Leaflet kemasan: Informasi untuk pengguna

Vaksin konjugat pneumokokal 20-valen

Prevenar 20®

Baca isi leaflet ini dengan teliti sebelum Anda menggunakan vaksin ini karena berisi informasi penting untuk Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Vaksin ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, sekali pun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 13.

Apa isi leaflet ini

1. Nama vaksin

Prevenar 20®

2. Bentuk sediaan

Suspensi untuk injeksi dalam syringe yang telah diisi dosis tunggal.

3. Deskripsi vaksin

Vaksin berupa suspensi putih untuk injeksi yang disediakan dalam syringe yang telah diisi dosis tunggal (0,5 ml).

4. Apa kandungan vaksin ini?

Bahan aktifnya adalah konjugat CRM_{197} polisakarida yang terdiri dari:
- 2,2 mikrogram polisakarida untuk serotipe 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, dan 33F
- 4,4 mikrogram polisakarida untuk serotipe 6B

Satu dosis (0,5 ml) mengandung sekitar 51 mikrogram protein pembawa CRM_{197} yang diserap pada aluminium fosfat (0,125 mg aluminium).

Bahan lainnya adalah natrium klorida, asam suksinat, polisorbat 80, dan air untuk injeksi.

5. Kekuatan vaksin

Vial sekali pakai: 0,5 ml.

6. Apa kegunaan vaksin ini?

Prevenar 20® adalah vaksin pneumokokal yang diberikan kepada:

- **anak mulai usia 6 minggu hingga kurang dari 18 tahun** untuk membantu mencegah penyakit seperti: meningitis (peradangan di sekitar otak), sepsis atau bakteremia (bakteri di dalam aliran darah), pneumonia (infeksi paru), dan infeksi telinga yang disebabkan oleh 20 jenis bakteri *Streptococcus pneumoniae.*

- **individu berusia 18 tahun ke atas** untuk membantu mencegah penyakit seperti: pneumonia (infeksi paru), sepsis atau bakteremia (bakteri di dalam aliran darah), dan meningitis (peradangan di sekitar otak) yang disebabkan oleh 20 jenis bakteri *Streptococcus pneumoniae.*

Prevenar 20® memberikan perlindungan terhadap 20 jenis bakteri *Streptococcus pneumoniae*.

Vaksin bekerja dengan membantu tubuh membentuk antibodi sendiri, yang melindungi Anda dari penyakit-penyakit ini.

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan vaksin ini?

Dokter atau perawat akan menginjeksikan dosis vaksin yang dianjurkan (0,5 ml) ke lengan atas Anda atau lengan atau otot kaki anak Anda.

Tidak ada atau hanya tersedia data terbatas untuk Prevenar 20 pada bayi di bawah usia 6 minggu, bayi dan anak-anak yang belum divaksinasi atau hanya sebagian divaksinasi. Rekomendasi dosis berikut sebagian besar didasarkan pada pengalaman dengan Prevenar 13.

Bayi berusia antara 6 minggu hingga 15 bulan

Anak Anda harus menerima rangkaian awal tiga injeksi vaksin diikuti dengan satu dosis penguat menurut anjuran resmi atau petugas kesehatan mungkin akan menggunakan jadwal alternatif. Penting untuk mematuhi petunjuk dari dokter atau perawat untuk menyelesaikan rangkaian injeksi.

- Injeksi pertama dapat diberikan paling cepat pada usia 6 minggu hingga 8 minggu.
- Setiap injeksi akan diberikan pada waktu berbeda dengan selang minimal 4 minggu antara dosis kecuali untuk injeksi terakhir (dosis penguat), yang akan diberikan antara usia 11 dan 15 bulan.

Anda akan diberi tahu kapan anak Anda harus kembali untuk injeksi berikutnya.

Bayi yang belum divaksinasi berusia 7 bulan hingga kurang dari 12 bulan

Bayi berusia **7 bulan hingga kurang dari 12 bulan** harus menerima tiga injeksi. Dua injeksi pertama diberikan dengan selang minimal 4 minggu. Injeksi ketiga akan diberikan saat anak berusia dua tahun.

Anak yang belum divaksinasi berusia 12 bulan hingga kurang dari 24 bulan

Anak berusia **12bulan hingga kurang dari 24 bulan** harus menerima dua injeksi yang diberikan dengan selang minimal 8 minggu.

Anak yang belum divaksinasi berusia 2 tahun hingga kurang dari 5 tahun

Anak berusia **2 tahun hingga kurang dari 5 tahun** harus menerima satu injeksi.

Anak berusia 12 bulan hingga kurang dari 5 tahun yang sebelumnya telah menerima vaksinasi lengkap Prevenar 13

Anak berusia **12 bulan hingga kurang dari 5 tahun** yang sebelumnya telah menerima vaksinasi lengkap Prevenar 13 akan menerima satu injeksi.

Anak dan remaja berusia 5 tahun hingga kurang dari 18 tahun terlepas dari apakah sudah menerima vaksinasi Prevenar 13 sebelumnya

Anak dan remaja berusia **5 tahun hingga kurang dari 18 tahun** akan menerima satu injeksi.

Jika anak Anda sebelumnya telah menerima Prevenar 13, harus diberikan selang minimal 8 minggu sebelum menerima Prevenar 20®.

Penting kiranya mematuhi petunjuk dari dokter, apoteker, atau perawat Anda sehingga anak Anda mendapatkan rangkaian injeksi yang lengkap. Pastikan anak Anda menyelesaikan rangkaian vaksinasi yang dianjurkan. Jika tidak, anak Anda mungkin tidak terlindungi sepenuhnya dari penyakit.

Jika anak Anda melewatkan satu injeksi, penting bagi Anda untuk mengatur janji temu lagi. Dengan demikian Anda dan dokter Anda dapat membicarakan tentang langkah-langkah yang perlu diambil untuk melindungi anak Anda.

Orang Dewasa

Orang dewasa harus menerima satu kali injeksi.

Informasikan kepada dokter, apoteker, atau perawat Anda jika Anda sebelumnya pernah menerima vaksin pneumokokal.

Jika Anda memiliki pertanyaan lebih lanjut mengenai penggunaan Prevenar 20®, konsultasikan dengan dokter, apoteker, atau perawat Anda.

Populasi khusus

Tidak ada data klinis dengan Prevenar 20® pada populasi khusus [orang dewasa dan anak-anak yang berisiko lebih tinggi terkena infeksi pneumokokus termasuk orang dewasa dengan sistem imun yang lemah dan anak-anak dengan infeksi human immunodeficiency virus (HIV) atau transplantasi sel induk hematopoietik (HSCT), dan anak-anak dengan penyakit sel sabit (SCD)].

8. Kapan seharusnya Anda tidak menggunakan vaksin ini?

Jangan gunakan Prevenar 20®
Jika Anda atau anak Anda alergi terhadap bahan aktif atau terhadap bahan lain dalam vaksin ini (tercantum di bagian 4), atau terhadap vaksin lain yang mengandung difteria toksoid.

9. Apa yang harus dipertimbangkan saat menggunakan vaksin ini?

Konsultasikan dengan dokter, apoteker, atau perawat sebelum vaksinasi dilakukan jika Anda atau anak Anda:

- sedang atau pernah mengalami gangguan kesehatan setelah pemberian dosis Prevenar 20® seperti reaksi alergi atau masalah pernapasan,
- mengalami sakit yang berat atau demam tinggi. Namun demikian, demam ringan dan infeksi saluran pernapasan atas (misalnya terkena selesma) saja tidak menjadi alasan untuk menunda vaksinasi,
- mengalami gangguan perdarahan atau mudah memar,
- mengalami penurunan sistem kekebalan tubuh (seperti akibat infeksi HIV); Anda mungkin tidak akan menerima manfaat penuh dari Prevenar 20®.

Konsultasikan dengan dokter, apoteker, atau perawat Anda sebelum vaksinasi jika anak Anda lahir sangat prematur (pada atau sebelum usia gestasi 28 minggu), sebab dapat terjadi jeda antar-napas yang lebih panjang dibanding jeda normal yang terjadi selama 2–3 hari setelah vaksinasi. Lihat juga bagian 13.

Seperti vaksin lainnya, Prevenar 20® tidak akan melindungi semua orang yang divaksinasi.

Prevenar 20® hanya akan melindungi dari infeksi telinga yang disebabkan oleh jenis-jenis *Streptococcus pneumoniae* sesuai tujuan pembuatan vaksin ini. Vaksin ini tidak akan melindungi dari agen penginfeksi lainnya yang dapat menyebabkan infeksi telinga.

10. Apa saja obat/vaksin lain atau makanan yang harus dihindari selama menggunakan vaksin ini?

Anak Anda dapat diberi Prevenar 20® secara bersamaan dengan vaksin anak lainnya.

Pada orang dewasa, Prevenar 20® dapat diberikan secara bersamaan dengan vaksin flu (vaksin influenza yang tidak aktif) pada tempat injeksi yang berbeda. Bergantung pada penilaian risiko individu yang dilakukan penyedia layanan kesehatan Anda, misalnya mungkin akan disarankan selang 4 minggu antara kedua vaksinasi.

Prevenar 20® dapat diberikan secara bersamaan dengan vaksin mRNA COVID-19.

Informasikan kepada dokter, apoteker, atau perawat Anda jika Anda atau anak Anda sedang, baru-baru ini atau mungkin akan meminum obat-obatan lain, atau baru-baru ini telah menerima vaksin lain.

11. Apakah vaksin ini aman untuk ibu hamil dan menyusui?

Jika Anda sedang hamil atau menyusui, mengira bahwa Anda mungkin hamil, atau berencana untuk hamil, konsultasikan dengan dokter atau apoteker Anda sebelum menerima vaksin ini.

12. Apakah pasien diperbolehkan mengemudi dan mengoperasikan mesin selama menggunakan vaksin ini?

Pengaruh Prevenar 20® terhadap kemampuan mengemudi atau menjalankan mesin terbilang nihil atau dapat dikesampingkan. Namun demikian, sebagian efek yang disebutkan di bagian 13 potensi efek yang tidak diinginkan dapat memengaruhi untuk sementara waktu kemampuan mengemudi atau mengoperasikan mesin.

13. Apa saja potensi efek yang tidak diinginkan dari penggunaan vaksin ini?

Seperti semua vaksin yang ada, Prevenar 20® dapat menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping serius Prevenar 20®

Beri tahu dokter Anda segera jika Anda merasakan tanda-tanda efek samping serius berikut ini (lihat juga bagian 9): pembengkakan wajah, bibir, mulut, lidah, atau tenggorokan (edema), sesak napas (dispnea), mengi (bronkospasme) – ini mungkin merupakan tanda-tanda reaksi alergi berat seperti anafilaksis, termasuk syok.

Efek samping lainnya

Berikut ini mencakup efek samping yang dilaporkan untuk Prevenar 20® pada bayi dan anak-anak (6 minggu hingga kurang dari 5 tahun):

Sangat umum: dapat terjadi pada lebih dari 1 di antara 10 dosis vaksin
- Penurunan nafsu makan.
- Mudah marah.
- Rasa mengantuk.
- Demam.
- Di tempat injeksi yang dialami semua anak: kemerahan, pembengkakan atau pengerasan, nyeri atau nyeri tekan.
- Di tempat injeksi setelah dosis penguat dan pada anak berusia 2 hingga 5 tahun: kemerahan, pembengkakan, atau pengerasan berukuran lebih dari 2,0 hingga 7,0 cm.

Umum: dapat terjadi hingga 1 di antara 10 dosis vaksin
- Diare.
- Muntah.
- Ruam.
- Demam (suhu tinggi 38,9℃ atau lebih).
- Di tempat injeksi setelah rangkaian awal injeksi: kemerahan, pengerasan, pembengkakan berukuran lebih dari 2,0 hingga 7,0 cm; nyeri atau nyeri tekan yang membatasi gerakan.

Tidak umum: dapat terjadi hingga 1 di antara 100 dosis vaksin
- Kejang, termasuk yang disebabkan oleh suhu yang tinggi.
- Biduran (urtikaria atau ruam menyerupai urtikaria).
- Di tempat injeksi: kemerahan, pembengkakan, atau pengerasan lebih besar daripada 7,0 cm.

Jarang: dapat terjadi hingga 1 di antara 1000 dosis vaksin
- Reaksi alergi (hipersensitivitas) di tempat injeksi.

Efek samping berikut ini teramati dengan Prevenar 13 dan dapat juga teramati dengan Prevenar 20®:
- Pingsan atau kondisi menyerupai syok (episode hipotonik-hiporesponsif).
- Reaksi alergi (hipersensitivitas), termasuk pembengkakan wajah dan/atau bibir.
- Menangis.
- Tidur tidak nyenyak.

Berikut ini adalah efek samping yang dilaporkan dialami anak-anak dan remaja yang menerima Prevenar 20® (berusia 5 hingga kurang dari 18 tahun):

Sangat umum: dapat terjadi pada lebih dari 1 di antara 10 dosis vaksin
- Sakit kepala.
- Nyeri otot.
- Di tempat injeksi: nyeri, nyeri tekan, kemerahan, pembengkakan, atau pengerasan.
- Kelelahan.

