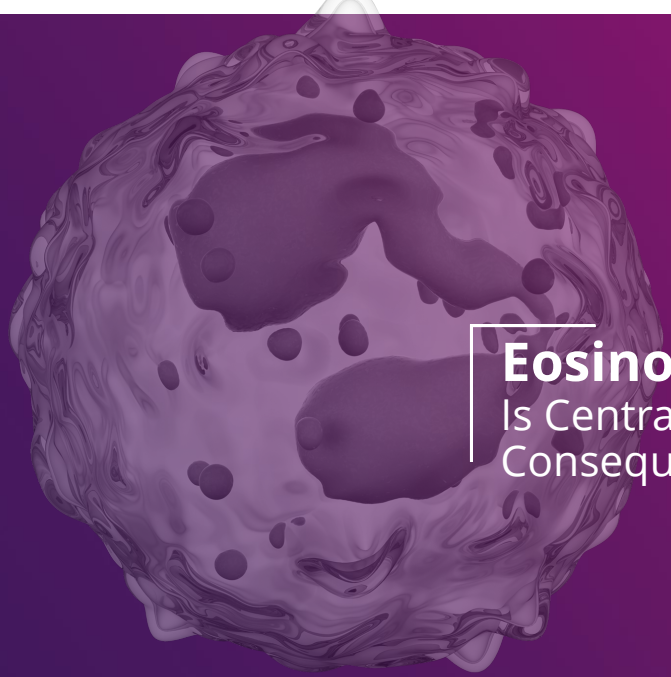


Eosinophilic Inflammation

Is Central to the Key Pathological Features and Clinical Consequences of Severe Eosinophilic Asthma

Developed by AstraZeneca for health care professionals

ID:NO-13874-03-2025-FA

AstraZeneca

Eosinophil Recruitment and Activation in Severe Eosinophilic Asthma[1]

