FAKULTAS KEDOKTERAN
UNIVERSITAS TRISAKTI

Indacaterol Inside

The Role of Indacaterol in Modern Respiratory Care

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NVS/BD&L/RESPI/SLID/022025/05

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Respiratory Breezhaler Portfolio

Once Daily, Once Inhalation, One Inhaler

Indacaterol Inside

Fast onset · Once daily · Controllable

Onbrez · Ultibro · Atectura · Enerzair

ASTHMA

LABA/ICS

ONCE DAILY ATECTURA breezhaler
Indacaterol acetate / mometasone furoate inhalation powder

150/80 mcg,
150/160 mcg or
150/320 mcg
Once Daily

LABA/LAMA/ICS

ONCE DAILY ENERZAIR breezhaler
Indacaterol acetate / glycopyrronium bromide / mometasone furoate inhalation powder

150/50/160 mcg
Once Daily

COPD

LABA

Once Daily onbrez breezhaler
indacaterol inhalation powder

150 mcg or
300 mcg
Once Daily

LABA/LAMA

ONCE DAILY ultibro breezhaler
indacaterol maleate / glycopyrronium bromide inhalation powder

110/50 mcg
Once Daily

✓ FAST ONSET

✓ ONCE DAILY

✓ CONTROLLABLE

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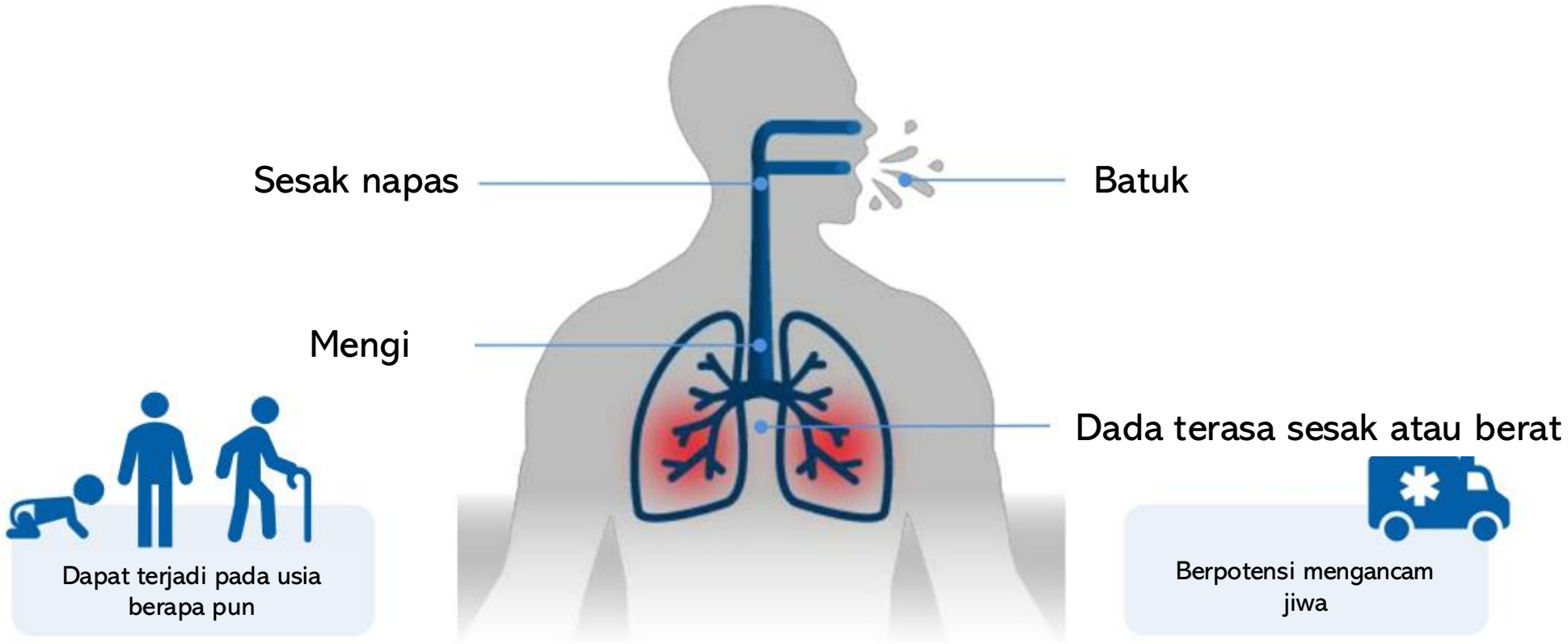
Definisi Asma

- Asma adalah penyakit heterogen, yang biasanya memiliki karakteristik inflamasi kronik saluran napas. Penyakit ini ditandai dengan riwayat gejala pernapasan seperti mengi, sesak napas, dada terasa berat dan batuk yang bervariasi dalam hal waktu dan intensitas, disertai variasi hambatan aliran udara ekspirasi.

Referensi : Global Initiative for Asthma (GINA) 2024

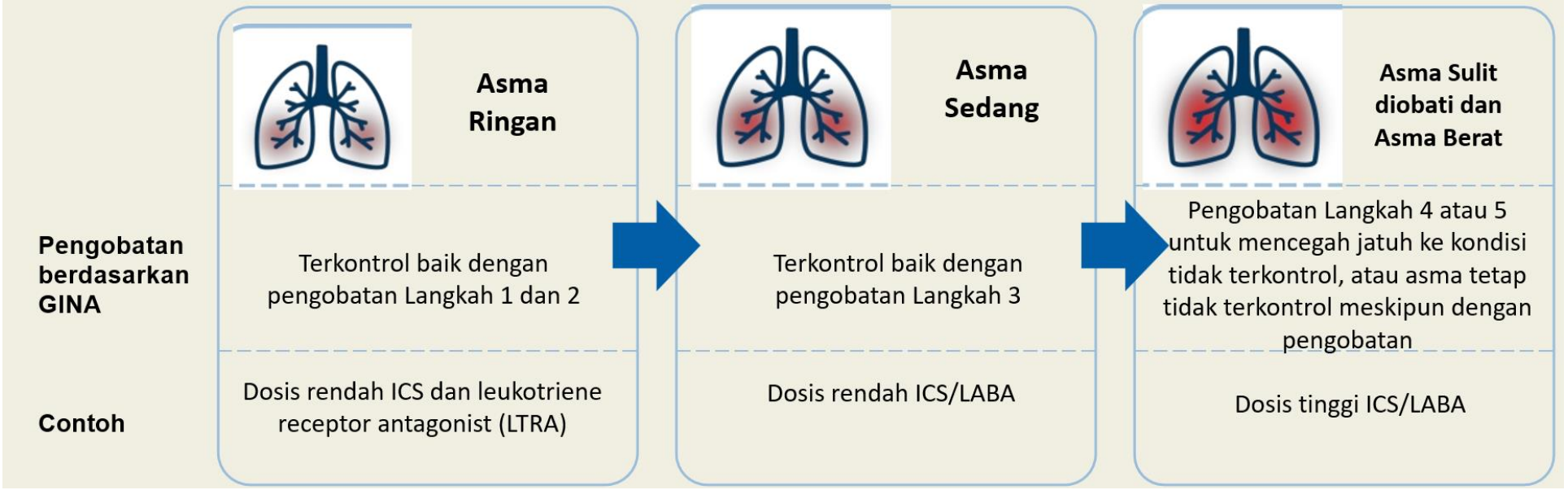
Gejala pada asma



Referensi : Global Initiative for Asthma (GINA) 2024

Klasifikasi Asma

Menurut GINA, keparahan asma didasarkan pada tingkat pengobatan yang diperlukan untuk mengendalikan gejala dan eksaserbasi daripada beban gejala.

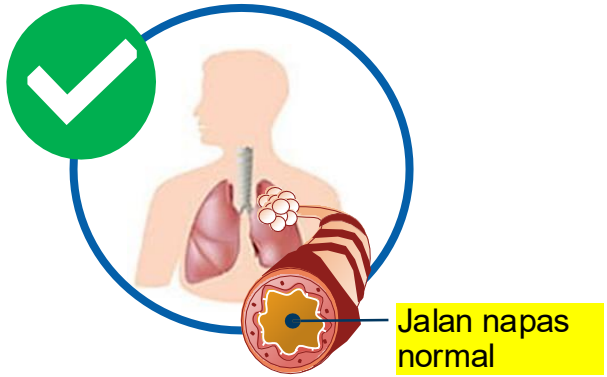


Asma yang sulit diobati vs asma berat

Referensi : Global Initiative for Asthma (GINA) 2024

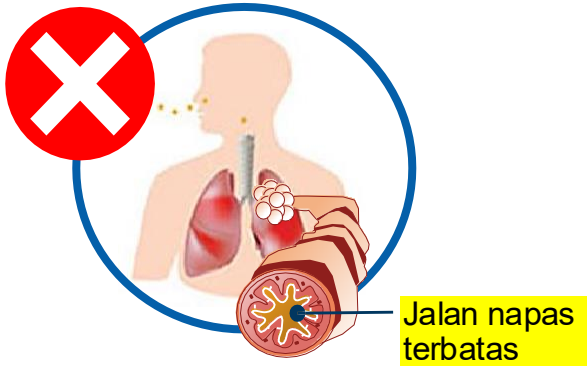
Tujuan Penatalaksanaan Asma

- **Tujuan penatalaksanaan Asma pada anak dan dewasa seperti dinyatakan oleh *Global Initiative for Asthma (GINA)* dapat diringkas sebagai berikut:**



Untuk mencapai kontrol gejala yang baik dan mempertahankan tingkat aktivitas normal

+



Untuk meminimalkan risiko eksaserbasi di masa depan, perbaikan pembatasan aliran udara, dan efek samping

- **Penting juga untuk mengetahui tujuan pasien sendiri mengenai asma mereka, karena ini mungkin berbeda dari tujuan medis konvensional.**