Umum: dapat terjadi hingga 1 di antara 10 dosis vaksin
- Nyeri sendi.
- Di tempat injeksi: nyeri atau nyeri tekan yang membatasi gerakan.

Tidak umum: dapat terjadi hingga 1 di antara 100 dosis vaksin
- Biduran (urtikaria atau ruam menyerupai urtikaria).
- Demam.

Berikut ini efek samping yang teramati dalam penggunaan Prevenar 13 dan mungkin juga teramati dalam penggunaan Prevenar 20®:
- Diare.
- Muntah.
- Penurunan nafsu makan.
- Mudah marah.
- Rasa mengantuk.
- Tidur tidak nyenyak.

- Ruam.

Anak-anak dan remaja yang terinfeksi HIV, terkena penyakit sel bulan sabit, atau memiliki transplantasi sel punca hematopoeitik menunjukkan efek samping yang serupa, akan tetapi frekuensi sakit kepala, muntah, diare, demam, kelelahan, nyeri sendi dan otot tergolong sangat sering.

Pada bayi yang lahir sangat prematur (pada atau sebelum usia gestasi 28 minggu), maka dapat terjadi jeda antar-napas yang lebih panjang dibanding jeda normal yang terjadi selama 2–3 hari setelah vaksinasi.

Efek samping berikut ini teramati dengan Prevenar 13 dalam pengalaman pascapemasaran pada anak-anak dan dapat juga teramati dengan Prevenar 20®:

- Reaksi alergi berat termasuk syok (kolaps kardiovaskular); pembengkakan bibir, wajah, atau tenggorokan (angioedema).
- Pembesaran nodus atau kelenjar limfa (limfadenopati) di dekat lokasi vaksinasi, seperti di bawah lengan atau di paha dalam.
- Di tempat injeksi: biduran (urtikaria), kemerahan dan iritasi (dermatitis), dan gatal-gatal (pruritus).
- Ruam yang menimbulkan bisul merah dan gatal (eritema multiforma).

Berikut ini adalah efek samping yang dilaporkan terkait pemberian Prevenar 20® pada orang dewasa:

Sangat umum: dapat terjadi pada lebih dari 1 di antara 10 dosis vaksin
- Sakit kepala.
- Nyeri sendi dan nyeri otot.
- Kelelahan.
- Nyeri/nyeri tekan di tempat injeksi dan kelelahan.

Umum: dapat terjadi hingga 1 di antara 10 dosis vaksin
- Pembengkakan di tempat injeksi, kemerahan di tempat injeksi, dan demam.

Tidak umum: dapat terjadi hingga 1 di antara 100 dosis vaksin
- Diare, mual, dan muntah.
- Ruam dan pembengkakan wajah, bibir, mulut, lidah, atau tenggorokan, yang dapat menyebabkan kesulitan menelan atau bernapas (angioedema).
- Gatal-gatal di tempat injeksi, pembengkakan kelenjar di leher, ketiak, atau paha (limfadenopati), biduran di tempat injeksi (urtikaria), dan menggigil.

Efek samping berikut ini teramati dengan Prevenar 13 dan dapat juga teramati dengan Prevenar 20®:
- Ruam yang menimbulkan bisul merah dan gatal (eritema multiforma).
- Iritasi di tempat injeksi.
- Penurunan nafsu makan.
- Terbatasnya gerakan lengan.

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam

leaflet ini. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih banyak mengenai keamanan vaksin ini.

Untuk melaporkan efek samping, hubungi www.pfizersafetyreporting.com atau email di IDN.AEReporting@pfizer.com.

14. Tanda-tanda dan gejala-gejala overdosis

Overdosis Prevenar 20® kemungkinan kecil terjadi karena disediakan dalam bentuk syringe yang telah diisi.

15. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?

Overdosis Prevenar 20® kemungkinan kecil terjadi karena disediakan dalam bentuk syringe yang telah diisi.

16. Bagaimana cara menyimpan vaksin ini?

Jauhkan vaksin ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan vaksin ini melebihi tanggal kedaluwarsa yang tertera pada karton dan label setelah tanda EXP. Tanggal kedaluwarsa mengacu pada tanggal terakhir pada bulan tersebut.

Simpan di lemari pendingin (2°C hingga 8°C).

Prevenar 20® harus digunakan sesegera mungkin setelah dikeluarkan dari lemari pendingin.

Jangan dibekukan. Buang vaksin jika telah dibekukan.

Data stabilitas menunjukkan bahwa vaksin stabil selama 96 jam jika disimpan pada suhu antara 8℃ hingga 25℃, atau 72 jam jika disimpan pada suhu antara 0℃ hingga 2℃. Di akhir periode waktu ini, Prevenar 20® harus segera digunakan atau dibuang. Data ini ditujukan sebagai panduan bagi petugas kesehatan jika hanya terjadi perubahan suhu sementara.

Syringe yang telah diisi harus disimpan dalam lemari pendingin secara horizontal untuk meminimalkan waktu suspensi ulang.

Jangan buang vaksin melalui saluran pembuangan air atau bersama sampah rumah tangga. Tanyakan kepada apoteker mengenai cara membuang vaksin yang sudah tidak digunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

17. Nomor izin edar

Prevenar 20® Dus, 1 syringe yang telah diisi @ 0,5 ml (No. Reg.: DKI2486102143A1)

18. Nama dan alamat pemohon dan/atau pemilik vaksin sesuai dengan ketentuan yang berlaku

Diproduksi dan kemas oleh:
Pfizer Ireland Pharmaceuticals Unlimited Company

Grange Castle Business Park
Nangor Road, Dublin 22
Irlandia

Dirilis oleh:
Pfizer Manufacturing Belgium NV,
Rijksweg 12,
2870 Puurs-Sint-Amands,
Belgia

Diimpor oleh:
PT. Pfizer Indonesia
Jakarta, Indonesia

19. Tanggal revisi

20. Peringatan khusus

HARUS DENGAN RESEP DOKTER

21. Tanggal Pertama Kali PIL Disetujui

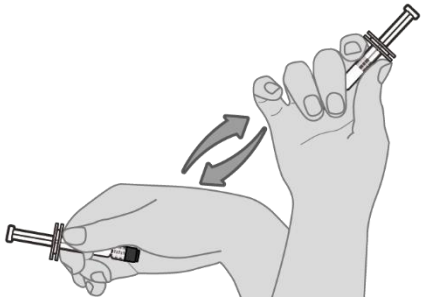
12 September 2024

Informasi berikut ini ditujukan untuk petugas kesehatan saja:

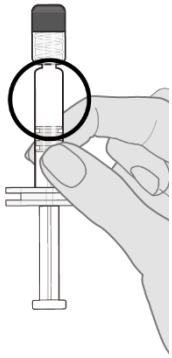
Selama penyimpanan, endapan putih dan supernatan jernih dapat teramati. Ini bukan merupakan tanda penurunan kualitas. Syringe yang telah diisi harus disimpan secara horizontal untuk meminimalkan waktu suspensi ulang.

Petunjuk pemberian

Langkah 1. Suspensi ulang vaksin
Pegang syringe yang telah diisi secara horizontal antara ibu jari dan jari telunjuk lalu kocok dengan kuat hingga isi syringe terlihat sebagai suspensi putih yang homogen. Jangan gunakan vaksin jika tidak dapat disuspensi ulang.

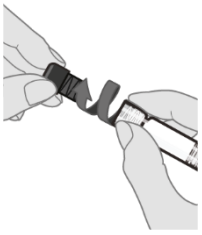


Langkah 2. Pemeriksaan visual
Periksa vaksin secara visual untuk melihat adanya bahan partikulat besar dan perubahan warna sebelum pemberian dilakukan. Jangan gunakan jika teramati adanya bahan partikulat besar atau perubahan warna. Jika vaksin bukan berupa suspensi putih yang homogen, ulangi langkah 1 dan 2.



Langkah 3. Lepas tutup syringe
Lepas tutup syringe dari adaptor kunci Luer dengan memutar tutup perlahan berlawanan arah jarum jam sambil memegang adaptor kunci Luer.

Catatan: Diperlukan kehati-hatian untuk memastikan bahwa piston yang diperpanjang tidak ditekan saat melepaskan tutup syringe.



Langkah 4. Pasang jarum steril
Pasang jarum yang sesuai untuk pemberian intramuskular pada syringe yang telah diisi dengan memegang adaptor kunci Luer dan memutar jarum searah jarum jam.

Berikan seluruh dosis.

Prevenar 20® hanya untuk penggunaan intramuskular.

Prevenar 20® tidak boleh dicampur dengan vaksin/produk obat lainnya dalam syringe yang sama.

Prevenar 20® dapat diberikan secara bersamaan dengan vaksin anak lainnya; dalam hal ini harus digunakan lokasi vaksinasi yang berbeda.

Prevenar 20® dapat diberikan kepada orang dewasa secara bersamaan dengan vaksin influenza musiman (QIV; antigen permukaan, dinonaktifkan, berajuvan). Pada individu dengan kondisi kesehatan tertentu yang dikaitkan dengan risiko tinggi berkembangnya penyakit pneumokokal yang mengancam nyawa, pertimbangan mungkin diperlukan untuk memberi selang antara pemberian QIV dan Prevenar 20® (misalnya selama sekitar 4 minggu). Penggunaan tempat vaksinasi yang berbeda perlu diperhatikan.

Prevenar 20® dapat diberikan kepada orang dewasa secara bersamaan dengan *vaksin mRNA COVID-19 (dengan modifikasi nukleosida).*

Setiap produk yang tidak terpakai atau bahan limbah harus dibuang sesuai persyaratan setempat.

PT. PFIZER INDONESIA
Local Product Document

Generic Name: 20-valent pneumococcal conjugate vaccine
Trade Name: Prevenar 20®
CDS Effective Date: 16-Jun-2023
Supersedes: NA

1. NAME OF THE MEDICINAL PRODUCT

PREVENAR 20 suspension for injection in pre-filled syringe. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Pneumococcal polysaccharide serotype 1[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 3[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 4[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 5[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 6A[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 6B[*,†]	4.4 µg
Pneumococcal polysaccharide serotype 7F[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 8[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 9V[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 10A[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 11A[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 12F[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 14[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 15B[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 18C[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 19A[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 19F[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 22F[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 23F[*,†]	2.2 µg
Pneumococcal polysaccharide serotype 33F[*,†]	2.2 µg

[*] Conjugated to CRM_{197} carrier protein (approximately 51 µg per dose)
† Adsorbed on aluminium phosphate (0.125 mg aluminium per dose)

3. PHARMACEUTICAL FORM

Suspension for injection in a single-dose pre-filled syringe.

The vaccine is a homogeneous white suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Active immunization for the prevention of invasive disease, pneumonia, and acute otitis media caused by *Streptococcus pneumoniae* in infants, children, and adolescents from 6 weeks to less than 18 years of age.

Active immunization for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older.

See sections 4.4 and 5.1 for information on protection against specific pneumococcal serotypes.

The use of PREVENAR 20 should be determined on the basis of official recommendations taking into consideration the risk of invasive disease and pneumonia in different age groups, underlying comorbidities as well as the variability of serotype epidemiology in different geographical areas.

4.2. Posology and method of administration

Posology

The immunisation schedules for PREVENAR 20 should be based on official recommendations.

It is recommended that infants who receive a first dose of PREVENAR 20 complete the vaccination course with PREVENAR 20.

Vaccination series

Vaccination schedule in infants 6 weeks to 15 months of age	
4-dose series (3-dose primary series followed by a booster dose)	PREVENAR 20 may be given as a 4-dose series, each of 0.5 mL. The primary infant series consists of three doses, with the first dose usually given at 2 months of age and with an interval of at least 4 weeks between doses. The first dose may be given as early as 6 weeks of age. The fourth (booster) dose is recommended between 11 and 15 months of age (see Section 5.1).
Vaccination schedule for individuals 18years of age and older	

Individuals 18years of age and older	PREVENAR 20 is to be administered as a single-dose to individuals 18 years of age and older. The need for revaccination with a subsequent dose of PREVENAR 20 has not been established. No data on sequential vaccination with other pneumococcal vaccines or a booster dose are available for PREVENAR 20.

Pediatric population

No or only limited data are available for Prevenar 20 in infants below 6 weeks, older unvaccinated, or partially vaccinated infants and children. The following dosing recommendations are predominantly based on experience with Prevenar 13.

Infants below 6 weeks of age

The safety and efficacy of PREVENAR 20 in infants below 6 weeks of age have not been established. No data are available.

Unvaccinated infants 7 months to less than 12 months of age

Two doses, each of 0.5 mL, with an interval of at least 4 weeks between doses. A third dose is recommended in the second year of life.

Unvaccinated children 12 months to less than 24 months of age

Two doses, each of 0.5 mL, with an interval of at least 8 weeks between doses.