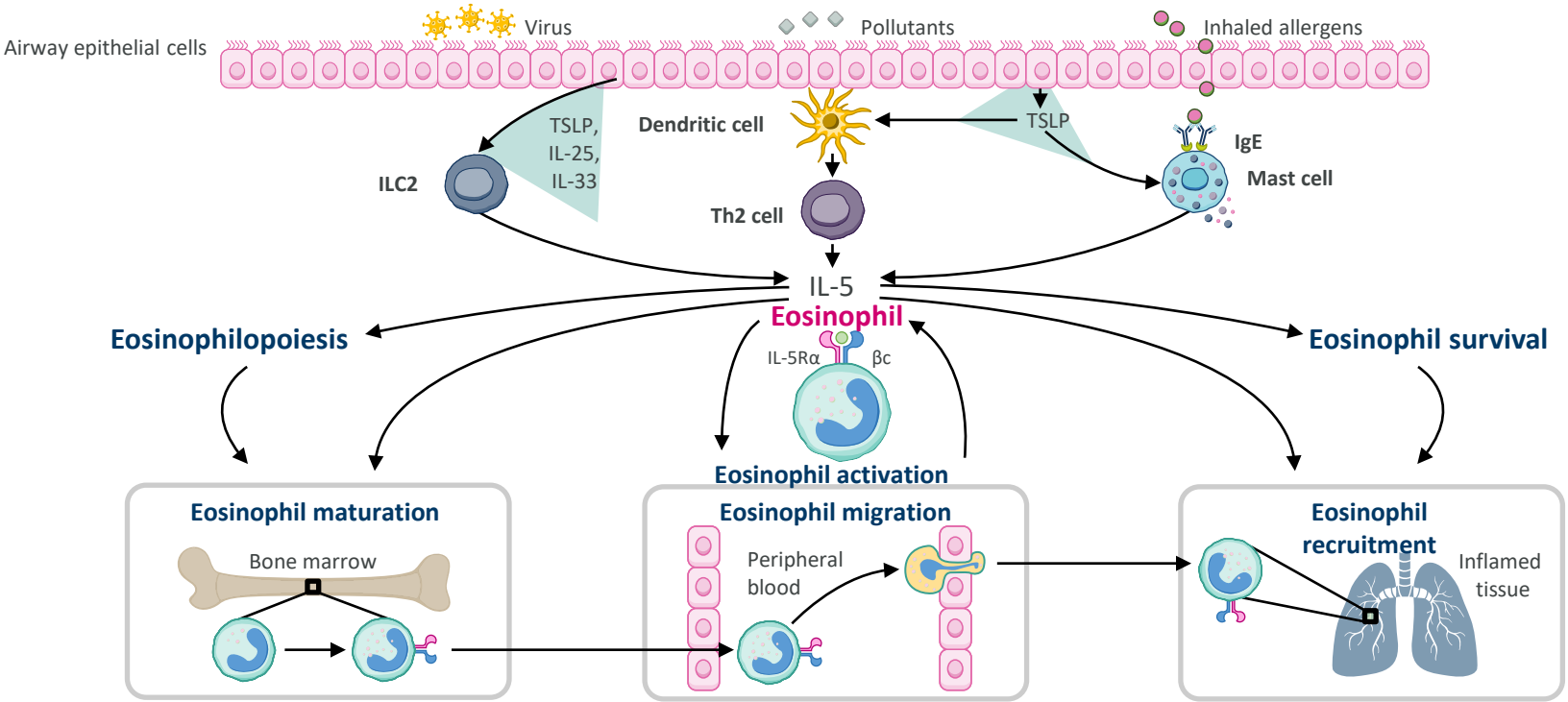


Illustration from figure 1 in Pelaia et al

IgE = Immunoglobulin E; IL = interleukin; ILC2 = Type 2 innate lymphoid cell; IL-5Rα = interleukin-5 receptor alpha; Th2 = T helper 2; TSLP = thymic stromal lymphopoietin.

1. Pelaia C, Paoletti G, Puggioni F et al. Interleukin-5 in the Pathophysiology of Severe Asthma Front Physiol. 2019;10:1514.

Mechanisms of action of biological drugs targeting IL-5 or its receptor.

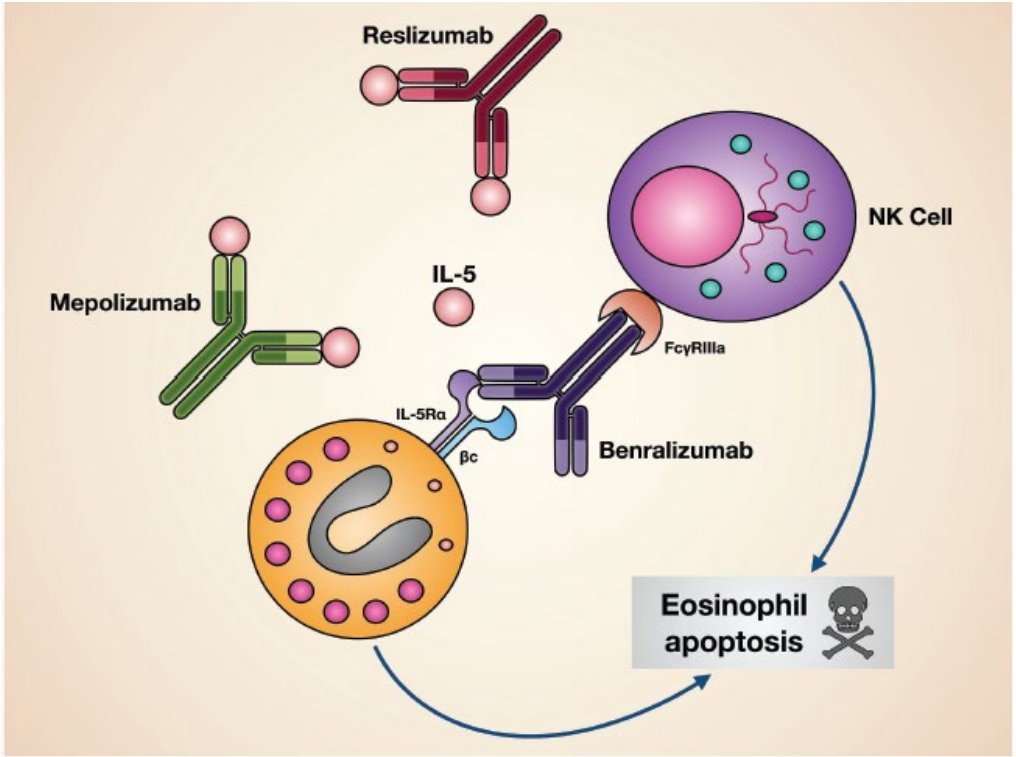
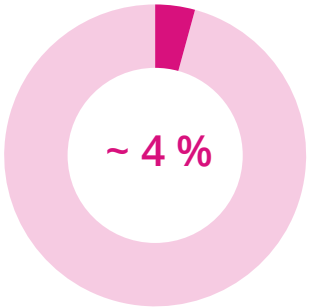