Referensi : Global Initiative for Asthma (GINA) 2024

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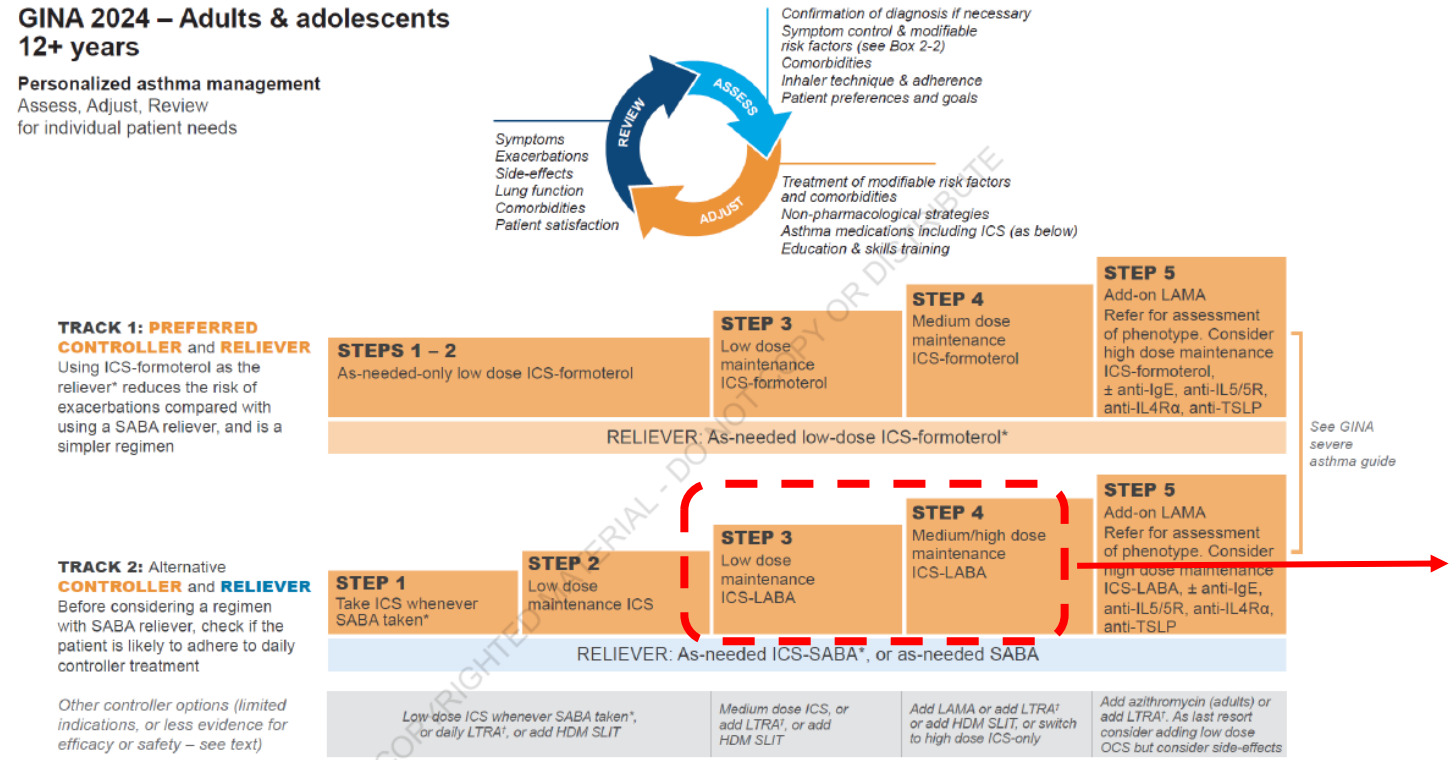
Penatalaksanaan Asma pada Terapi Pemeliharaan

ASTHMA TREATMENT STEPS IN ADULTS AND ADOLESCENTS

Box 4-6. Personalized management for adults and adolescents to control symptoms and minimize future risk



Pada Track 2 - Terapi Pemeliharaan (Maintenance Therapy)
Step 3 direkomendasikan LABA/ ICS dosis rendah
Step 4 direkomendasikan LABA/ICS dosis sedang - tinggi

References : Global Initiative for Asthma (GINA) 2024

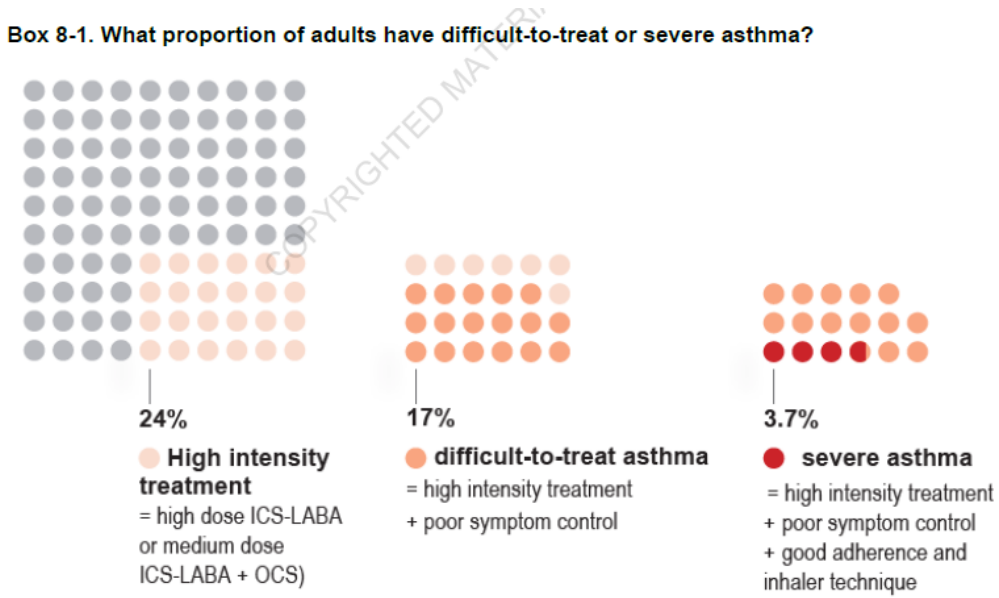
Asma Tidak Terkontrol

Definisi GINA 2024 mencakup salah satu atau kedua hal berikut:

- Kontrol gejala yang buruk (gejala yang sering atau penggunaan obat pelega yang sering, aktivitas terbatas akibat asma, terbangun di malam hari karena asma)
- Eksaserbasi yang sering (≥2 kali per tahun) yang memerlukan kortikosteroid oral, atau eksaserbasi berat (≥1 kali per tahun) yang memerlukan rawat inap.

Asma sulit-diobati adalah asma yang tetap tidak terkontrol meskipun telah menjalani pengobatan GINA Step 4 atau 5, akibat faktor-faktor seperti teknik inhalasi yang salah, kepatuhan yang buruk, merokok, komorbiditas, atau salah diagnosis.

Asma berat adalah asma yang tetap tidak terkontrol pada pengobatan GINA Step 4 atau 5 meskipun memiliki kepatuhan yang baik dan teknik inhalasi yang benar.



References : Global Initiative for Asthma (GINA) 2024

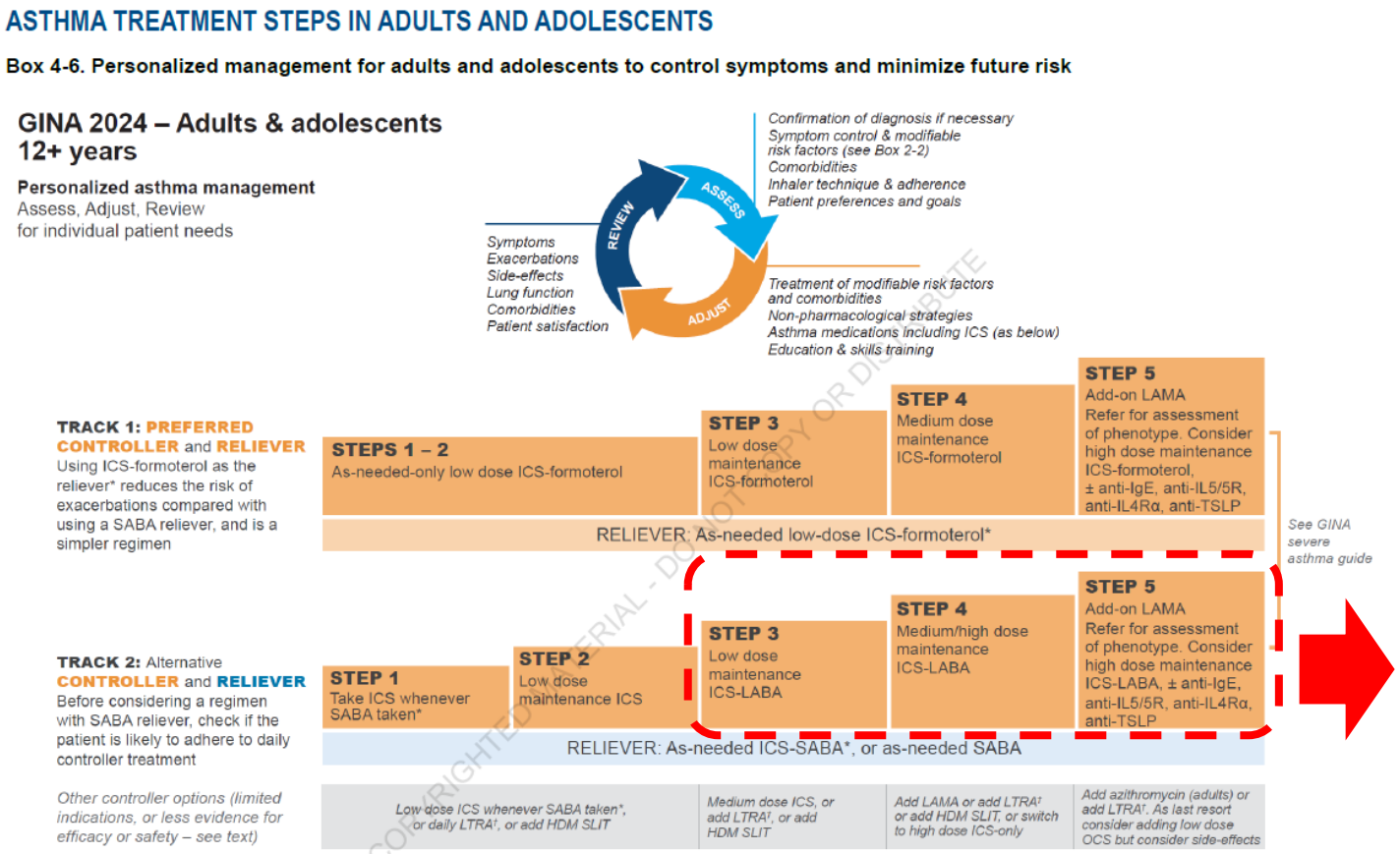
1 dari 3 pasien asma masih belum terkontrol walaupun sudah diberikan terapi inhalasi