Unvaccinated children 2 years to less than 5 years of age

One single dose of 0.5 mL.

Children 12 months to less than 5 years of age previously fully vaccinated with Prevenar 13

One single dose (0.5 mL) given on an individual basis according to official recommendations to elicit immune responses to the additional serotypes.

If Prevenar 13 was administered, at least 8 weeks should elapse before administering PREVENAR 20 (see section 5.1).

Children and adolescents 5 years to less than 18 years of age regardless of prior Prevenar 13 vaccination

One single dose (0.5 mL) given on an individual basis according to official recommendations.

If Prevenar 13 was administered, at least 8 weeks should elapse before administering PREVENAR 20 (see section 5.1).

Special populations

There are no clinical data with PREVENAR 20 in special populations [adults and children at higher risk of pneumococcal infection including immunocompromised adults and children with human immunodeficiency virus (HIV) infection or hematopoietic stem cell transplant (HSCT), and children with sickle cell disease (SCD)].

Method of administration

For intramuscular use only.

PREVENAR 20 (0.5 mL) should be given by intramuscular injection. The preferred sites are the anterolateral aspect of the thigh (vastus lateralis muscle) in infants or the deltoid muscle of the upper arm in children and adults. PREVENAR 20 should be administered with care to avoid injection into or near nerves and blood vessels.

For instructions on the handling of the vaccine before administration, see Section 6.6.

4.3. Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1, or to diphtheria toxoid.

4.4. Special warnings and precautions for use

Do not inject PREVENAR 20 intravascularly.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic event following the administration of the vaccine (see Section 4.8).

Concurrent illness

As with other vaccines, the administration of PREVENAR 20 should be postponed in individuals suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Thrombocytopenia and coagulation disorders

As with all injectable vaccines, the vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration.

The risk of bleeding in patients with coagulation disorders needs to be carefully evaluated before intramuscular administration of any vaccine, and subcutaneous administration should be considered if the potential benefit clearly outweighs the risks.

Protection against pneumococcal disease

PREVENAR 20 will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and will not protect against other microorganisms that cause invasive disease, pneumonia or otitis media.

As with any vaccine, PREVENAR 20 may not protect all individuals receiving the vaccine from pneumococcal disease.

Immunocompromised individuals

Safety and immunogenicity data on PREVENAR 20 are not available for individuals in immunocompromised groups and vaccination should be considered on an individual basis.

Based on experience with pneumococcal vaccines, some individuals with altered immunocompetence may have reduced immune responses to PREVENAR 20.

Individuals with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunization. The clinical relevance of this is unknown.

Pediatric population

As with all injectable pediatric vaccines, the potential risk of apnea should be considered when administering the primary immunization series to preterm infants. The need for monitoring for at least 48 hours after vaccination should be considered for every preterm infant born ≤28 weeks of gestation who remain hospitalized at the time of the recommended administration. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

4.5. Interaction with other medicinal products and other forms of interaction

Different injectable vaccines should always be administered at different vaccination sites.

Do not mix PREVENAR 20 with other vaccines/products in the same syringe.

Pediatric population

In infants and children 6 weeks to less than 5 years of age, PREVENAR 20 can be administered concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b, inactivated poliomyelitis, hepatitis B, measles, mumps, rubella (MMR) and varicella vaccines. The vaccine has been safely administered with influenza and rotavirus vaccines.

Adults 18 years of age and older

PREVENAR 20 can be administered concomitantly with influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV]) and COVID-19 mRNA vaccine (nucleoside modified) (see Section 5.1).

No data are currently available regarding concomitant use with other vaccines.

4.6. Fertility, pregnancy and lactation

Pregnancy

Safety during pregnancy for PREVENAR 20 has not been established in humans.

Lactation

Safety during lactation for PREVENAR 20 has not been established in humans.

It is not known whether vaccine antigens or antibodies are excreted in human milk.

Fertility

No human data on the effect of PREVENAR 20 on fertility are available.

Animal studies do not indicate direct or indirect harmful effects with respect to female fertility or reproductive toxicity (see Section 5.3).

4.7. Effects on ability to drive and use machines

PREVENAR 20 has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under Section 4.8 “Undesirable effects” may temporarily affect the ability to drive or use machines.

4.8. Undesirable effects

Summary of the safety profile

The safety of PREVENAR 20 was evaluated in 5,987 participants 6 weeks to less than 18 years of age, in five clinical trials (one Phase 2 and four Phase 3): four randomized, double-blind, active-controlled clinical trials and one single-arm clinical trial; 3,664 participants received at least 1 dose of PREVENAR 20, and 2,323 participants received 13vPnC (control vaccine).

Infants and children 6 weeks to less than 15 months of age

Clinical trials were conducted in healthy infants and children 6 weeks to less than 15 months of age using a 3-dose series (Phase 3 trial B7471012 [Study 1012]) or a 4-dose series (Phase 3 trials B7471011 and B7471013 [Studies 1011 and 1013] and the Phase 2 trial B7471003 [Study 1003]). In these 4 infant trials 5,156 participants received at least 1 dose of vaccine: 2,833 received PREVENAR 20 and 2,323 received 13vPnC. Overall, approximately 90% of participants in each group received all doses through the study-specified toddler dose. In all studies, local reactions and systemic events were collected after each dose, and adverse events were collected from the first dose through 1 month after the last infant vaccination and from the toddler dose through 1 month after vaccination in all studies. Serious adverse events were evaluated through 1 month after the last dose in Studies 1012 and 6 months after the last dose in Studies 1011, 1013, and 1003.

PREVENAR 20 was well tolerated when administered on a 3-dose and a 4-dose series, in the infant study populations with low rates of severe local reactions and systemic events, and most reactions resolving within 1 to 3 days. The percentages of participants with reactogenicity events after PREVENAR 20 were generally similar to those after 13vPnC. Based on the infant data, the most frequently reported local reactions and systemic events after any dose of PREVENAR 20 were irritability, drowsiness, and pain at injection site. In these studies, PREVENAR 20 was co-administered or permitted to be administered with certain routine pediatric vaccines (see Section 4.5).

Study 1012 was a pivotal double-blind, active-controlled Phase 3 trial, in which 601 healthy infants, 2 months (≥42 to ≤112 days) of age and born at >36 weeks of gestation received PREVENAR 20 in a 3-dose series. The most frequently reported adverse reactions (>10%) after any dose of PREVENAR 20 were irritability (71.0% to 71.9%), drowsiness/increased sleep (50.9% to 61.2%), pain at injection site (22.8% to 42.4%), decreased appetite (24.7% to 39.3%), redness at the injection site (25.3% to 36.9%), swelling at the injection site (21.4% to 29.8%) and fever of ≥38.0°C (8.9% to 24.3%). Most adverse reactions occurred within 1 to 2 days following vaccination and were mild to moderate in severity and of short duration (1 to 2 days).

Study 1011 was a pivotal double-blind, active-controlled Phase 3 trial, in which 1,001 healthy infants, 2 months (≥42 to ≤98 days) of age and born at >36 weeks of gestation received PREVENAR 20 in a 4-dose series. The most frequently reported adverse reactions (>10%) after any dose of PREVENAR 20 were irritability (61.0% to 71.6%), drowsiness/increased sleep (39.5% to 67.2%), pain at injection site (35.7% to 49.1%), decreased appetite (20.6% to 26.4%), redness (23.2% to 25.5%), swelling (14.9% to 17.1%) and fever of ≥38.0°C (10.3% to 17.3%). Most adverse reactions were mild or moderate following vaccination and severe reactions were reported infrequently.

Study 1013 was a double-blind, active-controlled Phase 3 safety trial, in which 1,000 healthy infants, 2 months (≥42 to ≤98 days) of age and born at ≥34 weeks of gestation received PREVENAR 20 in a 4-dose series. The most frequently reported adverse reactions (>10%) after any dose of PREVENAR 20 were irritability (54.8% to 68.2%), drowsiness/increased sleep (35.3% to 64.8 %), pain at injection site (24.7% to 40.5%), decreased appetite (23.6% to 28.4%), redness (21.2% to 23.5%), swelling (14.8% to 20.0%) and fever of ≥38.0°C (9.3% to 18.0%). In Study 1013, the local reactions and systemic events in the preterm subgroup (111 infants born at 34 to less than 37 weeks of gestation) were similar to or lower than the term infants in the study. In the preterm subgroup the frequency of any reported local reaction (31.7% to 55.3% in the PREVENAR 20 group and 37.9% to 47.1% in the 13vPnC group) and systemic event (65.0% to 85.5% in the PREVENAR 20 group and 59.4% to 77.4% in the 13vPnC group).

Study 1003 was a double-blind, active-controlled Phase 2 trial, in which 231 infants, 2 months (≥42 to ≤98 days) of age and born at >36 weeks of gestation received PREVENAR 20 in a 4-dose series. The most frequently reported adverse reactions (>10%) after any dose of PREVENAR 20 were irritability (62.4% to 79.5%), drowsiness/increased sleep (32.8% to 68.1%), pain at injection site (35.5% to 51.1%), decreased appetite (23.3% to 30.8%), redness (24.7% to 26.9%), and swelling (12.7% to 17.9%).

The frequency and severity of the adverse reactions in all infant clinical trials were generally similar in the PREVENAR 20 and 13vPnC groups.

Children 15 months to less than 18 years of age

In the Phase 3 trial B7471014 (Study 1014), 831 participants 15 months to less than 18 years of age received a single-dose of PREVENAR 20 in four age groups (209 participants 15 to less than 24 months of age; 216 participants 2 years to less than 5 years of age; 201 participants 5 years to less than 10 years age; and 205 participants 10 years to less than 18 years of age). The participants less than 5 years of age had received at least 3 prior doses of 13vPnC.

The most frequently reported adverse reactions (>10%) observed after any dose of PREVENAR 20 in participants less than 2 years of age were irritability (61.8%), pain at the injection site (52.5%), drowsiness/increased sleep (41.7%), redness at the injection

site (37.7%), decreased appetite (25.0%), swelling at the injection site (22.1%) and fever ≥38.0°C (11.8%). In participants aged 2 years and older, the most frequently reported adverse reactions were pain at the injection site (66.0% to 82.9%), muscle pain (26.5% to 48.3%), redness at the injection site (15.1% to 39.1%), fatigue (27.8% to 37.2%), headache (5.6% to 29.3%), and swelling at the injection site (15.6% to 27.1%).

Adults 18 years of age and older

The safety profile presented is based on analysis of over 7,000 individuals 18 years of age and older, of which 4,552 were vaccinated with PREVENAR 20 in three Phase 1 and Phase 2 clinical trials and three Phase 3 clinical trials. In the Phase 3 trials, 4,263 participants received PREVENAR 20, which included 1,798 adults 18 through 49 years of age, 334 adults 50 through 59 years of age, and 2,132 adults 60 years of age and older (1,138 were 65 years of age and older). Of the Phase 3 PREVENAR 20 recipients, 3,639 adults were naïve to pneumococcal vaccines, 253 had previously received Pneumovax® 23 (pneumococcal polysaccharide vaccine [23-valent]; PPSV23) only, 246 had previously received 13vPnC only, and 125 had previously received both PPSV23 and 13vPnC.

In participants 18 to 49 years of age, the most frequently reported adverse reactions were pain at injection site (79.2%), muscle pain (62.9%), fatigue (46.7%), headache (36.7%), and joint pain (16.2%). In participants 50 to 59 years of age, the most frequently reported adverse reactions were pain at injection site (72.5%), muscle pain (49.8%), fatigue (39.3%), headache (32.3%), and joint pain (15.4%). In participants ≥ 60 years of age, the most frequently reported adverse reactions were pain at injection site (55.4%), muscle pain (39.1%), fatigue (30.2%), headache (21.5%), and joint pain (12.6%).

Adverse reactions from clinical trials with PREVENAR 20

As PREVENAR 20 contains the same 13 serotype-specific capsular polysaccharide conjugates and the same vaccine excipients as 13vPnC, the adverse reactions already identified for 13vPnC have been adopted for PREVENAR 20.

Tabulated list of adverse reactions

Table 1 present adverse reactions reported in the Phase 2 infant trial, and Phase 3 trials in pediatric and adult populations, based on the highest frequency among adverse events, local reactions, or systemic events, after vaccination in a PREVENAR 20 group in a study or integrated dataset. The data from clinical trials in infants reflect PREVENAR 20 administered simultaneously with other routine childhood vaccines. In the case of adverse reactions reported in clinical trials of 13vPnC, but not reported in PREVENAR 20 trials, the frequency is not known. In clinical trials, the safety profile of PREVENAR 20 was similar to that of 13vPnC.

Table 1. Adverse Drug Reactions (ADRs) by System Organ Class (SOC) and Council for International Organizations of Medical Science (CIOMS) Frequency

Category Listed in Order of Decreasing Medical Seriousness or Clinical Importance Within Each Frequency Category and SOC

Adverse reactions are listed by system organ class in decreasing order of frequency and seriousness. The frequency is defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from available data).

