# Three Months of SCY-247 EUCAST MIC Testing: Uniform Activity against *Candida* Species and no Cross-Resistance to Echinocandins

STATENS SERUM INSTITUT

P052

**Karin Meinike Jørgensen[1], Nissrine Abou-Chakra[1], Karen Marie Thyssen Astvad[1] and Maiken Cavling Arendrup[1,2,3]**

*[1]Unit of Mycology, Statens Serum Institut, Copenhagen, Denmark, [2]Dept. Clinical Microbiology, Rigshospitalet, Copenhagen, Denmark, [3]Dept. of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*

## Objectives

SCY-247 is a second-generation, IV/oral, novel antifungal agent of the triterpenoid class (1) targeting the glucan synthase enzyme via a site interaction distinct from that of the echinocandins.

Inclusion of SCY-247 in our routine MIC determination to generate MICs for future ECOFF setting.

We present here the first three months of EUCAST SCY-247 MICs and compare these to 1) anidulafungin and micafungin MICs tested in parallel, and 2) previously published ibrexafungerp MICs (2).

## Materials & methods

MICs of SCY-247 were determined according to the EUCAST E.Def 7.4 reference method.

Susceptibility testing

- 239 *Candida* isolates from Q1 of 2025.
- Thermo Scientific™ Nunc™ MicroWell™ 96-Well, Nunclon Delta-Treated, Flat-Bottom Microplate (Fisher Scientific, cat. no. 161093).
- RPMI medium (SSI Diagnostica, cat. no. 60984).
- SCY-247 (Scynexis, New Jersey, USA)
- Anidulafungin and micafungin (Molcan Corporation, Toronto, Ontario, Canada).

Data analysis and sequencing

- Modal MICs (mg/L) for species with ≥11 isolates.
- SCY-247 MICs compared to previously generated and published ibrexafungerp MICs (2).
- Isolates defined as non-wild-type to SCY-247 if the MIC was ≥ 3 two-fold dilutions above the modal MIC.
- EUCAST breakpoints applied for interpretation of anidulafungin and micafungin MICs.
- Isolates resistant or non-wild-type to ≥1 agent underwent *fks* sequencing.

## Results

### MIC distribution

The SCY-247 MIC distributions are Gaussian and narrow, spanning 2-4 two-fold dilutions (Table 1).

For the most prevalent *Candida* species

- the MIC ranges are identical for *C. albicans* and *C. glabrata* (0.06-0.5 mg/L), for *C. dubliniensis* and *C. parapsilosis* (0.25-0.5 mg/L), and for *C. krusei* and *C. tropicalis* (0.25-1 mg/L).
- the modal MICs fall within a ±1 two-fold dilution (0.125-0.5 mg/L).

### Comparison to ibrexafungerp

For our present data, a more uniform activity profile is seen for SCY-247 compared to ibrexafungerp (Table 1).

SCY-247 modal MICs appear slightly higher (by 2 two-fold dilutions) than those for ibrexafungerp for *C. albicans* and *C. dubliniensis*, comparable to *C. krusei*, *C. parapsilosis,* and *C. tropicalis* and slightly lower for *C. glabrata* (by 1 two-fold dilution), though data are limited.

### SCY-247 in FKS mutants

The *C. glabrata* and *C. tropicalis* isolates with FKS hot spot alterations were regarded SCY-247 wild-type with MICs 1-2 two-fold dilution steps above the modal MICs (Table 1 and 2). In comparison, anidulafungin and micafungin MICs were 2-5 and 1-6 two-fold dilution steps, respectively, above the modal MIC for the same isolates (Table 2).