- **39% pasien** asma masih **tidak terkontrol,** walaupun sudah diberikan terapi inhalasi[1]
- **50% pasien asma tidak dapat menggunakan alat inhaler dengan benar,** walaupun sudah diberikan edukasi[2]
- **Gejala asma yang persisten** meningkatkan risiko serangan asma pada pasien[3]

NVS/BD&L/RESPI/SLID/022025/05

Referensi: 1. Buhl R, et al. Respir Med 2020;162:105859; 2. Azzi E, et al. NPJ Prim Care Respir Med 2017;27:29; 3. Global Initiative for Asthma (GINA) 2024

Penatalaksanaan Asma Tidak Terkontrol



References : Global Initiative for Asthma (GINA) 2024

Pada Track 2

- Pada **Step 3** direkomendasikan LABA/ ICS dosis rendah pada pasien dengan gejala hampir setiap hari atau terbangun di malam hari sekali seminggu atau lebih, atau fungsi paru yang rendah.
- Pada **Step 4** direkomendasikan LABA/ICS dosis sedang – tinggi pada pasien dengan gejala harian, terbangun di malam hari sekali seminggu atau lebih, serta fungsi paru yang rendah atau eksaserbasi terbaru.
- Pada **Step 5** direkomendasikan LABA/LAMA/ICS pada pasien yang sudah tidak terkontrol dengan LABA/ICS dosis sedang - tinggi

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Dual Fixed Dose Combination

LABA/ICS

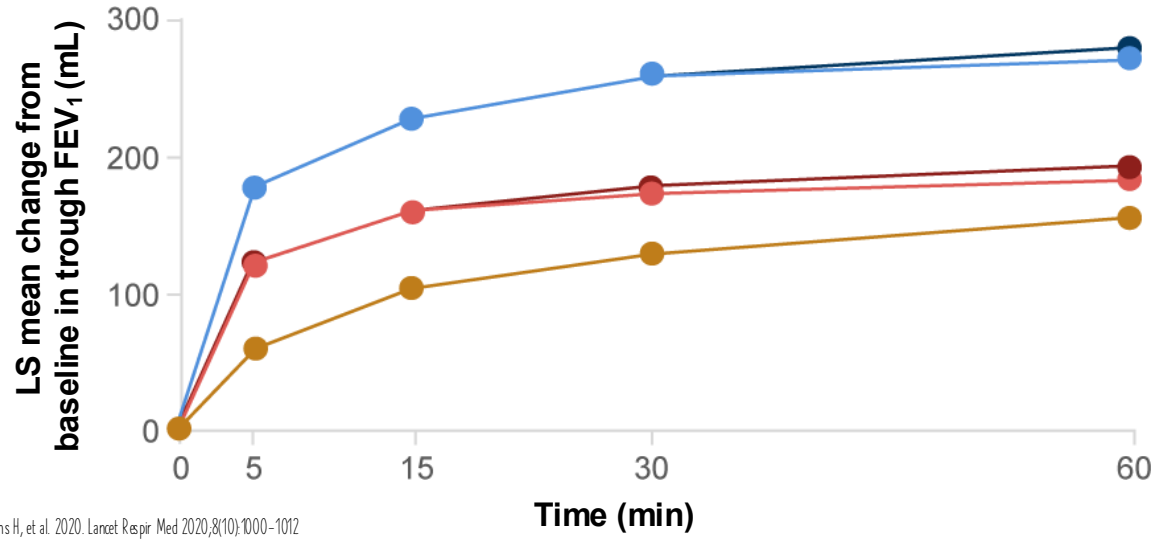
Indacaterol/Mometasone

NVS/BD&L/RESPI/SLID/022025/05

IRIDIUM

Indacaterol/Mometasone Terbukti Melegakan Napas dalam 5 Menit*

Dalam analisis sekunder,† IND/MF meningkatkan fungsi paru dibandingkan SAL/FLU dosis tinggi (dua kali sehari).



References: Kerstjens H, et al. 2020. Lancet Respir Med 2020;8(10):1000-1012

Onset kerja‡,

5 menit

- IND/GLY/MF high-dose (once-daily)
- IND/GLY/MF medium-dose (once-daily)
- IND/MF high-dose (once-daily)
- IND/MF medium-dose (once-daily)
- SAL/FLU high-dose (twice-daily)

*In symptomatic asthma patients, despite treatment with medium- or high-dose LABA/ICS. †Secondary analysis, analyzed using a mixed model for repeated measures, not controlled for multiplicity. ‡As measured by FEV_1 5 minutes post-dose on Day 1.
The IRIDIUM trial is a 52-week randomized study in 3,092 asthma patients, inadequately controlled on LABA/ICS.
Primary endpoint was met: Triple FDCssignificantly improved trough FEV_1 by +76 mL (95% CI: 41, 111) and +65 mL (95% CI: 31, 99) at Week 26 vs IND/MF for medium- and high-doses respectively, p<0.001. **Key secondary endpoint,** improvement in ACQ-7 score for Triple FDCsvs IND/MF at Week 26, **was not met**; however, all 5 arms demonstrated similarly high and clinically relevant improvement from baseline. Refer to ClinicalTrials.gov for more information about other secondary analyses.
Triple FDCshigh-dose = IND/GLY/MF 150/50/160 µg (once-daily); Triple FDCsmedium-dose = IND/GLY/MF 150/50/80 µg (once-daily); IND/MF high-dose = IND/MF 150/320µg (once-daily); IND/MF medium-dose = IND/MF 160/160 µg (once-daily); SAL/FLU high-dose = SAL/FLU 50/500 µg (twice-daily).
ACQ-7, Asthma Control Questionnaire-7; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; GLY, glycopyrronium; IND, indacaterol acetate; LS, least squares; MF, mometasone furoate.

Onset Kerja

Referensi: Kerstjens H, et al. 2020. Lancet Respir Med 2020;8(10):1000-1012

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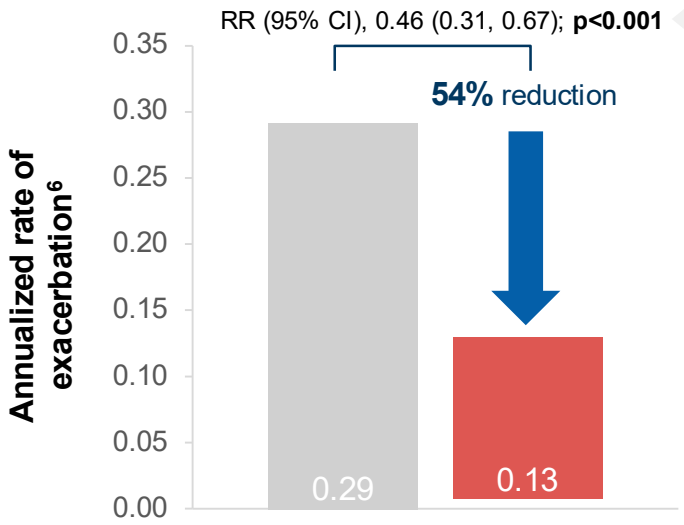
PALLADIUM

Indacaterol/Mometasone Terbukti Lebih Baik Menurunkan Angka Kekambuhan vs monoterapi ICS*



Analisis sekunder:

54%

Penurunan angka kekambuhan eksaserbasi berat dengan IND/MF dosis sedang (sekali sehari) dibandingkan MF dosis sedang (sekali sehari) selama 52 minggu†

IND/MF medium-dose (once-daily)

MF medium-dose (once-daily)

Data presented as annualized rate.

*For asthma patients ≥12 years not adequately controlled with ICS and inhaled SABA. †Secondary analysis, analyzed using a generalized linear model, not controlled for multiplicity.
The PALLADIUM trial is a 52-week randomized study in 2,216 asthma patients ≥12 years and ≤75 years, inadequately controlled on medium- or high-dose ICS and/or low-dose LABA/ICS.
Primary endpoint was met: Dual FDCssignificantly improved trough FEV_1 by +211 mL (95% CI: 167, 255) and +132 mL (95% CI: 88, 176) for medium- and high-doses respectively at Week 26 vs MF, p<0.001. Measured by trough FEV_1. Defined as the highest bronchodilator effect on FEV_1 approximately 24 hours after the last dose of each treatment period. **Key secondary endpoint**, superiority in ACQ-7 score (combined doses of Dual FDCsvs MF) at Week 26, **was met** with Dual FDCscombined doses significantly improving ACQ-7 vs MF combined doses (treatment difference was –0.209 [95% CI: –0.270, –0.149]; p<0.001). Refer to ClinicalTrials.gov for more information about other secondary analyses.
Dual FDCsmedium-dose = IND/MF 150/160 µg (once-daily); MF medium-dose = MF 400 µg (once-daily).
ACQ-7, Asthma Control Questionnaire-7; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; IND, indacaterol acetate; MF mometasone furoate; RR rate ratio; SABA, short-acting β_2-agonist.