Illustration from figure 3 in Pelaia et al

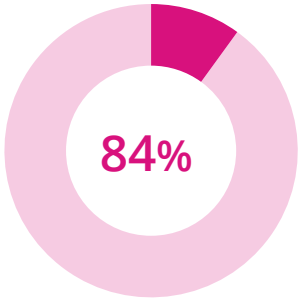
Mepolizumab and reslizumab interact with IL-5, thus *inhibiting* its biological effects on eosinophils. Benralizumab *blocks* via its Fab fragments IL-5Rα, thereby neutralizing IL-5 bioactivity, Moreover, through its Fc constant region benralizumab binds to the FcγIIIRa receptor expressed by natural killer cells, enabling them to induce eosinophil apoptosis.

Pelaia C, Paoletti G, Puggioni F et al. Interleukin-5 in the Pathophysiology of Severe Asthma Front Physiol. 2019;10:1514.

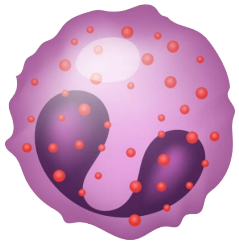
Prevalence & Clinical Characteristics of Severe Eosinophilic Asthma



of patients with asthma suffer from severe asthma[1]



of patients with severe asthma are likely to have an eosinophilic phenotype[2]*



Eosinophilic Asthma May Be Associated with:

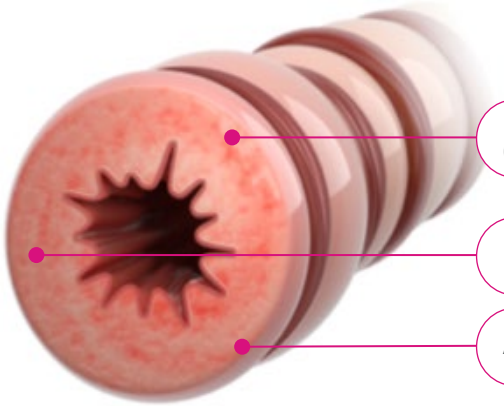
- Elevated blood eosinophil counts[2] (≥150 cells/µL)
- Frequent exacerbations[3] (≥2 exacerbations annually)
- Steroid dependence[3]
- Adult-onset disease[2]
- Nasal polyps[2]
- Low FEV_1 with persistent airflow limitation[3]

***The majority of patients with severe asthma (Grade 3 = most likely eosinophilic) had a blood eosinophil count ≥300 cells/µL OR were on anti-IL-5/IL-5Rα therapy.**
Severe disease was also characterized by a blood eosinophil count ≥150 to 300 cells/µL and being on maintenance OCS therapy or the presence of ≥2 nasal polyps, elevated fractional exhaled nitric oxide, and late-onset disease[2]
FEV_1, forced expiratory volume in 1 second.

1. Norsk forening for Lungemedisin (2019) Praktisk veileder for alvorlig astma. (https://www.legeforeningen.no/contentassets/9768b9ea8ed94cfaa89598e18fb2945b/praktisk-veileder-for-alvorlig-astma-hos-voksne.pdf cited 1302.2025)
2. Heaney LG, de Llano LP, Al-Ahmad M et al. Eosinophilic and Noneosinophilic Asthma. Chest 2021; 160(3):814-830.
3. de Groot JC, ten Brinke A, Bel EHD. Management of the patient with eosinophilic asthma: a new era begins ERJ Open Res 2015;1:00024-2015

Clinical Impact of Eosinophilic Inflammation in the Airways

Airway Pathology in Severe Asthma



Eosinophil airway inflammation (Type 2)[1]

Epithelial damage[2]

Airway remodeling[1]

- Goblet cell hyperplasia[2]
- Mucus production[1]
- Smooth muscle contractility & hypertrophy[1]

Clinical Impact:

- **Exacerbations**[1]
- **Decline in lung function**[1]
- **Symptoms**[1]
- **Bronchial Hyperresponsiveness**[1,2]

Figure adapted from: Israel E.