System Organ Class	Adverse Reactions	Frequency		
		Infants/Children/Adolescents		Adults
		6 weeks to less than 5 years of age	5 to less than 18 years of age	18 years of age and older
Immune System Disorders	Hypersensitivity reaction including face edema, dyspnea, bronchospasm	Not known[a]	-	Uncommon
Metabolism and Nutrition Disorders	Decreased appetite	Very common	Not known[c]	-
Psychiatric Disorders	Irritability	Very common	Not known[c]	-
	Crying	Not known[a]	-	-
Nervous System Disorders	Seizures (including febrile seizures)	Uncommon	-	-
	Hypotonic-hyporesponsive episode	Not known[a]	-	-
	Drowsiness/increased sleep	Very common	Not known[c]	-
	Restless sleep/decreased sleep	Not known[a]	Not known[c]	-
	Headache	-	Very common	Very common
Gastrointestinal Disorders	Vomiting	Common	Not known[c]	Uncommon[e]
	Diarrhea	Common	Not known[c]	Uncommon[e]
	Nausea	-	-	Uncommon
Skin and Subcutaneous Tissue Disorders	Angioedema	-	-	Uncommon[f]
	Urticaria or urticaria-like rash	Uncommon	Uncommon	-
	Rash	Common	Not known[c]	Uncommon[e]
Musculoskeletal and Connective Tissue Disorders	Muscle pain	-	Very common[d]	Very common
	Joint pain	-	Common[d]	Very common
General Disorders and Administration Site Conditions	Fever greater than 38.9°C	Common	-	-
	Vaccination-site erythema or induration/swelling (>7.0 cm)	Uncommon	-	-
	Vaccination-site pain/tenderness causing	Common	Common	-

System Organ Class	Adverse Reactions	Frequency		
		Infants/Children/Adolescents		Adults
		6 weeks to less than 5 years of age	5 to less than 18 years of age	18 years of age and older
	limitation of limb movement			
	Chills	-	-	Uncommon[e]
	Vaccination-site erythema or induration/swelling (>2.0 – 7.0 cm)	Very common (after toddler dose and in older children [age 2 to <5 years])	-	-
		Common (after infant series)	-	-
	Vaccination-site urticaria	-	-	Uncommon[f]
	Vaccination-site hypersensitivity	Rare[b]	-	-
	Fever	Very common	Uncommon	Common
	Lymphadenopathy	-	-	Uncommon[g]
	Fatigue	-	Very common[d]	Very common
	Vaccination-site induration/swelling	Very common	Very common	Common[e]
	Vaccination-site pain/tenderness	Very common	Very common	Very common
	Vaccination-site erythema	Very common	Very common	Common[e]
	Vaccination-site pruritus	-	-	Uncommon[f]

a. Adverse reactions (ARs) reported in clinical trials with 13vPnC in infants and children 6 weeks to 5 years of age with frequencies of very common (Restless sleep/decreased sleep), uncommon (Crying), and rare (Hypersensitivity reaction including face edema, dyspnea, bronchospasm; Hypotonic-hyporesponsive episode).
b. AR not reported for 13vPnC, although injection-site urticaria, injection-site pruritus, and injection-site dermatitis were reported in 13vPnC postmarketing experience.
c. ARs reported in clinical trials with 13vPnC in children and adolescents 5 years to less than 18 years of age with frequencies of very common (Decreased appetite; Irritability; Drowsiness/increased sleep; Restless sleep/decreased sleep) and common (Vomiting; Diarrhea; Rash).
d. ARs reported only in clinical trials of PREVENAR 20 in children and adolescents 5 years to less than 18 years.
e. Event reported in 13vPnC clinical trials in adults with very common frequency (>1/10).
f. Event reported spontaneously in 13vPnC postmarketing experience in adults; therefore, frequency was "Not known."
g. Event reported in 13vPnC clinical trials in adults as "lymphadenopathy localized to the region of the vaccination site" with uncommon frequency (≥1/1,000 to <1/100).

Not all ARs reported in 13vPnC Phase 3 trials in adults were reported in the PREVENAR 20 trials. The following ARs were not reported in the PREVENAR 20 Phase 3 trials in adults:

- General disorders and administration site conditions:
  - Limitation of arm movement (reported in 13vPnC clinical trials with Very Common frequency [≥1/10])
- Metabolism and nutrition disorders:
  - Decreased appetite (reported in 13vPnC clinical trials with Very Common frequency [≥1/10])

Safety with concomitant vaccine administration

Infants and children

The safety profile of PREVENAR 20 was acceptable, and similar to 13vPnC when administered concomitantly with routine pediatric vaccines containing diphtheria, tetanus, acellular pertussis, hepatitis B virus, poliovirus, and *Haemophilus influenzae* type b antigens (Infanrix hexa); measles, mumps, and rubella antigens (MMRVaxPro); and varicella antigens (Varilrix).

Adults

The safety profile was similar when PREVENAR 20 was administered with or without influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV]).

PREVENAR 20 administered together with COVID-19 mRNA vaccine (nucleoside modified) was observed to have a tolerability profile similar to COVID-19 mRNA vaccine (nucleoside modified) administered alone, and an overall safety profile consistent with PREVENAR 20 or COVID-19 mRNA vaccine (nucleoside modified) given alone.

Adverse reactions from post marketing experience

The following adverse events have been reported through passive surveillance since market introduction of 13vPnC. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine. The following adverse events were included based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to 13vPnC and are, therefore, considered adverse reactions. Although these adverse reactions reported in the postmarketing experience of 13vPnC in pediatric and adult populations were not observed in the PREVENAR 20 clinical trials, they are considered adverse reactions for PREVENAR 20 as the components of 13vPnC are also contained in PREVENAR 20.

Table 2. Adverse Reactions From Pneumococcal 13-valent Conjugate Vaccine Postmarketing Experience

System Organ Class	Frequency Not Known (cannot be estimated from available data)
Blood and lymphatic system disorders	Lymphadenopathy localized to the region of the vaccination site
Immune system disorders	Anaphylactic/anaphylactoid reaction including shock
Skin and subcutaneous tissue disorders	Angioedema; Erythema multiforme
General disorders and administration site conditions	Vaccination-site dermatitis; Vaccination-site urticaria; Vaccination-site pruritus

Events reported spontaneously in 13vPnC postmarketing experience; therefore, the frequencies could not be estimated from the available data and are considered as not known.

Three events (angioedema, vaccination-site pruritus, vaccination-site urticaria) that had been reported as adverse reactions from the 13vPnC postmarketing experience were reported in the PREVENAR 20 Phase 3 adult clinical trials, so they are listed in Table 1 for the adult populations. Lymphadenopathy localized to the region of the vaccination site had been reported in both 13vPnC clinical trials and in the postmarketing period. Since the term lymphadenopathy was reported in Phase 3 adult clinical trials of PREVENAR 20, it is noted in Table 1 for the adult population.

Additional information in special populations in studies with 13vPnC

Children and adolescents with sickle cell disease, HIV infection or a hematopoietic stem cell transplant had similar frequencies of adverse reactions as children and adolescents 2-17 years of age, except that headaches, vomiting, diarrhea, pyrexia, fatigue, arthralgia and myalgia were very common.
Adults with HIV infection had similar frequencies of adverse reactions as adults 18 years of age and older, except that fever and vomiting had a frequency category of very common (≥1/10) and nausea had a frequency category of common (≥1/1000 to <1/10).

Adults with HSCT have similar frequencies of adverse reactions as adults 18 years and older, except that fever, diarrhea and vomiting had a frequency category of very common (≥1/10).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560

Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com
Website: www.pfizersafetyreporting.com

4.9. Overdose

Overdose with PREVENAR 20 is unlikely due to its presentation as a pre-filled syringe.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological class, therapeutic class

Vaccines (J07AL02)

Mechanism of action

S. pneumoniae (pneumococcus) is a gram-positive diplococcus that can cause invasive disease including meningitis, sepsis, and pneumonia with bacteremia and noninvasive disease such as pneumonia without bacteremia and acute otitis media (AOM). Over 100 different serotypes of pneumococcus have been identified.

PREVENAR 20 contains 20 pneumococcal capsular polysaccharides all conjugated to CRM_{197} carrier protein, which modifies the immune response to the polysaccharide from a T-cell independent response to a T-cell dependent response. The T-cell dependent response leads to a higher antibody response, and induces antibodies that enhance opsonization, phagocytosis and killing of pneumococci to protect against pneumococcal disease, as well as generation of memory B-cells, allowing for an anamnestic (booster) response on re-exposure to the bacteria.

Vaccination with PREVENAR 20 induces serum antibody production and immunologic memory against the serotypes contained within the vaccine. Antibodies to some polysaccharides may cross-react with related types and provide some protection against additional serotypes.

In adults, the levels of circulating antibodies, and in pediatric populations the serotype-specific levels, that correlate with protection against pneumococcal disease have not been clearly defined.

Disease burden for infants and children

Despite reductions in disease due to 7vPnC (pneumococcal 7-valent conjugate vaccine) and 13vPnC, a significant burden of pediatric pneumococcal disease remains, with a substantial proportion caused by the PREVENAR 20 serotypes – mainly the 7 additional PREVENAR 20 serotypes. By 2015, although pediatric pneumococcal deaths had declined by an estimated 51% since 2000, *S pneumoniae* still accounted for 3.7 million cases of severe pneumococcal disease and 294,000 deaths in children <5 years of age globally. The incidence of pneumococcal disease is age specific, with the highest incidence among children <5 years of age (particularly among <2 years of age) and older adults. *S pneumoniae* was included as 1 of the 12 World Health Organization (WHO) global priority pathogens in 2017 because of its high burden of disease and increasing rates of antibiotic resistance in many countries. The incidence of pneumococcal disease varies by clinical presentation, with the majority of cases due to mucosal diseases, including non-bacteremic pneumonia and otitis media. Invasive pneumococcal disease (IPD), including meningitis and sepsis, are less common but more severe, often associated with a high case fatality ratio and risk of long-term sequelae.

The unmet need for pediatric pneumococcal disease is substantial. In the United States (US), a recent study estimated 940,605 cases of IPD, community-acquired pneumonia (CAP), and AOM and 72 deaths among US children <5 years of age were caused by PREVENAR 20 serotypes in 2020. A modeling analysis of 9 European countries (Austria, Finland, France, Germany, Italy, Netherlands, Spain, Sweden, United Kingdom) estimated that 1082 IPD cases, 65,124 pneumonia cases, 780,236 AOM cases per year in children <5 years of age are caused by PREVENAR 20 serotypes, representing an annual direct healthcare cost of approximately €166 million per year.

The 7 additional serotypes were not only selected based on their prevalence in IPD and mucosal disease around the world, but also on characteristics that make them medically important, including antibiotic resistance (10A, 11A, 15B and the closely related 15C, 22F, and 33F), association with outbreaks (8, 12F), and a tendency to greater disease severity such as an association with meningitis or higher case fatality rates (10A, 11A, 12F, 15B/C, 22F, 33F) (Table 3).

Table 3. Epidemiological Characteristics of the 7 Additional Pneumococcal Serotypes of PREVENAR 20 in Children

Epidemiological Characteristic	8	10A	11A	12F	15B/C*	22F	33F
Cause of any IPD[a]**	++	++	+	++	+++	++	++
Case fatality ratio for IPD[b]	+	++++	++	++	++++	+++	++
Cause of any non-IPD[a]**	+	+++	+	+	++++	NR	+
Cause of pneumococcal meningitis**	+++	++	+	++	++++	+++	++
Cause of pneumococcal bacteremic pneumonia[a]	++	++	+	++	++	+	++

Table 3. Epidemiological Characteristics of the 7 Additional Pneumococcal Serotypes of PREVENAR 20 in Children

Cause of pneumococcal AOM[a]	+	+++	+++	+	++++	++	+

* 15B and 15C are reported together.
** In settings with later-period 13vPnC programs.
a. +: ≤2%; ++: 3-5%; +++: 6-8%; ++++: >8%.
b. +: all studies ≤1%; ++: ≥1 study 2-5%; +++: ≥1 study >5%; ++++: all studies >5% or 1 study >10%.