Eksaserbasi Berat

References: Van Zyl-Smit RN, et al. Lancet Respir Med. 2020

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Triple Fixed Dose Combination

LABA/LAMA/ICS

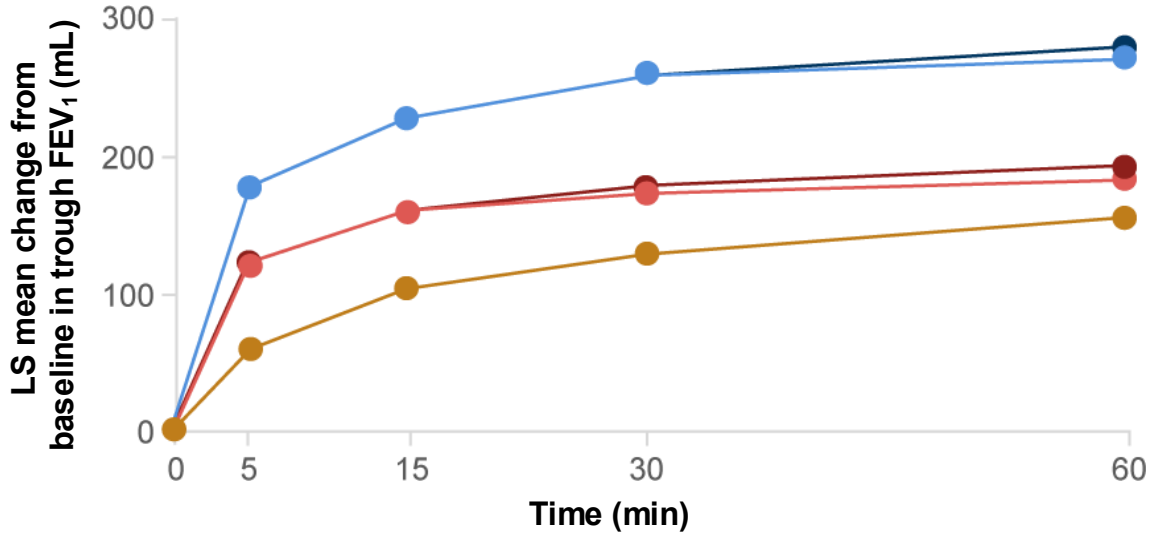
Indacaterol/Glycopyrronium/
Mometasone

NVS/BD&L/RESPI/SLID/022025/05

IRIDIUM

Indacaterol/Glycopyrronium/Mometasone Terbukti Melegakan Napas dalam 5 Menit*

Dalam analisis sekunder,† Triple FDC dosis tinggi (sekali sehari) meningkatkan fungsi paru dibandingkan SAL/FLU dosis tinggi (dua kali sehari).



Onset kerja‡,

5 menit

- IND/GLY/MF high-dose (once-daily)
- IND/GLY/MF medium-dose (once-daily)
- IND/MF high-dose (once-daily)
- IND/MF medium-dose (once-daily)
- SAL/FLU high-dose (twice-daily)

*In symptomatic asthma patients, despite treatment with medium- or high-dose LABA/ICS. †Secondary analysis, analyzed using a mixed model for repeated measures, not controlled for multiplicity. ‡As measured by FEV_1 5 minutes post-dose on Day 1.
The IRIDIUM trial is a 52-week randomized study in 3,092 asthma patients, inadequately controlled on LABA/ICS.
Primary endpoint was met: Triple FDCssignificantly improved trough FEV_1 by +76 mL (95% CI: 41, 111) and +65 mL (95% CI: 31, 99) at Week 26 vs IND/MF for medium- and high-doses respectively, p<0.001. **Key secondary endpoint,** improvement in ACQ-7 score for Triple FDCsvs IND/MF at Week 26, **was not met**; however, all 5 arms demonstrated similarly high and clinically relevant improvement from baseline. Refer to ClinicalTrials.gov for more information about other secondary analyses.
Triple FDCshigh-dose = IND/GLY/MF 150/50/160 µg (once-daily); Triple FDCsmedium-dose = IND/GLY/MF 150/50/80 µg (once-daily); IND/MF high-dose = IND/MF 150/320µg (once-daily); IND/MF medium-dose = IND/MF 160/160 µg (once-daily); SAL/FLU high-dose = SAL/FLU 50/500 µg (twice-daily).
ACQ-7, Asthma Control Questionnaire-7; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; GLY, glycopyrronium; IND, indacaterol acetate; LS, least squares; MF mometasone furoate.

Referensi: Kerstjens H, et al. 2020. Lancet Respir Med 2020;8(10):1000-1012

Onset Kerja

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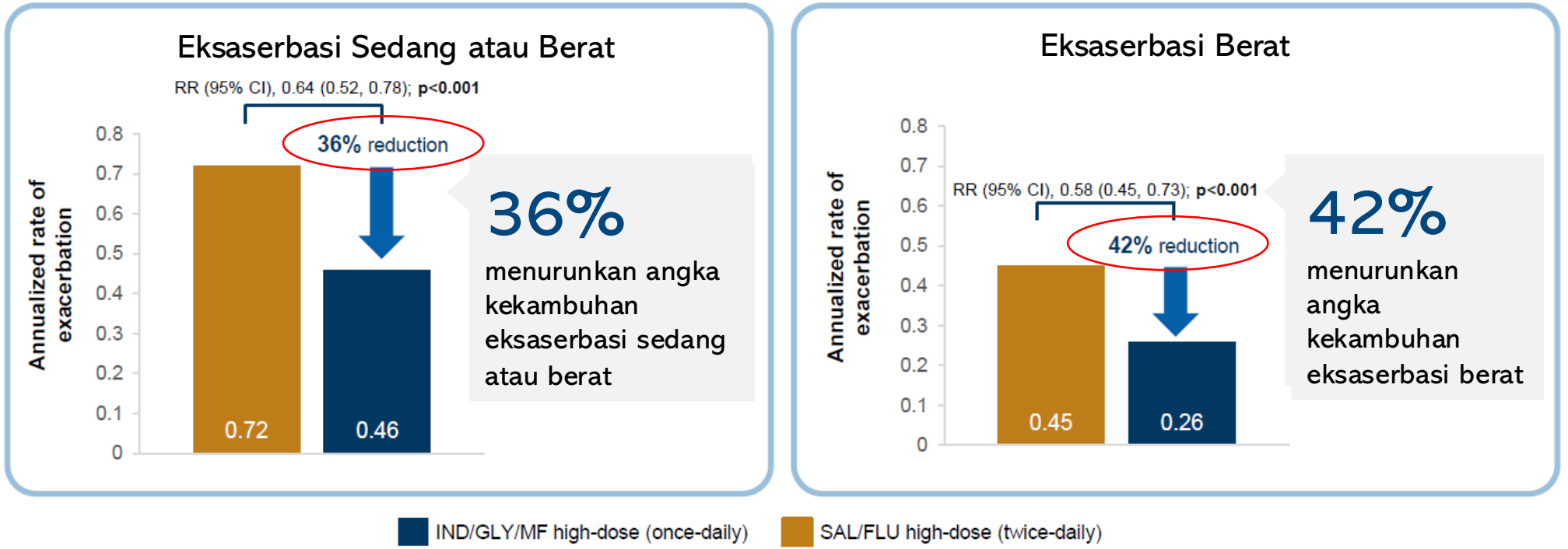
IRIDIUM

Indacaterol/Glycopyrronium/Mometasone Terbukti Lebih Baik Menurunkan Angka Kekambuhan vs LABA/ICS*

Dalam analisis sekunder,† Triple FDC dosis tinggi (sekali sehari) mengurangi kejadian eksaserbasi dibandingkan SAL/FLU dosis tinggi (dua kali sehari).



*In symptomatic asthma patients, despite treatment with medium- or high-dose LABA/ICS. †Secondary analysis, not controlled for multiplicity—analyzed using a generalized linear model assuming the negative binomial distribution.
The IRIDIUM trial is a 52-week randomized study in 3,092 asthma patients, inadequately controlled on LABA/ICS.
Primary endpoint was met: ENERZAIR® BREEZHALER® significantly improved trough FEV1 by +76 mL (95% CI: 41, 111) and +65 mL (95% CI: 31, 99) at Week 26 vs IND/MF for medium- and high-doses respectively, p<0.001.
Key secondary endpoint, improvement in ACQ-7 score for ENERZAIR® BREEZHALER® vs IND/MF at Week 26, was not met; however, all 5 arms demonstrated similarly high and clinically relevant improvement from baseline.
Refer to ClinicalTrials.gov for more information about other secondary analyses.
ENERZAIR® BREEZHALER® high-dose = IND/GLY/MF 150/50/160 µg (once-daily); SAL/FLU high-dose = SAL/FLU 50/500 µg (twice-daily).
ACQ-7, Asthma Control Questionnaire-7; CI, confidence interval; FEV1, forced expiratory volume in 1 second; GLY, glycopyrronium; IND, indacaterol acetate; MF mometasone furoate; RR rate ratio.

Referensi: Kerstjens H, et al. 2020. Lancet Respir Med 2020;8(10):1000-1012

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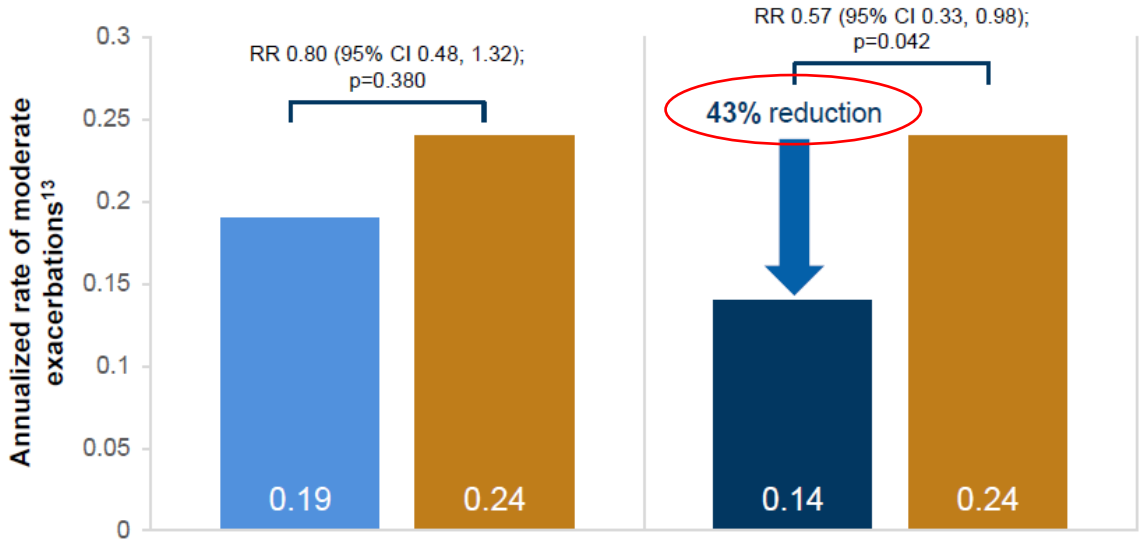
ARGON

Indacaterol/Glycopyrronium/Mometasone Terbukti Lebih Baik Menurunkan Angka Kekambuhan vs Tripel Kombinasi Terpisah*

Dalam analisis eksplorasi, Tripel FDC dosis tinggi (sekali sehari) mengurangi eksaserbasi vs Tripel Kombinasi SAL/FLU dosis tinggi + TIO (dua kali sehari)

Dosis-tinggi IND/GLY/MF secara signifikan mengurangi tingkat eksaserbasi sedang dibandingkan Tripel Kombinasi Terpisah dosis tinggi SAL/FLU + TIO selama 24 minggu. Pengurangan tingkat eksaserbasi pada semua analisis kelompok yang telah ditentukan sebelumnya sebanding antara dosis tinggi dan sedang IND/GLY/MF serta dosis tinggi SAL/FLU + TIO.