1. Israel E, Reddel HK.Severe and Difficult-to-Treat Asthma in Adults N Engl J Med. 2017;377:965–976; 2. McBrien CN, Menzies-Gow A. The Biology of Eosinophils and Their Role in Asthma Front Med (Lausanne). 2017;4:93.

Eosinophilic Inflammation Is Central to the Key Pathological Features and Clinical Consequences of Asth

"Studies support a crucial role for eosinophils as drivers of type 2 immune-inflammatory responses in asthma"[1]

Michael C Peters, Sally E Wenzel

Eosinophil activation

Asthma airway pathology

Eosinophil airway inflammation (Type 2)[2,3]

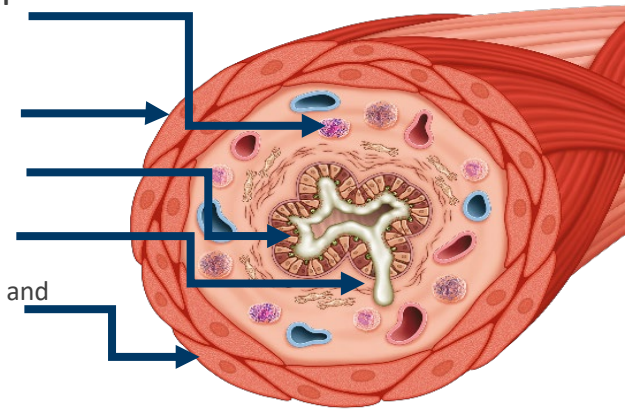
Epithelial damage[4]

Goblet cell hyperplasia[5]

Mucus production[3]

Smooth muscle contractility and hypertrophy[3]

Airway remodelling[2,3]



EOS = eosinophil.

Clinical consequences

- ✓ Exacerbations[2,3]
- ✓ Airway obstruction[2,3] (eg, ↓ lung function)
- ✓ Symptoms[2,3]
- ✓ Airway hyperresponsiveness[2,3]

1.Peters MC, Wenzel SE. Intersection of biology and therapeutics: type 2 targeted therapeutics for adult asthma. *Lancet*. 2020;395;371-383. 2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention 2024. Cited 12.03.2025. 3. Israel E, Reddel HK.Severe and Difficult-to-Treat Asthma in Adults N Engl J Med. 2017;377:965–976 4. Gandhi NA, Bennett BL, Graham NMH et al. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov*. 2016;15:35-50; 5. McBrien et al. *Front Med*. 2017;4.

Case Report

PATIENT EVALUATION

- 65-years, female
  168 cm/79.0 kg, BMI 28 kg/m2
  Ex- smoking (15 packyears)
- Increasing shortness of breath
- Cough
- Exacerbations 2/year (always + OCS)
- Asthma diagnosed 12 years before
  Initial ICS/LABA
  since 4 year LABA/LAMA/ICS
  Low dose OCS

HISTORY

- Asthma in childhood (until age of 20)
- Hypertension ↑
- CAD
- Diabetes Type II
- 2x Rehab´s
- exercise program 2x/week
- sometimes vaccination

LUNG FUNCTION

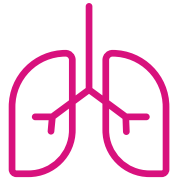
- pre FEV_1: 0.72 l (29.6% pred.)
- post FEV_1: 0,85 l (37.1% pred.)
- RV: 190 %

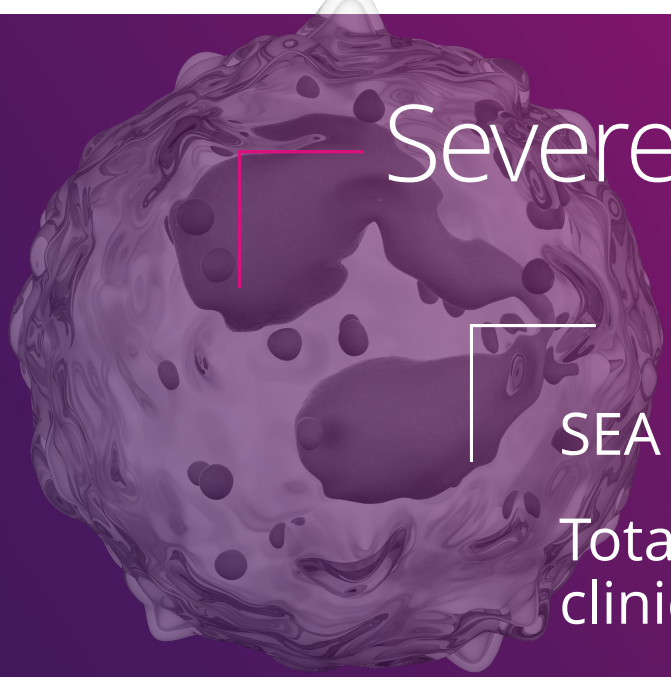
Diffusion capacity

- TLCO : 76.3 pred.