**Table 1.** SCY-247 and ibrexafungerp (ibrexa) EUCAST MICs against isolates received at the SSI during Q1 2025 (SCY-247, *N* =239) and 2020-2021 (ibrexafungerp, *N* =1852), respectively. Modal MICs are highlighted in bold.

| Species | Agent | *N* | MIC (mg/L) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 0.016 | 0.03 | 0.06 | 0.125 | 0.25 | 0.5 | 1 | 2 | 4 | 8 |
| *C. albicans* | SCY-247 | 103 | | | 13 | 37 | **50** | 3 | | | | |
| | Ibrexa | 896 | 5 | 91 | **574** | 213 | 10 | | 2 | 1 | | |
| *C. dubliniensis* | SCY-247 | 14 | | | | | 6 | **8** | | | | |
| | Ibrexa | 117 | | | 15 | **64** | 33 | 4 | | 1 | | |
| *C. glabrata* | SCY-247 | 58 | | | 9 | **37** | 11 | 1 | | | | |
| | Ibrexa | 475 | | | | 5 | **319** | 148 | 2 | 1 | | |
| *C. krusei* | SCY-247 | 21 | | | | | 5 | **14** | 2 | | | |
| | Ibrexa | 110 | | | | | 14 | **74** | 22 | | | |
| *C. parapsilosis* | SCY-247 | 7 | | | | | 1 | 6 | | | | |
| | Ibrexa | 78 | | | | 1 | 23 | **44** | 2 | 1 | 6 | 1 |
| *C. tropicalis* | SCY-247 | 17 | | | | | 5 | **11** | 1 | | | |
| | Ibrexa | 146 | | | | 8 | 44 | **75** | 16 | | 2 | 1 |
| *C. guilliermondii* | SCY-247 | 2 | | | | | | 1 | 1 | | | |
| | Ibrexa | 4 | | | | | | 1 | 3 | | | |
| *C. kefyr* | SCY-247 | 2 | | | | | 1 | 1 | | | | |
| | Ibrexa | 5 | | | | | 3 | 2 | | | | |
| *C. lusitaniae* | SCY-247 | 7 | | | | | 1 | 1 | 5 | | | |
| | Ibrexa | 9 | | | | | | | 4 | 5 | | |
| *C. metapsilosis* | SCY-247 | 1 | | | | | 1 | | | | | |
| | Ibrexa | 1 | | | | 1 | | | | | | |
| *S. cerevisiae* | SCY-247 | 4 | | | | 1 | 3 | | | | | |
| | Ibrexa | 11 | | | | 1 | 2 | **8** | | | | |

**Table 2**. Comparison of FKS amino acid sequences and MICs (mg/L) (MIC elevation above the modal MIC*) for isolates non-wild type to SCY-247 or echinocandin agents.

| Species | Fks alteration | Hot spot | SCY-247 | Anidulafungin | Micafungin |
|---|---|---|---|---|---|
| *C. glabrata* | F659S | FKS2 HS1 | 0.5 (2) | 0.125 (2) | 0.03 (1-2)* |
| *C. glabrata* | S663P | FKS2 HS1 | 0.25 (1) | 0.5 (4) | 0.5 (5-6)* |
| *C. glabrata* | D666G | FKS2 HS1 | 0.25 (1) | 0.25 (3) | 0.016 (0-1)* |
| *C. lusitaniae* | M689I | Outside HS | 1 (0) | 0.5 (3-4)* | 0.5 (3) |
| *C. tropicalis* | S654P | FKS1 HS1 | 1 (1) | 0.5 (5) | 1 (6) |

*For anidulafungin, the modal MIC against *C. lusitaniae* straddled 0.03 and 0.06; and for micafungin, the modal MIC against *C. glabrata* straddled 0.008 and 0.016 mg/L. Therefore, a 2 two-fold dilution range is given for the determined MIC elevation. HS: hot spot.

## Conclusion

- SCY-247 displayed uniform activity against the 11 *Candida* species included with no indication of cross-resistance to the echinocandins.
- However, more isolates, particularly of the rarer species, and more isolates with Fks alterations need to be investigated before firm conclusions can be drawn.

## References

1. Chu S, Long L, McCormick TS, *et al*. 2021. A second-generation fungerp analog, SCY-247, shows potent in vivo activity in a murine model of hematogenously disseminated *Candida albicans*. Antimicrob Agents Chemother. 2021, 65:e01989-20.
2. Jørgensen KM, Astvad KMT, Hare RK *et al*. 2022. EUCAST Ibrexafungerp MICs and Wild-Type Upper Limits for Contemporary Danish Yeast Isolates. J. Fungi, 8, 1106.

## Acknowledgements:

The study was supported by an unrestricted grant from Scynexis

SCYNEXIS

**Contact:** MACA@ssi.dk or KMJ@ssi.dk