43%
menurunkan angka kekambuhan eksaserbasi sedang

- Medium-dose IND/GLY/MF
- High-dose IND/GLY/MF
- High-dose SAL/FLU + TIO

Data presented are annualized rate.

ARGON population: symptomatic despite treatment with medium/high stable dose of LABA/ICS: 80% of patients had ≥1 exacerbation requiring treatment in the past year
IND/GLY/MF doses: high dose = 150/50/160 µg QD, medium dose =150/50/80 µg QD. SAL/FLU doses: high dose = 50/500 µg BID. Tiotropium dose = 5 µg QD.

Referensi: Gessner C, et al. 2020. Respir Med 2020;170:106021

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Single and Dual Bronchodilator

LABA and LABA/LAMA

Indacaterol and Indacaterol/Glycopyrronium

PENCEGAHAN DINI TERHADAP KEJADIAN EKSASERBASI SANGAT PENTING PADA PENATALAKSANAAN PPOK[1]

Eksaserbasi berulang menyebabkan penurunan status kesehatan dan peningkatan risiko kematian[1]

1 dari 4

pasien PPOK meninggal dalam 1 tahun* setelah eksaserbasi berat pertama[1]

(Dibandingkan dengan infark miokard: 8-19%)[2†]

*Data mortalitas 1 tahun dari 102.274 pasien setelah eksaserbasi berat pertama yang memerlukan rawat inap antara tahun 1990 dan 2005 di Quebec, Kanada.[1]
†Data mortalitas 1 tahun dari 5.383 pasien setelah infark miokard yang memerlukan rawat inap antara tahun 1997 dan 2005 di Worcester, MA, AS.[2]

Referensi: 1. Suissa S, et al. Thorax 2012;67:957–963; 2. McManus DD, et al. Am J Med 2011;124:40–47

Penatalaksanaan pada PPOK

Menurut data dari WHO, sebanyak

6% kematian

di Indonesia disebabkan oleh **Penyakit Paru Obstruktif Kronis (PPOK)**[1]

Berdasarkan tatalaksana PPOK,

2/3 pasien

direkomendasikan menggunakan terapi pengobatan **LABA+LAMA**[2]

Pedoman Penatalaksanaan PPOK PDPI 2023

LABA+LAMA diberikan pada kelompok penderita PPOK di group B dan E[2]

Kelompok penderita PPOK GOLD 2023	Obat pilihan utama
A	Agonis beta-2 kerja panjang **(LABA)**, atau Antikolinergik kerja panjang **(LAMA)**
B	Kombinasi agonis beta-2 kerja panjang dan antikolinergik kerja panjang **(LABA+LAMA)***
E	Kombinasi agonis beta-2 kerja panjang dan antikolinergik kerja panjang **(LABA+LAMA)***, atau Kombinasi tripel agonis beta-2 kerja panjang dan Antikolinergik kerja panjang dan kortikosteroid inhalasi **(LABA+LAMA+ICS)***§

*Pemberian melalui inhaler tunggal direkomendasikan dibandingkan dengan inhaler multipel karena lebih nyaman dan efektif
§ Pertimbangan pemberian tripel terapi jika kadar eos 300 sel/µL

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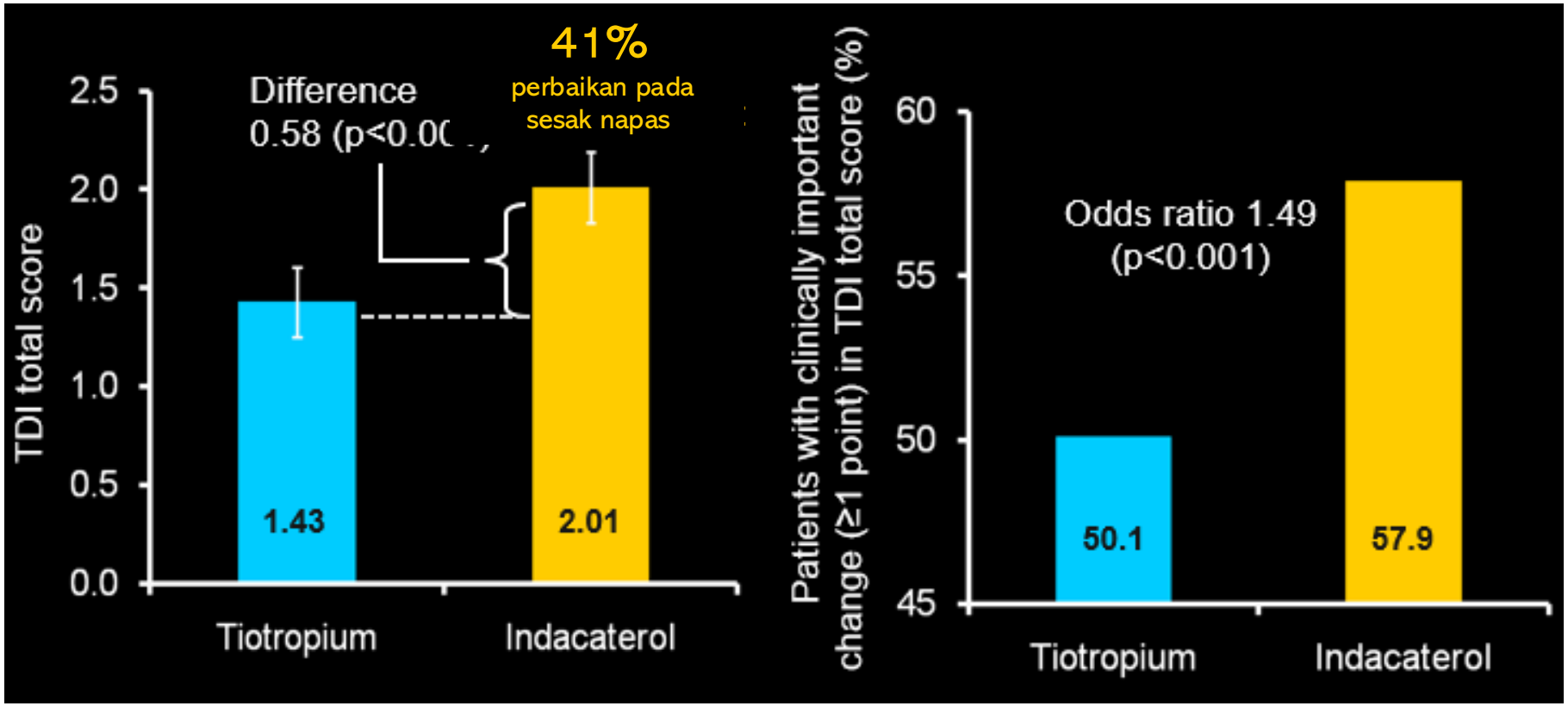
References : 1. Finansialku, detik health, WHO, naskah publikasi farmasi Universitas Muhammadiyah Surakarta 2013; 2. Penatalaksanaan PPOK, PDPI 2023

Indacaterol Terbukti Lebih Baik Mengurangi Gejala Sesak Napas Pada Pasien PPOK vs Tiotropium



TDI : Transition Dyspnea Index
MCID : Minimal Clinically Important Differences

Referensi: Buhl, R. et al., 2011. Eur Respir J 2011; 38: 797–803

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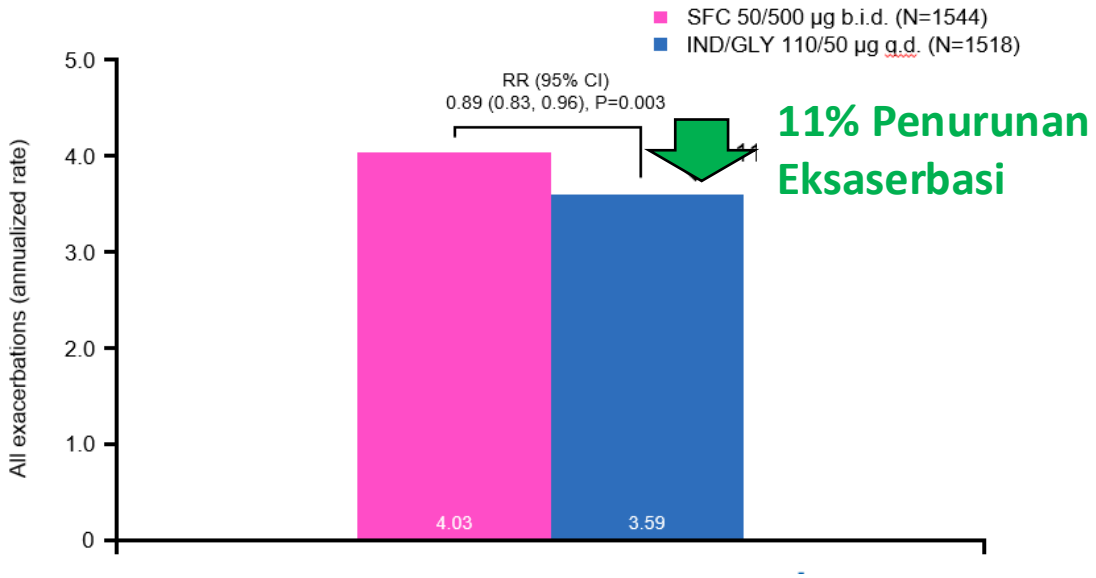
FLAME