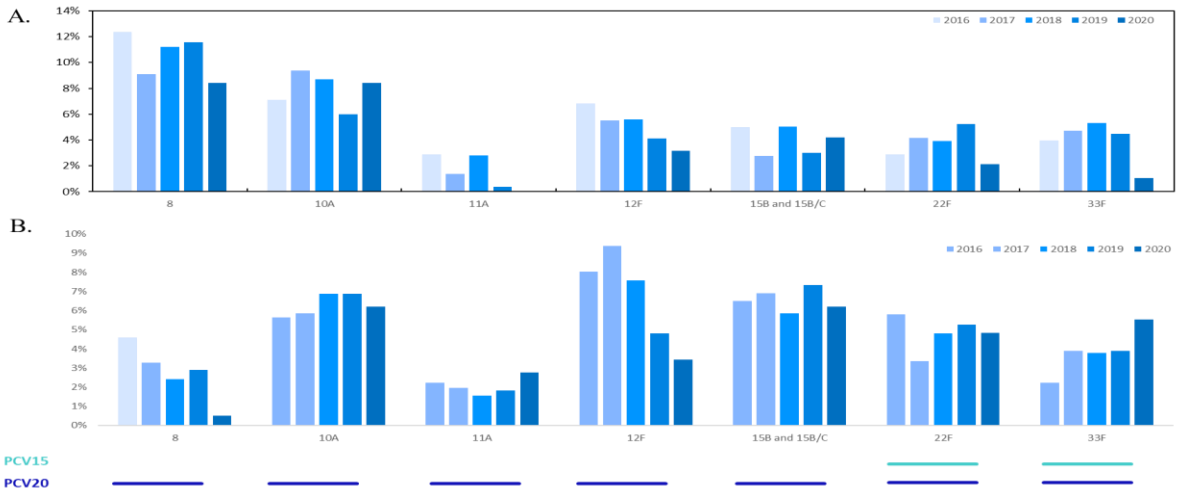
Invasive pneumococcal disease

Serotypes causing pneumococcal disease are evolving, highlighting the need to expand protection against additional medically relevant serotypes and to maintain protection against the 13vPnC serotypes. A global meta-analysis of surveillance data from 42 sites with mature 13vPnC pediatric programs estimated that the 7 additional PREVENAR 20 serotypes account for approximately 36% of IPD cases in children <5 years of age. Eight serotypes accounted for approximately 52% of IPD in 13vPnC-using sites, including serotypes 15B/C (9.5%), 12F (5.8%), 10A (5.5%), 22F (5.3%), and 33F (4.3%).

In the USA, the serotypes causing pneumococcal disease are evolving, highlighting the need to expand protection against additional medically relevant serotypes as well as the need to maintain the protection achieved against the 13vPnC serotypes. Based on the US Active Bacterial Core surveillance (ABCs) system, PREVENAR 20 serotypes (plus cross-reactive 6C) were responsible for 53% of IPD among US children <5 years of age in 2018–19. The 7 additional serotypes were responsible for 32% of IPD, and the 13vPnC serotypes (plus 6C), 21%.

In Europe, an estimated 35% and 33% of IPD in 2019 were due to the 7 additional PREVENAR 20 serotypes among children <1 and 1 through 4 years of age, respectively, based on IPD surveillance from 26 European countries. The most common PREVENAR 20 serotypes were 8 and 10A among children <1 year of age and 10A and 15B/C among children 1 to 4 years of age in 2019 (Figure 1). In 2020 during the COVID-19 pandemic, a substantial decline in the number of IPD cases was observed but IPD rates have rebounded to at or above pre-COVID levels.

Figure 1. Proportion of IPD Due to PREVENAR 20 non-13vPnC Serotypes Among Children Less Than 1 Year of Age (A) and 1 to 4 Years of Age (B) in 26 Countries in Europe[a,b]



a. Proportions based on reported serotype-specific IPD cases from Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom.
b. Countries may report 15B and the closely related, cross-reactive serotype 15C separately or as a group. If grouped, 15B/C included in analysis.

Pneumonia

A substantial burden of bacteremic pneumonia including parapneumonic effusions and empyemas are caused by the PREVENAR 20 serotypes. While the serotype distribution of non-bacteremic pneumonia currently cannot be determined due to the lack of sensitive and specific diagnostic tests, evidence of the substantial proportion of bacteremic pneumonia due to the PREVENAR 20 serotypes and the impact of pneumococcal conjugate vaccines on all-cause pneumonia suggest PREVENAR 20 will likely help protect against childhood pneumonia.

Acute otitis media

AOM is a common infection in young children worldwide — one of the most common reasons for clinic visits and antimicrobial prescriptions in developed countries. The majority of AOM is due to bacteria, and among bacterial OM globally, *S pneumoniae* is one of the most common causes, causing 24% and approximately 26% of cases as reported from studies in the USA and Israel, respectively, during the 13vPnC period. Studies in France, Germany, Israel, and USA during the 13vPnC period found that 12% to 31% of acute or complicated pneumococcal OM cases were caused by the 7 additional PREVENAR 20 serotypes not covered by 13vPnC. While mortality is rare, certain clinical presentations of OM, especially those caused by *S pneumoniae*, are associated with significant morbidity given their severity, complexity, and propensity for sequelae including hearing loss.

Disease burden in older children

Although the incidence of pneumococcal disease is lower in older children and adolescents than in younger children, healthy older children and adolescents still have some risk of pneumococcal disease. Incidence, severity, and case fatality rates are significantly elevated among older children with risk factors for pneumococcal disease, such as chronic medical conditions, cochlear implants, asthma, and SCD, and particularly among children with immunosuppression or immunodeficiencies. Risk of 13vPnC-type IPD was 27, 122, and 822 times higher among US children 6 through 18 years of age with SCD, HIV/AIDS, and hematologic malignancies, respectively, than among those without these conditions.

Disease burden for adults

Pneumonia is the most common clinical presentation of pneumococcal disease in adults.

The reported incidence of CAP and IPD in Europe varies by country, increases with age from 50 years and is highest in individuals 65 years of age and older. *S. pneumoniae* is the most frequent bacterial cause of CAP and has been estimated to be responsible for approximately 30% of all CAP cases requiring hospitalization in adults in developed countries, with the majority of cases considered non-bacteremic.

Bacteremic pneumonia (approximately 80% of IPD in adults), bacteremia without a focus, and meningitis are the most common manifestations of IPD in adults. Based on surveillance data, in the context of established childhood pneumococcal conjugate vaccination programs, the pneumococcal serotypes in PREVENAR 20 may be responsible for at least 63% to 76% (depending on country) of IPD in older adults in Europe.

The risk for CAP and IPD in adults also increases with chronic underlying medical conditions, specifically, anatomical or functional asplenia, diabetes mellitus, asthma, chronic cardiovascular, pulmonary, kidney or liver disease, and it is highest in those who are immune-suppressed such as those with malignant hematological diseases or HIV infection.

PREVENAR 20 effectiveness

Effectiveness studies using PREVENAR 20 were not conducted.

The efficacy and effectiveness of 13vPnC are relevant to PREVENAR 20, since the vaccines are manufactured similarly and contain 13 of the same polysaccharide conjugates.

13vPnC effectiveness in children

Invasive pneumococcal disease

Four years after the introduction of 7vPnC as a two dose primary series plus booster dose in the second year of life and with a 94% vaccine uptake a 98% (95% CI 95; 99) reduction of disease caused by the 7 vaccine serotypes was reported in England and Wales. Subsequently, four years following the switch to 13vPnC, the additional reduction in incidence of IPD due to the 7 serotypes in 7vPnC ranged from 76% in children less than 2 years of age to 91% in children 5-14 years of age. The serotype specific reductions for each of the 5 additional serotypes in 13vPnC (no cases of serotype 5 IPD were observed) by age group are shown in Table 4 and ranged from 68% (serotype 3) to 100% (serotype 6A) for children less than 5 years of age. Significant incidence reductions were also observed in older age groups who had not been vaccinated with 13vPnC (indirect effect).

Table 4. Serotype Specific Number of Cases and Incidence Reductions of IPD in 2013/14 Compared to 2008/09-2009/10 (2008/10) by Age in England and Wales

	<5 years of age			5 to 64 years of age			≥65 years of age		
	2008-10§	**2013/14§**	**% Incidence reduction (95% CI*)**	**2008-10§**	**2013/14§**	**% Incidence reduction (95% CI*)**	**2008-10§**	**2013/14§**	**% Incidence reduction (95% CI*)**
Additional serotypes covered by 13vPnC									
1	59 (54)	5 (5)	91% (98%; 68%)**	458 (382)	77 (71)	83% (88%; 74%)**	102 (89)	13 (13)	87% (94%; 72%)**
3	26 (24)	8 (8)	68% (89%; 6%)	178 (148)	73 (68)	59% (72%; 38%)**	256 (224)	143 (146)	44% (57%; 27%)**
6A	10 (9)	0 (0)	100% (100%; 62%)**	53 (44)	5 (5)	90% (97%; 56%)**	94 (82)	5 (5)	95% (99%; 81%)**
7F	90 (82)	8 (8)	91% (97%; 74%)**	430 (361)	160 (148)	63% (71%; 50%)**	173 (152)	75 (77)	56% (70%; 37%)**
19A	85 (77)	7 (7)	91% (97%; 75%)**	225 (191)	104 (97)	54% (65%; 32%)**	279 (246)	97 (99)	65% (75%; 53%)**

§ Corrected for proportion of samples serotyped, missing age, denominator compared with 2009/10, and for the trend in total invasive pneumococcal disease up to 2009/10 (after which no trend correction was applied).
* 95% CI inflated from a Poisson interval based on over-dispersion of 2·1 seen from modelling of 2000-06 pre-7vPnC all IPD data.
** p<0·005 to cover 6A where p=0.002.

Otitis media (OM)

In a two dose primary series plus booster dose in the second year of life the impact of 13vPnC on OM was documented in a population-based active-surveillance system in Israel middle ear fluid collected via tympanocentesis from children less than 2 years of age with OM. Following the introduction of 7vPnC and subsequently 13vPnC there was a decline in incidence of 96% of OM for the 7vPnC serotypes plus serotype 6A and a decline in incidence of 85% for the additional serotypes 1, 3, 5, 7F, and 19A in 13vPnC.

In a prospective, population-based, long-term surveillance study conducted in Israel between 2004 and 2015 following the introduction of 7vPnC and subsequently 13vPnC, reductions of non-pneumococcal bacteria isolated from children <3 years of age with OM were 75% for all NTHi cases, and 81% and 62% for cases of OM due to *M. catarrhalis* and *S. pyogenes*, respectively.

Pneumonia

In a multicenter observational study in France comparing the periods before and after the switch from 7vPnC to 13vPnC, there was 16% reduction in all community-acquired pneumonia (CAP) cases in emergency departments in children 1 month to 15 years of age. Reductions were 53% ($p<0.001$) for CAP cases with pleural effusion and 63% ($p<0.001$) for microbiologically confirmed pneumococcal CAP cases. In the second year after the introduction of 13vPnC the total number of CAP cases due to the 6 additional vaccine serotypes in 13vPnC was reduced by 74% (27 to 7 isolates).

In an ongoing surveillance system (2002 to 2013) to document the impact of 7vPnC and subsequently 13vPnC on CAP in children less than 5 years in Southern Israel using a 2 - dose primary series with a booster dose in the second year of life, there was a reduction of 68% (95% CI 73; 61) in outpatient visits and 32% (95% CI 39; 22) in hospitalizations for alveolar CAP following the introduction of 13vPnC when compared to the period before the introduction of 7vPnC was introduced.

Reduction of antimicrobial resistance (AMR)

Following the introduction of 7vPnC and subsequently 13vPnC, a reduction in AMR has been shown as a result of direct reduction of serotypes and clones associated with AMR from the population (including 19A), reduction of transmission (herd effects), and reduction in the use of antimicrobial agents.

In a double–blind, randomized, controlled study in Israel comparing 7vPnC and 13vPnC that reported the acquisition of *S. pneumoniae,* reductions of serotypes 19A, 19F, and 6A not susceptible to either penicillin, erythromycin, clindamycin, penicillin plus erythromycin, or multiple drugs (≥3 antibiotics) ranged between 34% and 62% depending on serotype and antibiotic.

Analyses of data from the United States Centers for Disease Control and Prevention evaluated temporal trends for four antibiotic classes and showed that compared to 2009 (the last year of 7vPnC use in the US, following which it was replaced with 13vPnC), by 2013 the annual incidence of IPD due to pneumococci non-susceptible to macrolides, cephalosporins, penicillins, and tetracyclines had decreased by 63%, 81%, 83%, and 81% in children less than 5 years of age and 24%, 49%, 57%, and 53% in persons 65 years of age and older.

13vPnC effect on nasopharyngeal carriage

In a surveillance study in France in children presenting with AOM, changes in nasopharyngeal (NP) carriage of pneumococcal serotypes were evaluated following the introduction of 7vPnC and subsequently 13vPnC. 13vPnC significantly reduced NP carriage of the 6 additional serotypes (and serotype 6C) combined and individual serotypes 6C, 7F, 19A when compared with 7vPnC. A reduction in carriage was also seen for serotype 3 (2.5% vs 1.1%; p=0.1). There was no carriage of serotypes 1 or 5 observed.

The effect of pneumococcal conjugate vaccination on NP carriage was studied in a randomized double-blind study (6096A1-3006) in which infants received either 13vPnC or 7vPnC at 2, 4, 6 and 12 months of age in Israel. 13vPnC significantly reduced newly identified NP acquisition of the 6 additional serotypes (and serotype 6C) combined and of individual serotypes 1, 6A, 6C, 7F, 19A when compared with 7vPnC. There was no reduction seen in serotype 3 and for serotype 5 the colonization was too infrequent to assess impact. For 6 of the remaining 7 common serotypes, similar rates of NP acquisition were observed in both vaccine groups; for serotype 19F a significant reduction was observed.