BIOMARKERS

- IgE: 38 U/l (NW < 25)
- bloood eosinophiles: 213 /ul
- FENO: 33 ppb





Severe eosinophilic asthma

SEA is mostly eosinophilic[1]

Total depletion of eosinophils results in clinical benefits[2,3]

No side effects due to total depletion reported[2,3]

1.Heaney LG, de Llano LP, Al-Ahmad M et al. Eosinophilic and Noneosinophilic Asthma. Chest 2021; 160(3):814-830 2. Pelaia C, Paoletti G, Puggioni F et al. Interleukin-5 in the Pathophysiology of Severe Asthma Front Physiol. 2019;10:1514. 3. Korn S, Bourdin A, Chupp G et al. Integrated Safety and Efficacy Among Patients Receiving Benralizumab for Up to 5 Years. J Allery Clin Immunol Pract 2021; https://doi.org/10.1016/j.jaip.2021.07.058.g.

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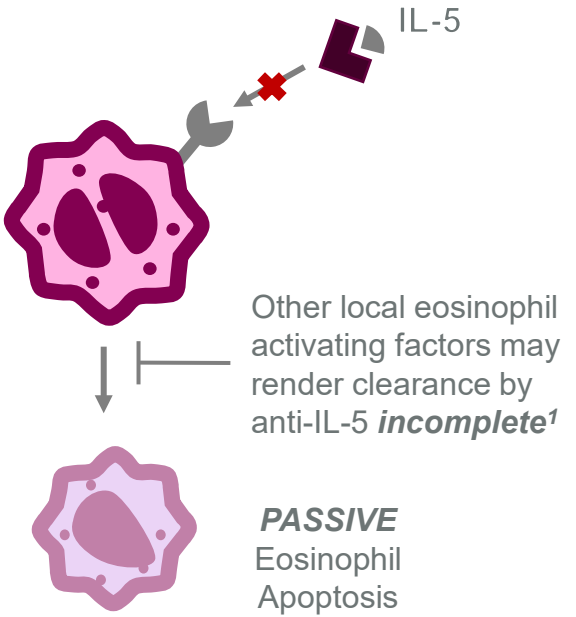
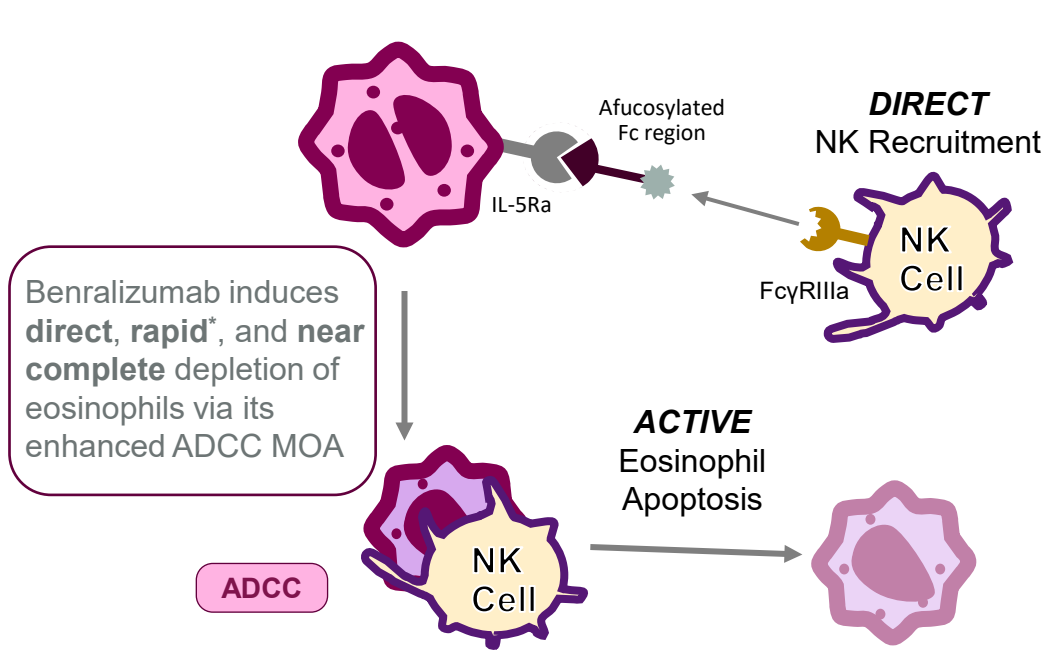
Mechanism of Action:
IL-5 Cytokine Targeted versus Eosinophil Targeted