Indacaterol Inside

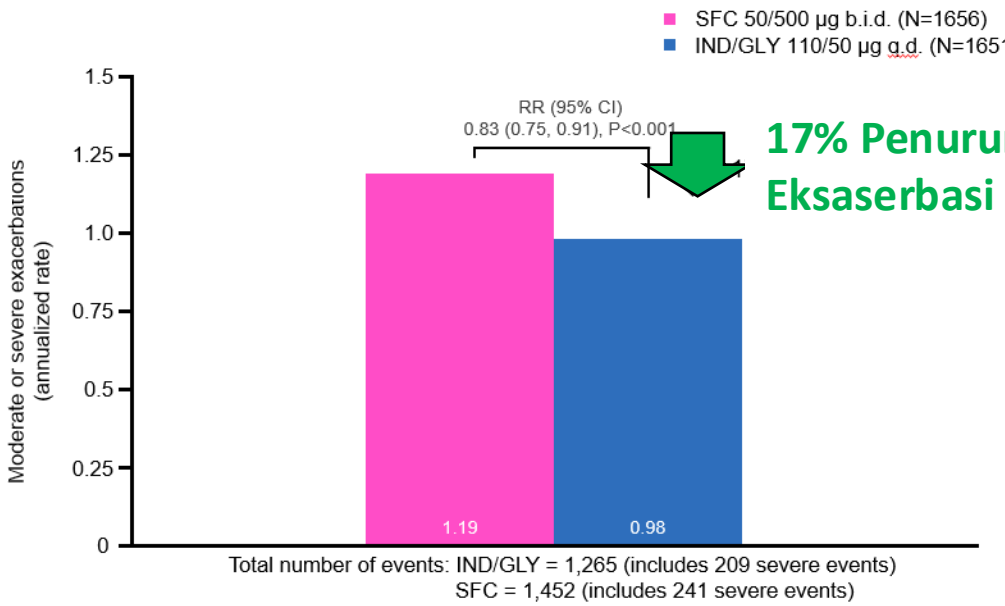
Pergantian Langsung (*Direct Switching*) dari LABA/ICS ke Indacaterol/Glycopyrronium menurunkan angka kekambuhan pada pasien PPOK

IND/GLY secara signifikan mengurangi tingkat semua eksaserbasi vs SAL/FLU selama 52 minggu.



11% Penurunan Eksaserbasi

IND/GLY secara signifikan mengurangi eksaserbasi sedang atau berat vs SAL/FLU selama 52 minggu.



17% Penurunan Eksaserbasi

NVS/BD&L/RESPI/SLID/022025/05

Referensi: Wedzicha JA, et al; FLAME Investigators. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. N Engl J Med. 2016 Jun 9;374(23):2222-34

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Kesimpulan

- Kombinasi dosis tetap membantu dokter memaksimalkan potensi terapi inhalasi pada pasien asma & PPOK
- Terapi kombinasi telah menunjukkan: Perbaikan pada fungsi paru dengan memberikan kelegaan pada saat bernapas, Mengurangi kejadian eksaserbasi asma & PPOK, Memperbaiki kontrol asma & PPOK serta meningkatkan kualitas hidup dengan mengurangi gejala asma & PPOK

Perbandingan LABA/ICS

Molekul	ATECTURA	FOR/BUD	SAL/FLU	FOR/BPD
Onset[1]	~ 5 menit	~ 7 menit	~ 15 menit	~ 7 menit
Dosis[1]	1x sehari	2x sehari	2x sehari	2x sehari
Penurunan Eksaserbasi	++++[2]	++[3]	+++[4]	NS

Perbandingan brondkodilator tunggal

Molekul	ONBREZ	Tiotropium
Onset	~ 5 menit[1]	~ 30 menit[7]
Dosis	1x sehari	1x sehari 2 puff[7]
Perbaikan sesak napas[6]	57,9%	50,1%

Perbandingan Tripel Terapi

Molekul	ENERZAIR	VI/UMEC/FF
Onset[1]	~ 5 menit	~ 5 menit
Dosis[1]	1x sehari	1x sehari
Penurunan Eksaserbasi[5]	Signifikan	NS

Perbandingan dual bronkodilator

Molekul	ULTIBRO	OLO/TIO
Onset	~ 5 menit[1]	~ 30 menit[7]
Dosis	1x sehari[1]	1x sehari 2 puff[7]
Perbaikan sesak napas* (Nilai FEV_1)	136 ml[8]	117 ml[9]

Referensi: 1. Billington CK, et al. Handb Exp Pharmacol. 2017;237:23–40; 2. Van Zyl-Smit R, et al. Lancet Respir Med 2020;8(10):987-999; 3. Peters SP, et al. N Engl J Med 2016; 375:850-60; 4. Stempel DA, et al. N Engl J Med 2016;374:1822-30; 5. Kerstjens H, et al. 2020. Lancet Respir Med 2020;8(10):1000-1012; 6. Product Information Onbrez BPOM Approval 11 Maret 2022; 7. Koumis T, et al. Clin Ther 2005;27(4):377-92; 8. Bateman ED, et al. Eur Respir J. 2013;42(6):1484-1494; 9. Beeh KM, et al. Pulm Pharmacol Ther 2015;32:53–59

NVS/BD&L/RESPI/SLID/022025/05

Respiratory Breezhaler Portfolio

Once Daily, Once Inhalation, One Inhaler

Indacaterol Inside
Fast onset · Once daily · Controllable
Onbrez Ultibro Atectura Enerzair

ASTHMA

LABA/ICS

ONCE DAILY ATECTURA breezhaler
Indacaterol acetate / mometasone furoate inhalation powder

150/80 mcg,
150/160 mcg or
150/320 mcg
Once Daily

LABA/LAMA/ICS

ONCE DAILY ENERZAIR breezhaler
Indacaterol acetate / glycopyrronium bromide / mometasone furoate inhalation powder

150/50/160 mcg
Once Daily

COPD

LABA

Once Daily onbrez breezhaler
indacaterol inhalation powder

150 mcg or
300 mcg
Once Daily

LABA/LAMA

ONCE DAILY ultibro breezhaler
indacaterol maleate / glycopyrronium bromide inhalation powder

110/50 mcg
Once Daily

Untuk informasi lebih lanjut, mohon membaca Informasi Produk yang dapat diakses pada QR Code terlampir.

Atectura PI

Enerzair PI

Onbrez PI

Ultibro PI

NVS/BD&L/RESPI/SLID/022025/05

NOVARTIS

For healthcare professionals only

Wellesta cpi
A HEALTHCARE COMPANY

Atectura® Breezhaler® Product Information

Important note: Before prescribing, consult full prescribing information.Presentation: Inhalation powder hard capsules containing indacaterol 150 micrograms and mometasone furoate 80 or 160 or 320 micrograms respectively. Indications: Atectura Breezhaler is indicated as a once-daily maintenance treatment of asthma in adults and adolescents 12 – 75 years of age where use of a combination of long-acting beta2-agonist and inhaled corticosteroid is appropriate: •patients not adequately controlled with inhaled corticosteroids, or •patients not adequately controlled with long-acting beta2-agonist and low dose of inhaled corticosteroids (for Atectura Breezhaler 150/160 and 150/320 micrograms). Dosage regimen and administration:General target population Inhalation of the content of one capsule of Atectura Breezhaler 150/80 micrograms once daily is recommended in patients who require a combination of a long-acting beta2-agonist and a low dose of inhaled corticosteroid. Inhalation of the content of one capsule of Atectura Breezhaler 150/160 micrograms or 150/320 micrograms once-daily is recommended in patients who require a combination of a long-acting beta2-agonist and a medium or high dose of inhaled corticosteroid. Patients usually experience an improvement in lung function within 5 minutes of inhaling Atectura Breezhaler. However, the patient should be informed that regular daily use is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. The maximum recommended dose is Atectura Breezhaler 150/320 micrograms once daily. Special populations Renal impairment No dose adjustment is required in patients with renal impairment. Hepatic impairment No dose adjustment is required in patients with mild or moderate hepatic impairment. No data are available for Atectura Breezhaler in subjects with severe hepatic impairment, therefore Atectura Breezhaler should be used in these patients only if the expected benefit outweighs the potential risk (see section 12 Clinical pharmacology). Pediatric patients (below 12 years) Atectura Breezhaler may be used in pediatric patients (12 years of age and older) at the same posology as in adults. The safety and efficacy of Atectura Breezhaler in pediatric patients below 12 years of age have not been established. Geriatric patients (65 years or above) No dose adjustment is required in elderly patients 65 years of age or older (see section 12 Clinical pharmacology). Method of administration For inhalation use only. Atectura Breezhaler capsules must not be swallowed.Patients should be instructed on how to administer the medicinal product correctly. Patients who do not experience improvement in breathing should be asked if they are swallowing the capsule rather than inhaling it. The capsules must be administered only using the Atectura Breezhaler inhaler. The inhaler provided with each new prescription should be used. Atectura Breezhaler should be administered at the same time of the day each day. It can be administered irrespective of the time of the day. The capsules must always be stored in the blister to protect from moisture and light, and only removed immediately before use (see section 15 Pharmaceutical information). After inhalation, patients should rinse their mouth with water without swallowing. If a dose is missed, it should be taken as soon as possible. Patients should be instructed not to take more than one dose in a day. Contraindications: ♦Hypersensitivity to any of the active substances or excipients. Warnings and precautions: ♦Acute asthma: Should not be used to treat acute asthma including acute bronchospasm. A short acting bronchodilator should be used. ♦Hypersensitivity: If hypersensitivity reaction occurs, Atectura Breezhaler should be discontinued immediately and alternative therapy instituted. ♦Paradoxical bronchospasm: As with other inhalation therapy, administration may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, Atectura Breezhaler should be discontinued immediately and alternative therapy instituted. ♦Cardiovascular effects: Like other medicinal products containing beta2-adrenergic agonists, may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. Should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension, known or suspected prolongation of the QT interval), convulsive disorders, thyrotoxicosis, or in patients who are unusually responsive to beta2-adrenergic agonists. ♦Hypokalemia: Beta2-adrenergic agonists may produce significant hypokalemia in some patients, which has the potential to produce adverse cardiovascular effects. In patients with severe condition, hypokalemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias ♦Hyperglycemia: Inhalation of high dose of beta2-adrenergic agonist may produce increase in plasma glucose. Upon initiation of treatment with Atectura Breezhaler, plasma glucose should be monitored more closely in diabetic patients. ♦Systemic effects of corticosteroids: Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Should be administered with caution in patients with pulmonary tuberculosis or in patients with chronic or untreated infections. Pregnancy: Should only be used if the expected benefit to the patient justifies the potential risk to the fetus. Lactation: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Atectura Breezhaler or from the underlying maternal condition. Labor and delivery: Like other medicinal products containing beta2-adrenergic agonist, indacaterol may inhibit labor due to a relaxant effect on uterine smooth muscle. Adverse reactions: ♦Very common (≥1/10): nasopharyngitis, asthma (exacerbation). ♦Common (≥1/100 to <1/10): Upper respiratory tract infection, hypersensitivity, headache, oropharyngeal pain, dysphonia, musculoskeletal pain. ♦Uncommon (≥1/1,000 to <1/100): candidiasis, angioedema, hyperglycaemia, vision blurred, cataract, tachycardia, rash, pruritus, muscle spasms. Interactions: ♦Beta-adrenergic blockers: Should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use ♦Medicinal products prolong QTc interval: Should be administered with caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QT-interval. ♦Hypokalemic treatment: Concomitant treatment with methylxanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate the possible hypokalemic effect of beta2-adrenergic agonists. ♦CYP3A4 and P-glycoprotein inhibitors: Inhibition of CYP3A4 and P-gp has no impact on the safety of therapeutic doses of Atectura Breezhaler. ♦Other long acting beta2-adrenergic agonists: Co-administration with other medicinal products containing long-acting beta2-adrenergic agonists is not recommended. Packs and prices: Atectura Breezhaler 150/80 mcg Box, 3 blisters @ 10 capsules + 1 inhaler Reg. No. DKI2297301467A1 Atectura Breezhaler 150/160 mcg Box, 3 blisters @ 10 capsules + 1 inhaler Reg. No. DKI2297301467B1 Atectura Breezhaler 150/320 mcg Box, 3 blisters @ 10 capsules + 1 inhaler Reg. No. DKI2297301467C1 ON MEDICAL PRESCRIPTION ONLY HARUS DENGAN RESEP DOKTER