13vPnC efficacy study in adults 65 years of age and older

Efficacy against vaccine-type (VT) pneumococcal CAP and IPD was assessed in a large-scale, randomized, double-blind, placebo-controlled study (Community-Acquired Pneumonia Immunization Trial in Adults [CAPiTA]) in the Netherlands. A total of 84,496 participants 65 years of age and older received a single vaccination of either 13vPnC or placebo in a 1:1 randomization.

The CAPiTA study enrolled participants 65 years of age and older whose demographic and health characteristics may differ from those seeking vaccination. Chronic medical conditions (asthma, diabetes, heart, liver, and/or lung diseases) were reported in 42.3% of study participants at baseline.

A first episode of hospitalized, chest X-ray-confirmed pneumonia was identified in about 2% of this population (n=1814 participants) of which 329 cases were confirmed pneumococcal CAP and 182 cases were VT pneumococcal CAP in the per-protocol and modified intent-to-treat (mITT) populations.

Efficacy was demonstrated for the primary and secondary endpoints in the per-protocol population (Table 5).

Table 5. Vaccine Efficacy for the Primary and Secondary Endpoint of the CAPiTA Study (Per-protocol Population)

Efficacy Endpoint	Total Number of Episodes	Vaccine Group		VE (%)	(95.2% CI)	p-value
		13vPnC	Placebo			
		n	n			
Primary endpoint						
First case of confirmed VT pneumococcal CAP	139	49	90	45.6	(21.8, 62.5)	0.0006
Secondary endpoints						
First episode of confirmed NB/NI VT pneumococcal CAP	93	33	60	45	(14.2, 65.3)	0.0067
First episode of VT-IPD	35	7	28	75	(41.1, 90.9)	0.0005

Abbreviations: CAP=community-acquired pneumonia; CAPiTA=Community-Acquired Pneumonia Immunization Trial in Adults; CI=confidence interval; n=number of participants; NB/NI=non-bacteremic/noninvasive; IPD=invasive pneumococcal disease; 13vPnC=13-valent pneumococcal conjugate vaccine; VE=vaccine efficacy; VT=vaccine-type.

The duration of protective efficacy against a first episode of VT pneumococcal CAP, NB/NI VT pneumococcal CAP, and VT-IPD extended throughout the 4-year study.

The study was not designed to demonstrate efficacy in subgroups, and the number of participants 85 years of age and older was not sufficient to demonstrate efficacy in this age group.

A post-hoc analysis was used to estimate the following public health outcomes against clinical CAP (as defined in the CAPiTA study, and based on clinical findings regardless of radiologic infiltrate or etiologic confirmation): VE, incidence rate reduction (IRR), and number needed to vaccinate (NNV) (Table 6).

IRR, also referred to as vaccine-preventable disease incidence, is the number of cases of vaccine-preventable disease per 100,000 person-years of observation.

In Table 6, NNV is a measure that quantifies the number of people that need to be vaccinated in order to prevent one clinical CAP case.

Table 6. Vaccine Efficacy Against Clinical CAP*

	Episodes		VE[a] % (95% CI) (1-sided p-value)	Incidence per 100,000 PYO		IRR[b] (95% CI)	NNV[c]
	13vPnC	Placebo		13vPnC	Placebo		
All episodes analysis	1375	1495	8.1 (-0.6, 16.1) (0.034)	819.1	891.2	72.2 (-5.3, 149.6)	277
First episode analysis	1126	1214	7.3 (-0.4, 14.4) (0.031)	670.7	723.7	53.0 (-2.7, 108.7)	378

Abbreviations: CAP=community-acquired pneumonia; CI=confidence interval; IRR=incidence rate reduction; NNV=number needed to vaccinate; 13vPnC=13-valent pneumococcal conjugate vaccine; PYO=person-years of observation; VE=vaccine efficacy.

* Patients with at least 2 of the following: cough; purulent sputum, temperature >38°C or <36.1°C; pneumonia (auscultatory findings); leukocytosis; C-reactive protein value >3 times the upper limit of normal; hypoxemia with a partial oxygen pressure <60 mm Hg while breathing room air.

a. A Poisson regression model with random effects was used to calculate VE.

b. Per 100,000 person-years of observation. IRR is calculated as the incidence in the placebo group minus the incidence in the vaccine group, and was mathematically equivalent to VE × the incidence in the placebo group.

c. Based on a 5-year duration of protection. NNV is not a rate but instead indicates the number of cases prevented for a given number of persons vaccinated. NNV also incorporates the length of the trial or duration of protection and is calculated as 1 divided by the product of the IRR and duration of protection (or length of trial) (=1/[IRR × duration]).

PREVENAR 20 immunogenicity clinical studies in infants, children, and adolescents

Approval of PREVENAR 20 for the pediatric population was based on comparing the totality of the immune responses in infants after receiving PREVENAR 20 to the immune responses after receiving 13vPnC. The comparison, following the WHO guideline, included the percentage of participants with predefined IgG (immunoglobulin G) concentrations and IgG geometric mean concentrations (GMCs). The noninferiority criteria and other supportive data were agreed by the United States Food and Drug Administration (FDA) and Committee for Medicinal Products for Human Use (CHMP). This approach is largely based upon the observed relationship between immunogenicity and IPD efficacy from 3 placebo-controlled trials with either 7vPnC (see above section for 13vPnC Effectiveness) or the investigational 9-valent CRM_{197} conjugate polysaccharide vaccine conducted in Navajo and White Mountain Apache Indian infants (cluster randomized trial), infants in Soweto, South Africa, and infants in the Northern California Kaiser Permanente (NCKP) health organization. The predefined IgG concentration corresponding to 0.35 µg/mL in the WHO enzyme-linked immunosorbent assay (ELISA) is only applicable at the population level and cannot be used to predict individual or serotype-specific protection against IPD.

Immune responses elicited by PREVENAR 20 and 13vPnC in children were measured using a serotype-specific multiplex direct-binding Luminex immunoassay (dLIA), designed to determine the concentration of specific polysaccharide-binding IgG antibodies, and opsonophagocytic activity (OPA) assays to measure serotype-specific functional OPA titers. The Pfizer LUMINEX assay (dLIA) to measure IgG has been bridged to the standard ELISA assay.

PREVENAR 20 clinical trials in infants, children, and adolescents

Clinical studies evaluating the immunogenicity of PREVENAR 20 were conducted in infants following a 3-dose series at 2, 4 and 11 to 12 months of aged (2 infant doses and toddler dose) in a Phase 3 trial (Study 1012) or 4-dose series (3 infant doses and a toddler dose) at 2, 4, 6, and 12 to 15 months of age have been conducted in one randomized Phase 2 trial (Study 1003) and one Phase 3 trial (Study 1011) in USA/Puerto Rico.

The full infant immunization series for PREVENAR 20 consist of 3-dose with an alternative 4-dose immunization series.

Pneumococcal immune responses after 2 and 3 doses in a 3-dose vaccination series

In Study 1012, the immunogenicity of PREVENAR 20 was evaluated in infants when administered in a series of 2 infant doses and 1 toddler dose in infants enrolled from Europe and Australia. The study enrolled infants 2 months (≥42 to ≤112 days) of age and born at >36 weeks of gestation. Participants were randomized (1:1) to receive either PREVENAR 20 or 13vPnC with the first dose given at 42 to 112 days of age, a second dose given approximately 2 months later, and the third dose given at approximately 11 to 12 months of age. Participants received concomitant vaccines at these visits.

PREVENAR 20 elicited immune responses, as assessed by IgG GMCs, percentages of participants with predefined IgG concentrations, and OPA geometric mean titers (GMTs) for all 20 serotypes contained in the vaccine. The observed IgG GMCs and percentages of participants with predefined IgG concentrations 1 month after the third (last) dose of PREVENAR 20 were generally comparable to the 13vPnC group for the 13 matched serotypes and higher for the 7 additional serotypes (Table 7).

One month after the 2 infant doses, the observed IgG GMCs were generally comparable for most serotypes to the 13vPnC group and the percentages of participants with predefined IgG concentrations for the 13 matched serotypes were generally lower in the PREVENAR 20 group than the 13vPnC group (Table 8). The immune responses to the additional 7 serotypes were higher in the PREVENAR 20 group than the 13vPnC group after the 2nd dose.

Table 7. Percentages of Participants With Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month After Dose 3 of a 3-Dose Series, Study 1012[a]

	Percentages of Participants With Predefined IgG Concentrations[b]			IgG GMCs		
	PREVENAR 20 N[c]=493-495	13vPnC N[c]=501-502	PREVENAR 20 – 13vPnC	PREVENAR 20 N[c]=493-495	13vPnC N[c]=501-502	PREVENAR 20/13vPnC
	%	%	% (95% CI[d])	GMC[e]	GMC[e]	GMR[e] (95% CI[e])
Serotypes						
1	97.2	98.2	-1.0 (-3.1, 0.9)	1.71	2.53	0.67 (0.60, 0.75)
3	82.6	93.2	-10.6 (-14.7, -6.7)	0.72	1.09	0.66 (0.59, 0.73)
4	99.2	99.2	0.0 (-1.4, 1.3)	4.11	5.36	0.77 (0.68, 0.87)

5	98.4	98.0	0.4 (-1.4, 2.2)	1.74	2.41	0.72 (0.64, 0.81)
6A	98.8	98.8	0.0 (-1.6, 1.5)	7.75	11.82	0.66 (0.57, 0.75)
6B	98.4	97.6	0.8 (-1.1, 2.7)	2.64	4.63	0.57 (0.48, 0.67)
7F	99.6	100.0	-0.4 (-1.5, 0.4)	3.61	4.93	0.73 (0.67, 0.80)
9V	99.2	98.8	0.4 (-1.0, 1.9)	3.68	5.04	0.73 (0.66, 0.81)
14	96.6	98.0	-1.5 (-3.7, 0.6)	4.52	5.66	0.80 (0.69, 0.92)
18C	99.2	98.2	1.0 (-0.5, 2.7)	2.71	3.61	0.75 (0.67, 0.84)
19A	99.6	99.6	0.0 (-1.1, 1.1)	4.51	5.49	0.82 (0.72, 0.93)
19F	99.6	99.4	0.2 (-0.9, 1.4)	6.19	8.08	0.77 (0.68, 0.87)
23F	96.4	97.2	-0.9 (-3.2, 1.4)	2.64	4.40	0.60 (0.52, 0.69)
Additional Serotypes						
8	99.2	3.6	95.6 (93.4, 97.1)	3.57	0.03	113.37 (100.05, 128.46)
10A	97.8	1.6	96.2 (94.1, 97.6)	4.86	0.01	423.02 (372.25, 480.73)
11A	98.4	4.6	93.8 (91.3, 95.6)	3.74	0.02	229.66 (199.06, 264.96)
12F	96.6	0.2	96.4 (94.3, 97.7)	1.86	0.01	224.31 (204.73, 245.76)
15B	99.4	4.8	94.6 (92.3, 96.3)	13.09	0.02	527.47 (465.44, 597.77)
22F	99.2	1.4	97.8 (96.1, 98.8)	9.27	0.00	2193.09 (1908.27, 2520.41)
33F	98.6	1.8	96.8 (94.8, 98.0)	6.37	0.01	530.53 (470.15, 598.66)

Abbreviations: CI=confidence interval; GMC=geometric mean concentration; GMR=geometric mean ratio; IgG=immunoglobulin G; LLOQ=lower limit of quantitation.
Note: Noninferiority for a matched serotype was concluded if the lower bound of the 2-sided 95% CI for the percentage difference (PREVENAR 20 - 13vPnC) was > -10% or the lower bound of the 2-sided 95% CI for the GMR (PREVENAR 20 to 13vPnC) was >0.5 for that serotype.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
a. Study 1012 was conducted in Europe and Australia (NCT04546425).
b. The predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.
c. N=Number of participants with valid IgG concentrations.
d. Two-sided CI based on the Miettinen and Nurminen method.
e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (PREVENAR 20 - 13vPnC) of logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

Table 8. Percentage of Participants With Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month After Dose 2 of a 3-Dose Series, Study 1012[a]

