voriconazole, CRESEMBA® does not require dose adjustments in patients with mild or moderate hepatic impairment[1,26]

- CRESEMBA® has not been studied in patients with severe hepatic impairment; use in these patients is not recommended unless the potential benefit is considered to outweigh the risks[1]

While voriconazole and posaconazole prolong the QTc interval, CRESEMBA® shortens it[1,22,26,28]

- CRESEMBA® is contraindicated in patients with familial short QT syndrome; caution should be used when prescribing CRESEMBA® in combination with other medicines that decrease the QTc interval[1,22]

CRESEMBA® has fewer drug-drug interactions than other azoles[1,20]

- CRESEMBA® is contraindicated in coadministration with ketoconazole, high-dose ritonavir, and strong CYP3A4/5 inducers such as rifampicin, rifabutin, carbamazepine, long acting barbiturates, phenytoin and St. John's wort, or with moderate CYP3A4/5 inducers such as efavirenz, nafcillin and etravirine[1]

CRESEMBA® allows for simple and reliable IV and oral dosing[1,22,24,25]

- For both IV and oral administration, the recommended loading dose is 200 mg of CRESEMBA® every 8 hours for 48 hours, followed by a maintenance dose of 200 mg once daily[1]
- TDM is not routinely recommended for CRESEMBA®[29,30]

IV, intravenous; TDM therapeutic drug monitoring

Pfizer Hospital

WITH CRESEMBA® YOU CAN GO BEYOND SURVIVAL

CRESEMBA® is as effective as the standard of care in invasive aspergillosis and is also active against mucormycosis[13,20]

CRESEMBA® has better tolerability than the standard of care in invasive aspergillosis[13,17]

CRESEMBA® offers simplicity and flexibility to help you focus on your patient's underlying condition[1,6,13,17,23]

Prescribing information

Please click the links below to be directed to the EMA website.

CRESEMBA® - SmPC

VFEND - SmPC

References

1. CRESEMBA Summary of Product Characteristics. 2019.
2. Lin SJ *et al. Clin Infect Dis* 2001;**32**(3):358–366.
3. Garcia-Vidal C *et al. PLoS One* 2015;**10**(3):e0120370.
4. Guinea J *et al. PLoS One* 2017;**12**(6):e0179136.
5. Dignani MC. F1000Prime Rep 2014;**6**:81.
6. Mercier T and Maertens J. *J Antimicrob Chemother* 2017;**72**(suppl_1):i29–i38.
7. Chamilos G *et al. Clin Infect Dis* 2008;**47**(4): 503–509.
8. Donnelley MA *et al. Infect Drug Resist* 2016;**9**:79–86.
9. Lass-Florl C and Cuenca-Estrella M. *J Antimicrob Chemother* 2017;**72**(suppl_1):i5–i11.
10. Limper AH. *Proc Am Thorac Soc* 2010;**7**(3): 163–168.
11. Bongomin F *et al. J Fungi (Basel)* 2017;**3**(4).
12. Miceli MH and Kauffman CA. *Clin Infect Dis* 2015;**61**(10):1558–1565.
13. Falci DR and Pasqualotto AC. *Infect Drug Resist* 2013;**6**:163-174.
14. Arendrup MC *et al. Antimicrob Agents Chemother* 2015;**59**(12):7735–7742.
15. Guinea J *et al. Antimicrob Agents Chemother* 2008;**52**(4):1396–1400.
16. Sabatelli F *et al. Antimicrob Agents Chemother* 2006;**50**(6):2009-2015.
17. Maertens JA *et al. Lancet* 2016;**387**(10020): 760–769.
18. Marty FM *et al. Lancet Infect Dis* 2016;**16**(7): 828–837.
19. Mullane KM *et al.* ECCMID 2015. Poster presentation (EV0932).
20. Natesan SK and Chandrasekar PH. *Infect Drug Resist* 2016;**9**:291–300.
21. Horn D *et al. J Med Econ* 2016;**19**(7):728–734.
22. Mellinghoff SC *et al. Mycoses* 2018;**61**(4):256–260.
23. Perfect JR. *Nat Rev Drug Discov* 2017;**16**(9): 603–616.
24. Kaindl T *et al. J Antimicrob Chemother* 2019;**74**(3):761–767.
25. Schmitt-Hoffmann A *et al. Antimicrob Agents Chemother* 2006;**50**(1):279–285.
26. VFEND Summary of Product Characteristics. 2019.
27. Sporanox Summary of Product Characteristics. 2018.
28. Noxafil Summary of Product Characteristics. 2019.
29. Andes D *et al. Antimicrob Agents Chemother* 2018;**62**(7).
30. Desai AV *et al. Antimicrob Agents Chemother* 2017;**61**(12).

July 2020. PP-CRB-GLB-0495.

CRESEMBA® (ISAVUCONAZOLE)

BECAUSE SURVIVAL ISN'T ENOUGH