Enerzair® Breezhaler® Product Information

Important note: Before prescribing, consult full prescribing information. Presentation: Inhalation powder hard capsules containing indacaterol 150 micrograms, glycopyrronium 50 micrograms and mometasone furoate 160 micrograms respectively. Indications: ENERZAIR BREEZHALER (indacaterol / glycopyrronium / mometasone furoate) is indicated as a maintenance treatment of asthma in adult patients not adequately controlled with a maintenance combination of a long-acting beta2-agonist and a medium or high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous 12 months. ENERZAIR BREEZHALER is not indicated for the relief of acute bronchospasm. Dosage and administration: Dosage regimen General target population Inhalation of the content of one capsule of Enerzair Breezhaler 150/50/160 micrograms once-daily is recommended in adult patients not adequately controlled with a maintenance combination of a long acting beta2-agonist and a medium dose or high dose of an inhaled corticosteroid who experienced one or more asthma exacerbations in the previous 12 months. The recommended dose is one capsule to be inhaled once daily. The maximum recommended dose is Enerzair Breezhaler 150/50/160 micrograms once daily. Special populations Renal impairment No dose adjustment is required in patients with mild to moderate renal impairment. In patients with severe renal impairment or end-stage renal disease requiring dialysis, Enerzair Breezhaler should be used only if the expected benefit outweighs the potential risk (see sections 6 Warnings and precautions and 11 Clinical pharmacology). Hepatic impairment No dose adjustment is required in patients with mild or moderate hepatic impairment. No data are available for Enerzair Breezhaler in subjects with severe hepatic impairment, therefore Enerzair Breezhaler should be used in these patients only if the expected benefit outweighs the potential risk (see section 11 Clinical pharmacology). Pediatric patients (below 18 years) The safety and efficacy of Enerzair Breezhaler in pediatric patients below 18 years of age have not been established. Geriatric patients (65 years or above) No dose adjustment is required in elderly patients 65 years of age or older (see section 11 Clinical pharmacology). Method of administration For inhalation use only. Enerzair Breezhaler capsules must not be swallowed.Patients should be instructed on how to administer the medicinal product correctly. Patients who do not experience improvement in breathing should be asked if they are swallowing the capsule rather than inhaling it. The capsules must be administered only using the Enerzair Breezhaler inhaler. The inhaler provided with each new prescription should be used. Enerzair Breezhaler should be administered at the same time of the day each day. It can be administered irrespective of the time of the day. The capsules must always be stored in the blister to protect from moisture and light, and only removed immediately before use (see section 14 Pharmaceutical information). After inhalation, patients should rinse their mouth with water without swallowing. If a dose is missed, it should be taken as soon as possible. Patients should be instructed not to take more than one dose in a day. Contraindications: ♦Hypersensitivity to any of the active substances or excipients. Warnings and precautions: ♦Acute asthma: Should not be used to treat acute asthma including acute bronchospasm. A short acting bronchodilator should be used. ♦Hypersensitivity: If hypersensitivity reaction occurs, Enerzair Breezhaler should be discontinued immediately and alternative therapy instituted. ♦Paradoxical bronchospasm: As with other inhalation therapy, administration may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, Enerzair Breezhaler should be discontinued immediately and alternative therapy instituted. ♦Cardiovascular effects: Like other beta2-adrenergic agonists, may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. Should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension, known or suspected prolongation of the QT interval), convulsive disorders, thyrotoxicosis, or in patients who are unusually responsive to beta2-adrenergic agonists. ♦Hypokalemia: Beta2-adrenergic agonists may produce significant hypokalemia in some patients, which has the potential to produce adverse cardiovascular effects. In patients with severe condition, hypokalemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. ♦Hyperglycemia: Inhalation of high doses of beta2-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Enerzair Breezhaler, plasma glucose should be monitored more closely in diabetic patients. ♦Anticholinergic effects: Use with caution in patients with narrow-angle glaucoma and urinary retention. ♦Patients with severe renal impairment: To be used only if expected benefit outweighs potential risk in patients with severe renal impairment including end-stage renal disease requiring dialysis. ♦Systemic effects of corticosteroids: Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Should be administered with caution in patients with pulmonary tuberculosis or in patients with chronic or untreated infections. Pregnancy: Should only be used if the expected benefit to the patient justifies the potential risk to the fetus. Lactation: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Enerzair Breezhaler and any potential adverse effects on the breast-fed child from Enerzair Breezhaler or from the underlying maternal condition. Labor and delivery: Like other medicinal products containing beta2-adrenergic agonists, indacaterol may inhibit labor due to a relaxant effect on uterine smooth muscle. Adverse drug reactions: ♦Very common (≥1/10): nasopharyngitis, asthma (exacerbation). ♦Common (≥1/100 to <1/10): upper respiratory tract infection, candidiasis, urinary tract infection, hypersensitivity, headache, tachycardia, oropharyngeal pain, cough, dysphonia, gastroenteritis, musculoskeletal pain, muscle spasms, pyrexia. ♦Uncommon (≥1/1,000 to <1/100): hyperglycaemia, cataract, dry mouth, rash, pruritus, dysuria. Interactions: ♦Beta-adrenergic blockers: Should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use. ♦Medicinal products prolong QTc interval: Should be administered with caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QT-interval. ♦Hypokalemic treatment: Concomitant treatment with methylxanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate the possible hypokalemic effect of beta2-adrenergic agonists. ♦CYP3A4 and P-glycoprotein inhibitors: Inhibition of CYP3A4 and P-gp has no impact on the safety of therapeutic doses of Enerzair Breezhaler. ♦Other long acting antimuscarinics and long acting beta2-adrenergic agonists: Co-administration with other medicinal products containing long-acting muscarinic antagonists or long-acting beta2-adrenergic agonists is not recommended. ♦Cimetidine or other inhibitors of the organic cation transport: No clinically relevant drug interaction is expected. Packs: Box, 3 blisters @ 10 capsules + 1 inhaler Reg. No. DKI2297301367A1 ON MEDICAL PRESCRIPTION ONLY HARUS DENGAN RESEP DOKTER