	Percentages of Participants With Predefined IgG Concentrations[b]			IgG GMCs		
	PREVENAR 20 N[c]=564-567	13vPnC N[c]=561-562	PREVENAR 20 – 13vPnC	PREVENAR 20 N[c]=564-567	13vPnC N[c]=561-562	PREVENAR 20/13vPnC
	%	%	% (95% CI[d])	GMC[e]	GMC[e]	GMR (95% CI[e])
Serotypes						
1	70.7	84.2	-13.5 (-18.3, -8.7)	0.57	0.93	0.61 (0.54, 0.69)
3	58.0	75.8	-17.9 (-23.2, -12.4)	0.41	0.58	0.71 (0.64, 0.79)
4	68.6	79.5	-11.0 (-16.0, -5.9)	0.55	0.92	0.60 (0.52, 0.69)
5	63.4	76.0	-12.6 (-17.8, -7.2)	0.34	0.56	0.60 (0.52, 0.70)
6A	59.5	73.7	-14.1 (-19.5, -8.6)	0.45	0.84	0.54 0.45, 0.65)
6B	20.7	36.5	-15.8 (-21.0, -10.6)	0.03	0.06	0.51 (0.43, 0.61)
7F	87.6	90.2	-2.6 (-6.3, 1.1)	1.02	1.41	0.72 (0.64, 0.80)
9V	60.2	74.6	-14.3 (-19.7, -8.9)	0.45	0.77	0.59 (0.50, 0.69)
14	78.6	81.9	-3.3 (-7.9, 1.4)	1.05	1.28	0.82 (0.70, 0.96)

18C	71.0	76.5	-5.5 (-10.6, -0.4)	0.69	0.87	0.79 (0.67, 0.92)
19A	92.2	94.0	-1.7 (-4.8, 1.3)	0.67	1.13	0.59 (0.51, 0.69)
19F	94.3	95.7	-1.4 (-4.0, 1.2)	2.21	3.06	0.72 (0.64, 0.82)
23F	23.5	41.8	-18.3 (-23.6, -12.9)	0.13	0.25	0.52 (0.44, 0.62)
Additional Serotypes						
8	96.5	2.9	93.6 (91.2, 95.4)	1.62	0.02	91.19 (81.19, 102.43)
10A	28.9	2.7	26.3 (22.4, 30.3)	0.16	0.02	8.38 (7.20, 9.76)
11A	94.2	2.0	92.2 (89.7, 94.2)	1.62	0.02	74.53 (65.99, 84.17)
12F	30.3	0.2	30.2 (26.5, 34.1)	0.15	0.01	17.91 (15.66, 20.48)
15B	94.3	8.5	85.8 (82.5, 88.5)	3.33	0.04	83.56 (71.77, 97.28)
22F	94.4	2.0	92.4 (89.9, 94.3)	2.25	0.01	337.08 (287.86, 394.72)
33F	46.8	2.7	44.2 (39.8, 48.5)	0.31	0.03	12.19 (10.55, 14.09)

Abbreviations: CI=confidence interval; GMC=geometric mean concentration; GMR=geometric mean ratio; IgG=immunoglobulin G; LLOQ=lower limit of quantitation.
Note: Noninferiority for a matched serotype was concluded if the lower bound of the 2-sided 95% CI for the percentage difference (PREVENAR 20 – 13vPnC) was > -10% or the lower bound of the 2-sided 95% CI for the GMR (PREVENAR 20 to 13vPnC) was >0.5 for that serotype.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
a. Study 1012 was conducted in Europe and Australia (NCT04546425).
b. The Predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.
c. N=Number of participants with valid IgG concentrations.
d. Two-sided CI based on the Miettinen and Nurminen method.
e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (PREVENAR 20 – 13vPnC) of the logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

OPA responses after 2 and 3 doses in a 3-dose vaccination series

The OPA GMTs for the 13 matched serotypes at 1 month after Dose 2 and 1 month after Dose 3 in the PREVENAR 20 group were generally similar to the observed OPA GMTs in the 13vPnC group for most serotypes. The observed OPA GMTs were lower for serotype 6B after Dose 2 and serotype 1 after Dose 3 in the PREVENAR 20 group. OPA GMTs were higher after Dose 3 than after Dose 2 for all serotypes. The observed OPA GMTs for the 7 additional serotypes, both 1 month after the second dose and 1 month after the third dose were substantially higher in the PREVENAR 20 group than those in the 13vPnC group (Table 9).

Table 9. Pneumococcal OPA GMTs One Month After Doses 2 and 3 in a 3-Dose Series, Study 1012[a]

	PREVENAR 20 N[b]=96-116 After Dose 2	**13vPnC N[b]=97-118 After Dose 2**	**PREVENAR 20 N[b]=72-106 After Dose 3**	**13vPnC N[b]=92-109 After Dose 3**
	GMT[c] (95% CI[c])	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**
Serotypes				
1	14 (12, 16)	23 (19, 28)	54 (43, 69)	101 (79, 129)
3	31 (26, 36)	40 (34, 47)	99 (84, 117)	129 (111, 150)
4	333 (270, 413)	391 (314, 486)	904 (752, 1086)	992 (777, 1266)
5	21 (18, 23)	27 (23, 31)	60 (50, 72)	82 (66, 101)
6A	347 (273, 441)	409 (318, 527)	1101 (897, 1350)	1304 (1018, 1671)
6B	54 (42, 71)	105 (76, 144)	537 (408, 706)	864 (664, 1125)
7F	858 (736, 1000)	895 (781, 1027)	1811 (1553, 2112)	2197 (1905, 2533)
9V	233 (182, 298)	285 (228, 358)	3254 (2596, 4079)	4544 (3681, 5610)
14	287 (215, 383)	360 (264, 489)	738 (606, 899)	926 (751, 1142)
18C	588 (467, 741)	719 (590, 876)	1296 (1048, 1602)	1870 (1489, 2348)
19A	57 (43, 75)	91 (69, 121)	754 (627, 907)	707 (558, 896)
19F	97 (81, 116)	117 (94, 146)	183 (140, 237)	258 (192, 347)
23F	59 (42, 84)	68 (48, 96)	697 (530, 917)	975 (734, 1296)

Additional Serotypes				
8	164 (133, 203)	17 (15, 18)	1398 (1088, 1796)	31 (25, 39)
10A	855 (610, 1199)	39 (34, 44)	3403 (2600, 4455)	69 (52, 91)
11A	327 (253, 423)	49 (47, 51)	2966 (2212, 3978)	66 (51, 85)
12F	4788 (3779, 6067)	26 (23, 28)	5501 (4499, 6725)	29 (25, 35)
15B	846 (605, 1183)	17 (15, 19)	2676 (1948, 3677)	23 (18, 30)
22F	4444 (3666, 5386)	10 (9, 11)	6523 (4848, 8777)	17 (13, 24)
33F	2373 (1759, 3202)	178 (163, 195)	11315 (8107, 15794)	708 (545, 920)

Abbreviations: GMT=geometric mean titer; LLOQ=lower limit of quantitation; OPA=opsonophagocytic activity.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
Note: OPA titers were determined on serum from randomly selected subsets of participants assuring equal representation of both vaccine groups.
a. Study 1012 was conducted in Europe and Australia (NCT04546425).
b. N=Number of participants with valid OPA titers.
c. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student's t distribution).

Booster responses after the last dose in a 3-dose infant vaccination series

PREVENAR 20 immune responses show boosting in IgG GMCs and percentage of participants with a predefined IgG concentrations 1 month after Dose 3, that are higher than concentrations before Dose 3, and also increased relative to the levels 1 month after Dose 2, indicating that a memory response was elicited by the 2 infant doses (see Tables 7 and 8). For all serotypes, the OPA responses also show a generally similar pattern of boosting as observed with the IgG responses, with priming evidenced by the robust OPA responses geometric mean fold rise (GMFRs) and the percentages of participants with a ≥4-fold rise in OPA titers) from before to one month after Dose 3. In summary, PREVENAR 20 elicits immune responses that are comparable to 13vPnC for the 13 matched serotypes and the 7 additional serotypes after the third (toddler) dose.

The totality of data show that a 3-dose series of PREVENAR 20 elicited immune responses expected to provide children protection against pneumococcal disease similar to that of 13vPnC for all 20 vaccine serotypes.

Pneumococcal IgG immune responses after 3 and 4 doses in a 4-dose vaccination series

In Study 1011, healthy infants 2 months (≥42 to ≤98 days) of age at the time of consent and born at >36 weeks of gestation, were enrolled. Participants were randomized (1:1) to receive either PREVENAR 20 or 13vPnC at approximately 2, 4, 6, and 12 to 15 months of age. Routine pediatric vaccinations were administered concomitantly (see Section 4.5).

The IgG GMCs for PREVENAR 20 were noninferior for all 13 matched serotypes to 13vPnC one month after Dose 4, based on a 2-fold noninferiority criterion. The IgG GMCs for all 7 additional serotypes were noninferior to the lowest IgG GMC among 13vPnC serotypes (other than serotype 3) based on a 2-fold noninferiority criterion. This was also the case for the IgG GMCs for PREVENAR 20, 1 month after Dose 3. Noninferiority of the percentages of participants with predefined serotype-specific IgG concentrations one month after Dose 3 was met for 8 of the 13 serotypes and missed by small margins for 4 serotypes (serotypes 1, 4, 9V and 23F) based on a 10% noninferiority criterion. Six of the 7 additional serotypes met the noninferiority criterion; serotype 12F missed the statistical noninferiority criterion. At both 1 month

after Dose 3 and 1 month after Dose 4, the IgG GMCs and percentages of participants with predefined IgG concentrations for all 7 additional serotypes, including serotype 12F, were much higher than the corresponding serotype responses in the 13vPnC group, consistent with statistically greater antibody levels based on the lower bounds of the nominal 2-sided 95% confidence limits (not adjusted for multiplicity).

Table 10. Percentage of Participants With Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month After Dose 4 of a 4-Dose Series, Study 1011[a]

	Percentages of Participants With Predefined IgG Concentrations[b]			IgG GMCs		
	PREVENAR 20 N[c]=753-755	13vPnC N[c]=744-745	PREVENAR 20 – 13vPnC	PREVENAR 20 N[c]=753-755	13vPnC N[c]=744-745	PREVENAR 20/13vPnC
	%	%	% (95% CI[d])	GMC[e]	GMC[e]	GMR (95% CI[e])
Serotypes						
1	94.3	97.2	-2.9 (-5.0, -0.8)	1.47	2.12	0.69 (0.63, 0.76)
3	73.6	85.8	-12.1 (-16.2, -8.1)	0.56	0.85	0.66 (0.61, 0.73)
4	98.9	99.1	-0.1 (-1.3, 1.0)	3.77	4.84	0.78 (0.70, 0.86)
5	97.9	97.7	0.2 (-1.4, 1.7)	1.87	2.51	0.74 (0.67, 0.82)
6A	99.5	99.7	-0.3 (-1.1, 0.5)	9.01	11.69	0.77 (0.70, 0.85)
6B	99.1	99.5	-0.4 (-1.4, 0.6)	4.01	5.74	0.70 (0.62, 0.79)
7F	99.5	99.9	-0.4 (-1.2, 0.3)	3.91	5.18	0.76 (0.70, 0.82)
9V	98.5	98.9	-0.4 (-1.6, 0.8)	3.44	4.30	0.80 (0.73, 0.88)
14	98.9	99.5	-0.5 (-1.6, 0.4)	5.68	6.34	0.90 (0.81, 1.00)
18C	98.9	98.7	0.3 (-0.9, 1.5)	3.46	4.69	0.74 (0.67, 0.82)
19A	99.9	99.7	0.1(-0.5, 0.9)	3.53	4.13	0.85 (0.77, 0.94)
19F	98.8	98.9	-0.1 (-1.3, 1.1)	5.01	5.79	0.86 (0.78, 0.96)
23F	97.2	98.1	-0.9 (-2.5, 0.7)	3.95	6.18	0.64 (0.57, 0.72)
Additional Serotypes[f]						
8	99.5	[f]	2.3(1.1, 3.8)	3.97	[f]	1.87 (1.71, 2.06)
10A	97.7	[f]	0.6 (-1.1, 2.3)	6.22	[f]	2.94 (2.64, 3.26)
11A	98.8	[f]	1.6 (0.2, 3.2)	3.53	[f]	1.67 (1.51, 1.84)
12F	95.2	[f]	-1.9 (-4.0, 0.0)	1.85	[f]	0.88 (0.79, 0.97)
15B	99.7	[f]	2.6 (1.4, 4.0)	12.59	[f]	5.95 (5.39, 6.55)
22F	99.6	[f]	2.4 (1.3, 3.9)	10.60	[f]	5.01 (4.54, 5.52)
33F	99.5	[f]	2.3 (1.1, 3.8)	9.31	[f]	4.40 (3.99, 4.85)

Abbreviations: CI=confidence interval; GMC=geometric mean concentration; GMR=geometric mean ratio; IgG=immunoglobulin G; LLOQ=lower limit of quantitation.
Note: Noninferiority for a serotype was concluded if the lower bound of the 2-sided 95% CI for the GMR (PREVENAR 20 to 13vPnC) was >0.5 for that serotype.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
a. Study 1011 was conducted in the United States and the territory of Puerto Rico (NCT04382326).
b. The Predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.
c. N=Number of participants with valid IgG concentrations.
d. Two-sided CI based on the Miettinen and Nurminen method.
e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (PREVENAR 20 – 13vPnC) of the logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).
f. For the GMRs and the percentage differences of the 7 additional serotypes, the IgG results from serotype 1 (vaccine serotype with the lowest GMC and percentage excluding serotype 3) in the 13vPnC group was used in the comparisons.