Anti-IL-5 MOA1-4
indirect



Benralizumab MOA
Enhanced Antibody-Dependent Cell-mediated Cytotoxicity (ADCC)G



*Benralizumab induces eosinophil apoptosis within 6 hours *in vitro*[7]; blood eosinophils were depleted within 24 hours in a clinical study[6]

IL-5 = interleukin 5; IL-5Ra = interleukin 5 receptor alpha; MOA = mechanism of action; NK = natural killer.

1. Pelaia C, Paoletti G, Puggioni F et al. Interleukin-5 in the Pathophysiology of Severe Asthma Front Physiol. 2019;10:1514. 2. FASENRA SPC 5.1

FASENRA (benralizumab) - viktig informasjon (utvalg)

Indikasjon: Astma: Fasenra er indisert som tillegg til vedlikeholdsbehandling hos voksne med alvorlig eosinofil astma som er utilstrekkelig kontrollert til tross for høye doser inhalasjonskortikosteroider samt langtidsvirkende beta-agonister. **Eosinofil granulomatose med polyangiitt (EGPA):** Fasenra er indisert som tilleggsbehandling hos voksne pasienter med relapserende eller refraktær eosinofil granulomatose med polyangiitt. **Dosering:** Fasenra er beregnet til langtidsbehandling. Behovet for fortsatt behandling bør vurderes minst én gang årlig, basert på sykdommens alvorlighetsgrad, graden av sykdomskontroll og eosinofiltall i blod. Astma: Anbefalt dose er 30 mg som subkutan injeksjon hver 4. uke for de første 3 dosene, og deretter hver 8. uke. Behandlingen skal startes opp av lege med erfaring med diagnostisering og behandling av alvorlig astma. EGPA: Anbefalt dose er 30 mg som subkutan injeksjon hver 4. uke. Hos pasienter som utvikler livstruende maniifestasjoner av EGPA, skal behovet for fortsatt behandling vurderes, siden Fasenra ikke har blitt undersøkt i denne populasjonen. **Kontraindikasjoner:** Overfølsomhet overfor virkestoffet eller overfor noen av hjelpestoffene. **Vanlige bivirkninger:** Feber, reaksjon på injeksjonsstedet, overfølsomhetsreaksjon, faryngitt, hodepine. **Ukjent frekvens:** Anafylaktisk reaksjon. **Forsiktighetsregler**: Skal ikke brukes ved akutt forverring av astma. Pasienten bør instrueres om å søke medisinsk hjelp dersom astmaen forblir ukontrollert eller forverres. Bruk bør unngås under graviditet og amming. **Pakninger og priser**: Injeksjonsvæske, oppløsning i ferdigfylt penn (30 mg): 1 stk. kr 34065,90. Injeksjonsvæske, oppløsning i ferdigfylt sprøyte (30 mg): 1 stk. kr 34065,90. **Reseptgruppe: C. Refusjon:** H-resept. Refusjonsberettiget bruk: Der det er utarbeidet nasjonale handlingsprogrammer/nasjonal faglig retningslinje og/eller anbefalinger fra RHF/LIS spesialistgruppe skal rekvirering gjøres i tråd med disse. Vilkår: 216 Refusjon ytes kun etter resept fra sykehuslege eller avtalespesialist. Fasenra inngår i RHF anbefalinger for alvorlig ukontrollert T2-høy astma.

For fullstendig informasjon, les mer på www.felleskatalogen.no

AstraZeneca AS - www.astrazeneca.no – P. box 6050 Etterstad - 0601 Oslo

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