Onbrez® Breezhaler® Product Information

Important note: Before prescribing, consult full prescribing information. Presentation: Inhalation powder hard capsules containing indacaterol maleate equivalent to 150 microgram (mcg) indacaterol; inhalation powder hard capsules containing indacaterol maleate equivalent to 300 mcg indacaterol. Indications: ONBREZ BREEZHALER is indicated for maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). Dosage:Adults: The recommended dosage of ONBREZ BREEZHALER is the once-daily inhalation of the content of one 150 microgram capsule using the ONBREZ BREEZHALER inhaler. The dosage should only be increased on medical advice. Once-daily inhalation of the content of one 300 microgram capsule, using the ONBREZ BREEZHALER inhaler, has been shown to provide additional clinical benefit to some patients, e.g. with regard to breathlessness, particularly for patients with severe COPD. The maximum dose is 300 microgram once-daily. Children (<18 years): should not be used in patients under 18 years of age. Special patients population: No dosage adjustment is required for geriatric patients, patients with mild and moderate hepatic impairment, or renally impaired patients. No data is available for subjects with severe hepatic impairment (see section Clinical Pharmacology). Method of administration ONBREZ BREEZHALER capsules must be administered only by the oral inhalation route and only using the ONBREZ BREEZHALER inhaler. Capsules must not be swallowed. ONBREZ BREEZHALER should be administered at the same time of the day each day. If a dose is missed, the next dose should be taken at the usual time the next day. Capsules must always be stored in the blister, and only removed immediately before use. Patients should be instructed on how to administer the product correctly. Patients who do not experience improvement in breathing should be asked if they are swallowing the medicine rather than inhaling it. Contraindications: ♦Known hypersensitivity to indacaterol or to any of the excipients. Warnings/Precautions: ♦Asthma: should not be used in asthma. Long-acting beta2-adrenergic agonists may increase the risk of asthma-related serious adverse events, including asthma-related deaths, when used for the treatment of asthma ♦Paradoxical bronchospasm: as with other inhalation therapy, administration may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, ONBREZ BREEZHALER should be discontinued immediately and alternative therapy instituted ♦Hypersensitivity: If hypersensitivity reaction occurs, ONBREZ BREEZHALER should be discontinued immediately and alternative therapy instituted ♦Deterioration of disease: in case of deterioration of COPD whilst on treatment, a re-evaluation of the patient and COPD treatment regimen should be undertaken ♦Systemic effects: as with other beta2-adrenergic agonists, should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension, known or suspected prolongation of QT interval); in patients with convulsive disorders or thyrotoxicosis; in patients who are unusually responsive to beta2-adrenergic agonists ♦Cardiovascular effects: like other beta2-adrenergic agonists, may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes ♦Hypokalemia: beta2-adrenergic agonists may produce significant hypokalemia in some patients, which has the potential to produce adverse cardiovascular effects. In patients with severe COPD, hypokalemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias ♦Hyperglycemia: clinically notable changes in blood glucose and/or serum potassium were generally more frequent by 1 to 2% during clinical studies at the recommended doses than on placebo ♦should not be used in conjunction with other long-acting beta2-adrenergic agonists or medications containing long-acting beta2-adrenergic agonists. Pregnancy: should be used during pregnancy only if the expected benefit justifies the potential risk to the foetus. Breast-feeding: should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. Fertility: reproduction studies or other data in animals did not reveal a problem or potential problem concerning fertility in either males or females. Interactions: ♦should be administered with caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QT-interval ♦concomitant administration of other sympathomimetic agents may potentiate the undesirable effects ♦concomitant treatment with methylxanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate the possible hypokalemic effect of beta2-adrenergic agonists ♦should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use ♦inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, has no impact on safety of therapeutic doses. Adverse reactions: ♦Uncommon (0.1 to 1%) and potentially serious: hypersensitivity, paradoxical bronchospasm. ♦Very common (>10%): nasopharyngitis, upper respiratory tract infection. ♦Common (1 to 10%): headache, dizziness, cough, muscle spasm, oropharyngeal pain incl. throat irritation, sinusitis, peripheral edema, ischemic heart disease, palpitations, diabetes and hyperglycemia, rhinorrhea, musculoskeletal pain, chest pain, pruritus/rash. ♦Uncommon (0.1 to 1%): atrial fibrillation, tachycardia, paresthesia, myalgia. Packs Onbrez Breezhaler 150 mcg: Box, 3 blisters @ 10 capsules + 1 inhaler; Reg. No.: DKI2097300967A1 Onbrez Breezhaler 300 mcg: Box, 3 blisters @ 10 capsules + 1 inhaler; Reg. No.: DKI2097300967B1 Shelf-life The expiry date is indicated on the packaging HARUS DENGAN RESEP DOKTER

Ultibro® Breezhaler® Product Information

Important note: Before prescribing, consult full prescribing information. Presentation: Inhalation powder hard capsules containing indacaterol maleate equivalent to 110 microgram (mcg) indacaterol and glycopyrronium bromide equivalent to 50 microgram glycopyrronium. Indications: ULTIBRO BREEZHALER is indicated as once-daily maintenance bronchodilator treatment to relieve symptoms and reduce exacerbations in patients with moderate to very severe chronic obstructive pulmonary disease (COPD) who are still symptomatic despite treatment with indacaterol alone or glycopyrronium alone or the combination of salmeterol/fluticasone. ULTIBRO BREEZHALER is indicated as once-daily maintenance bronchodilator treatment to relieve symptoms in patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are still symptomatic despite treatment with tiotropium alone. Dosage and administration: General target population The recommended dosage of ULTIBRO BREEZHALER is the once-daily inhalation of the content of one 110/50 microgram capsule using the ULTIBRO BREEZHALER inhaler. Special populations Renal impairment: ULTIBRO BREEZHALER can be used at the recommended dose in patients with mild to moderate renal impairment. In patients with severe renal impairment or end-stage renal disease requiring dialysis ULTIBRO BREEZHALER should be used only if the expected benefit outweighs the potential risk. See also sections Warnings and precautions and Clinical pharmacology. Hepatic impairment: ULTIBRO BREEZHALER can be used at the recommended dose in patients with mild and moderate hepatic impairment. No data are available for subjects with severe hepatic impairment. See also section Clinical pharmacology. Pediatric patients (below 18 years): ULTIBRO BREEZHALER should not be used in patients under 18 years of age. Geriatric patients (75 years or above): ULTIBRO BREEZHALER can be used at the recommended dose in elderly patients 75 years of age and older. Method of administration ULTIBRO BREEZHALER capsules must be administered only by the oral inhalation route and only using the ULTIBRO BREEZHALER inhaler. ULTIBRO BREEZHALER capsules must not be swallowed (see also section Overdosage). ULTIBRO BREEZHALER should be administered at the same time of the day each day. If a dose is missed, it should be taken as soon as possible. Patients should be instructed not to take more than one dose in a day. ULTIBRO BREEZHALER capsules must always be stored in the blister to protect from moisture, and only removed IMMEDIATELY BEFORE USE (see also section Pharmaceutical information). When prescribing ULTIBRO BREEZHALER patients should be instructed on correct use of the inhaler. Patients who do not experience improvement in breathing should be asked if they are swallowing the medicine rather than inhaling it. Contraindications: ♦Hypersensitivity to indacaterol or glycopyrronium, which are components of ULTIBRO BREEZHALER, or to any of the excipients. Warnings and precautions: Serious Warnings and Precautions WARNING: ASTHMA RELATED DEATH Long-acting beta2-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large placebo controlled US study that compared the safety of another LABA (salmeterol) or placebo added to patients' usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including indacaterol maleate, one of the active ingredients of ULTIBRO BREEZHALER. ULTIBRO BREEZHALER is only indicated for COPD. The safety and efficacy of ULTIRBO BREEZHALER in patients with asthma have not been established. ULTIBRO BREEZHALER is not indicated for the treatment of asthma. ♦ULTIBRO BREEZHALER should not be administered concomitantly with other long-acting beta-agonists or long-acting muscarinic-antagonists. ♦asthma: should not be used in asthma, long-acting beta2-adrenergic agonists may increase the risk of asthma-related serious adverse events, including asthma-related deaths, when used for treatment of asthma. ♦not for acute use: should not be used as rescue therapy. ♦hypersensitivity: If hypersensitivity reaction occurs, ULTIBRO BREEZHALER should be discontinued immediately and alternative therapy instituted. ♦paradoxical bronchospasm: as with other inhalation therapy, administration may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, ULTIBRO BREEZHALER should be discontinued immediately and alternative therapy instituted. ♦anticholinergic effects related to glycopyrronium: use with caution in patients with narrow-angle glaucoma and urinary retention. ♦systemic effects of beta-agonists: as with other beta2-adrenergic agonists, should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension, known or suspected prolongation of the QT interval); in patients with convulsive disorders or thyrotoxicosis; in patients who are unusually responsive to beta2-adrenergic agonists. ♦patients with severe renal impairment: to be used only if expected benefit outweighs potential risk in patients with severe renal impairment including end-stage renal disease requiring dialysis. ♦cardiovascular effects of beta-agonists: like other beta2-adrenergic agonists, may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. ♦hypokalemia with beta-agonists: beta2-adrenergic agonists may produce significant hypokalemia in some patients, which has the potential to produce adverse cardiovascular effects. In patients with severe COPD, hypokalemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. ♦hyperglycemia with beta agonists: During long-term clinical studies ([ENLIGHTEN] and [RADIATE]), more patients on ULTIBRO BREEZHALER experienced clinically notable changes in blood glucose (4.9%) than on placebo (2.7%). ULTIBRO BREEZHALER has not been investigated in patients for whom diabetes mellitus is not well controlled. Pregnancy: should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus. Lactation: should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. Infertility: reproduction studies or other data in animals did not reveal a problem or potential problem concerning fertility in either males or females. Labor and delivery: Information related to indacaterol - Like other beta2-adrenergic agonist containing drugs, Indacaterol may inhibit labor due to a relaxant effect on uterine smooth muscle. ♦Information related to glycopyrronium: In pregnant women undergoing Caesarean section, 86 minutes after a single intramuscular injection of 0.006 mg/kg glycopyrronium bromide, the concentration of glycopyrronium in the umbilical venous (0.28 (0.25) ng/mL) and in the umbilical arterial (0.18 (0.11) ng/mL) plasma were low (clinically insignificant) Interactions: ♦No specific drug-drug interaction studies were conducted with ULTIBRO BREEZHALER. Information on the potential for interactions is based on the potential for each of its two components. ♦should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use. ♦should be administered with caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QT-interval. Drugs known to prolong the QT-interval may increase the risk of ventricular arrhythmia. ♦concomitant administration of other sympathomimetic agents may potentiate the undesirable effects. ♦concomitant treatment with methylxanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate the possible hypokalemic effect of beta2-adrenergic agonists. ♦inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, has no impact on safety of therapeutic doses. ♦co administration with other inhaled anticholinergic-containing drugs has not been studied and is therefore not recommended. ♦no clinically relevant drug interaction is expected when glycopyrronium is co-administered with cimetidine or other inhibitors of the organic cation transport. Adverse drug reactions: ♦Common (≥1% to <10%) and potentially serious: Hyperglycemia and diabetes mellitus, hypersensitivity ♦Uncommon (≥0.1% to <1%) and potentially serious: Glaucoma, ischemic heart disease, atrial fibrillation, paradoxical bronchospasm ♦Very common (≥10%): Upper respiratory tract infection ♦Common (≥1% to <10%): Nasopharyngitis, urinary tract infection, sinusitis, rhinitis, dizziness, headache, cough, oropharyngeal pain including throat irritation, dyspepsia, dental caries, pyrexia, chest pain, bladder obstruction including urinary retention ♦Uncommon (≥0.1% to <1%): Musculoskeletal pain, insomnia, tachycardia, palpitations, epistaxis, dry mouth, pruritus/rash, muscle spasm, myalgia, peripheral edema, fatigue, gastroenteritis, pain in extremity. ♦Rare (≥0.01% to <0.1%): Paresthesia Not known: Angioedema, dysphonia. Packaging size Box, 3 blister @ 10 capsules + 1 inhaler, No. Reg. DKI1897300767A1 Shelf life: the expiry date is indicated on the packaging ON MEDICAL PRESCRIPTION ONLY HARUS DENGAN RESEP DOKTER

For further information consult full prescribing information

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