Table 11. Percentage of Participants With Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month After Dose 3 of a 4-Dose Series, Study 1011[a]

	Percentages of Participants With Predefined IgG Concentrations[b]			IgG GMCs		
	PREVENAR 20 N[c]=831-833	13vPnC N[c]=801 - 802	PREVENAR 20 – 13vPnC	PREVENA R 20 N[c]=831-833	13vPnC N[c]=801-802	PREVENAR 20/13vPnC
	%	%	% (95% CI[d])	GMC[e]	GMC[e]	GMR (95% CI[e])
Serotypes						
1	79.8	88.4	-8.6 (-12.1, -5.1)	0.74	1.14	0.65 (0.59, 0.72)
3	52.1	67.6	-15.5 (-20.1, -10.8)	0.36	0.51	0.70 (0.64, 0.76)
4	79.7	88.2	-8.4 (-12.0, -4.9)	0.75	1.08	0.70 (0.63, 0.78)
5	82.5	86.8	-4.3 (-7.8, -0.8)	0.66	0.96	0.69 (0.61, 0.77)

6A	93.5	95.9	-2.4 (-4.6, -0.2)	1.95	2.69	0.72 (0.65, 0.81)
6B	88.3	92.4	-4.1 (-7.0, -1.2)	0.61	1.02	0.60 (0.51, 0.70)
7F	96.6	97.6	-1.0 (-2.7, 0.7)	1.71	2.29	0.75 (0.69, 0.81)
9V	81.9	89.8	-7.9 (-11.3, -4.6)	0.87	1.21	0.72 (0.65, 0.80)
14	93.4	94.1	-0.8 (-3.1, 1.6)	2.16	2.72	0.79 (0.71, 0.89)
18C	92.6	93.1	-0.6 (-3.1, 1.9)	1.31	1.71	0.77 (0.70, 0.84)
19A	97.1	98.1	-1.0 (-2.6, 0.5)	0.72	0.91	0.79 (0.72, 0.86)
19F	96.9	96.6	0.2 (-1.5, 2.0)	1.59	2.00	0.79 (0.73, 0.86)
23F	77.9	85.5	-7.6 (-11.4, -3.9)	0.82	1.25	0.66 (0.58, 0.75)
Additional Serotypes[f]						
8	96.8	[f]	11.2 (8.6, 14.0)	1.80	[f]	1.98 (1.81, 2.16)
10A	82.2	[f]	-3.3 (-6.9, 0.3)	1.21	[f]	1.32 (1.18, 1.49)
11A	92.7	[f]	7.1 (4.2, 10.2)	1.39	[f]	1.52 (1.39, 1.67)
12F	67.5	[f]	-18.1 (-22.1, -14.0)	0.55	[f]	0.60 (0.54, 0.67)
15B	98.2	[f]	12.7 (10.2, 15.4)	4.40	[f]	4.82 (4.39, 5.30)
22F	98.3	[f]	12.8 (10.3, 15.5)	3.71	[f]	4.06 (3.68, 4.48)
33F	86.7	[f]	1.1 (-2.2, 4.5)	1.49	[f]	1.64 (1.46, 1.83)

Abbreviations: CI=confidence interval; GMC=geometric mean concentration; GMR=geometric mean ratio; IgG=immunoglobulin G; LLOQ=lower limit of quantitation.
Note: Noninferiority for a serotype was concluded if the lower bound of the 2-sided 95% CI for the percentage difference (PREVENAR 20 – 13vPnC) was > -10% or the lower bound of the 2-sided 95% CI for the GMR (PREVENAR 20 to 13vPnC) was >0.5 for that serotype.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

a. Study 1011 was conducted in the United States and the territory of Puerto Rico (NCT04382326).
b. The Predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.
c. N=Number of participants with valid IgG concentrations.
d. Two-sided CI based on the Miettinen and Nurminen method.
e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (PREVENAR 20 – 13vPnC) of the logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).
f. For the GMRs and the percentage differences of the 7 additional serotypes, the IgG results from serotype 19A and 23F (vaccine serotype with the lowest GMC and percentage, excluding serotype 3) in the 13vPnC group was used in the comparisons.

Additional Important Measures of Immune Response

OPA responses after 3 and 4 doses of PREVENAR 20

The OPA GMTs for the 13 matched serotypes 1 month after Dose 3 and 1 month after Dose 4 in the PREVENAR 20 group were generally similar to the OPA GMTs in the 13vPnC group for most serotypes, and the observed OPA GMTs were substantially higher for the 7 additional serotypes at both timepoints in the PREVENAR 20 group than in the 13vPnC group.

PREVENAR 20 elicits OPA immune responses that are comparable to 13vPnC for the 13 matched serotypes and the 7 additional serotypes after 3 doses in infants and Dose 4 in toddlers. PREVENAR 20 also elicits functional antibody to all 20 serotypes that was observed 1 month after Dose 3 and 1 month after Dose 4. PREVENAR 20 immune responses also show boosting after Dose 4, indicating that a memory response was elicited by the 3 infant doses.

Table 12. Pneumococcal OPA GMTs One Month After Dose 3 and Dose 4 of a 4-Dose Series– Study 1011[a]

	PREVENAR 20 N[b]=85-105 After Dose 3	**13vPnC N[b]=84-113 After Dose 3**	**PREVENAR 20 N[b]=80-99 After Dose 4**	**13vPnC N[b]=77-103 After Dose 4**
	GMT[c] (95% CI[c])	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**
Serotypes				

Table 12. Pneumococcal OPA GMTs One Month After Dose 3 and Dose 4 of a 4-Dose Series– Study 1011[a]

	PREVENAR 20 N[b]=85-105 After Dose 3	13vPnC N[b]=84-113 After Dose 3	PREVENAR 20 N[b]=80-99 After Dose 4	13vPnC N[b]=77-103 After Dose 4
	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])
1	26 (21, 33)	34 (27, 42)	36 (27, 48)	66 (50, 87)
3	51 (43, 61)	63 (53, 76)	62 (49, 78)	102 (86, 120)
4	339 (252, 455)	280 (207, 378)	621 (435, 887)	961 (714, 1294)
5	32 (27, 39)	39 (32, 47)	55 (45, 67)	69 (54, 87)
6A	910 (763, 1084)	936 (757, 1156)	1384 (1092, 1753)	1767(1329, 2348)
6B	318 (242, 419)	516 (409, 651)	666 (489, 906)	1211 (861, 1703)
7F	1222 (1020, 1465)	1149 (926, 1424)	2022 (1673, 2444)	2099 (1741, 2531)
9V	661 (482, 906)	594 (421, 838)	2609 (1913, 3558)	3210 (2500, 4123)
14	415 (323, 535)	420 (330, 535)	667 (523, 850)	593 (462, 761)
18C	1153 (910, 1460)	996 (754, 1317)	1973 (1472, 2643)	2425 (1914, 3072)
19A	108 (78, 149)	109 (79, 151)	844 (622, 1145)	1357 (1007, 1829)
19F	84 (67, 105)	116 (90, 149)	246 (179, 337)	373 (272, 513)
23F	255 (186, 350)	295 (215, 406)	827 (554, 1235)	1532 (1118, 2100)
Additional Serotypes				
8	665 (503, 880)	18 (17, 20)	1228 (901, 1673)	26 (21, 31)
10A	2558 (1869, 3501)	37 (33, 42)	3674 (2746, 4916)	57 (44, 74)
11A	289 (212, 395)	50 (46, 55)	2728 (1975, 3768)	69 (53, 89)
12F	7677 (5952, 9901)	28 (24, 33)	9320 (7037, 12343)	31 (26, 37)
15B	1560 (1090, 2233)	18 (16, 22)	3035 (2138, 4308)	23 (17, 30)
22F	6797 (5170, 8936)	9 (9, 9)	11077 (7956, 15422)	15 (11, 20)
33F	7388 (4803, 11365)	198 (177, 220)	19216 (13193, 27990)	363 (292, 451)

Abbreviations: GMT=geometric mean titer; LLOQ=lower limit of quantitation; OPA=opsonophagocytic activity.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
Note: OPA titers were determined on serum from randomly selected subsets of participants assuring equal representation of both vaccine groups.
a. Study 1011 was conducted in the United States and the territory of Puerto Rico (NCT04382326).
b. N=Number of participants with valid OPA titers.
c. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student's t distribution).

Boosting responses after the last dose in a 4-dose infant vaccination series

PREVENAR 20 shows boosting of IgG and OPA responses after Dose 4, indicating that a memory response was elicited by the 3 infant doses (see Tables 10, 11, and 12).

In summary, PREVENAR 20 elicits immune responses that are comparable to 13vPnC for the 13 matched serotypes and the 7 additional serotypes after 3 doses in infants and a fourth dose in toddlers. PREVENAR 20 also elicits functional antibody and booster responses to all 20 serotypes from 1 month after Dose 3 and 1 month after Dose 4. Thus, the totality of data show that a 4-dose series of PREVENAR 20 elicited immune responses expected to provide children protection against pneumococcal disease similar to that of 13vPnC for all 20 vaccine serotypes.

Children 12 months to less than 24 months of age Study B7471027 (Study 1027)

In a multicenter, randomized, partially double-blinded Phase 3 Study (Study 1027), the immunogenicity of a single booster dose or 2 doses of PREVENAR 20 in toddlers 12 months to less than 24 months of age with 2 prior infant doses of 13vPnC was evaluated.

Children 12 months to less than 24 months of age previously vaccinated with 13vPnC

In children 12 months to less than 24 months of age with 2 prior infant doses of 13vPnC, 356 participants were enrolled and randomized to receive either 1 or 2 toddler doses of PREVENAR 20, or a single dose of 13vPnC (control). In the group receiving 2 doses of PREVENAR 20, the second dose was given approximately 2 months after Dose 1. Robust IgG immune responses to the 13 matched serotypes were observed after 1 or 2 doses of PREVENAR 20 with the observed IgG GMCs numerically higher for most of the 13 matched serotypes after 1 dose of PREVENAR 20 than after 2 doses of PREVENAR 20. Substantial IgG immune responses to all 7 additional serotypes were observed after 1 or 2 doses of PREVENAR 20, with the IgG responses to the 7 additional serotypes numerically higher after 2 doses of PREVENAR 20 than after a single dose. OPA responses were elicited for all 20 serotypes after 1 or 2 doses of PREVENAR 20.

Children 15 months to less than 18 years of age (Study 1014)

In a multicenter, single-arm trial (Study 1014), participants were enrolled into the study by age group (approximately 200 participants per group) to receive a single-dose PREVENAR 20 as described below.

Children 15 months to less than 5 years of age previously vaccinated with 13vPnC

In 15 months to less than 24 months and 2 years to less than 5 years age groups, participants had been previously vaccinated with 3 or 4 doses of 13vPnC. Increases in IgG concentrations from before to 1 month after PREVENAR 20 were observed for all 20 vaccine serotypes in participants 15 months to less than 5 years of age with prior vaccination with 13vPnC. The observed IgG GMFRs to the 7 additional serotypes ranged from 27.9 to 1847.7 and increases in IgG GMCs were observed in all 20 vaccine serotypes from before to 1 month after PREVENAR 20 (Table 13). In children 15 months to less than 24 months of age 83.2% to 100.0% had predefined IgG concentrations to 6 of the 7 additional serotypes, serotype 12F was 40.0%.

Table 13: Pneumococcal IgG GMCs in Participants 15 Months to Less Than 5 Years of Age – Before and 1 Month After Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥15 to <24 Months N[b]=186-190		≥2 to <5 Years N[b]=179-183	
	Before Vaccination GMC[c] (95% CI[c])	After Vaccination GMC[c] (95% CI[c])	Before Vaccination GMC[c] (95% CI[c])	After Vaccination GMC[c] (95% CI[c])
Serotypes				
1	0.43 (0.37, 0.49)	1.46 (1.28, 1.67)	0.20 (0.17, 0.24)	4.21 (3.62, 4.90)
3	0.14 (0.12, 0.16)	0.54 (0.47, 0.61)	0.08 (0.06, 0.10)	1.21 (1.04, 1.42)
4	0.61 (0.52, 0.72)	2.59 (2.27, 2.96)	0.30 (0.25, 0.37)	8.37 (7.28, 9.62)
5	0.43 (0.36, 0.50)	1.53 (1.32, 1.77)	0.18 (0.15, 0.22)	5.09 (4.32, 5.99)
6A	1.61 (1.38, 1.88)	7.59 (6.67, 8.63)	0.71 (0.58, 0.88)	31.99 (27.85, 36.75)
6B	0.85 (0.71, 1.02)	4.27 (3.69, 4.94)	0.52 (0.42, 0.63)	17.78 (15.43, 20.48)
7F	1.17 (1.03, 1.33)	3.53 (3.16, 3.94)	0.51 (0.44, 0.60)	6.42 (5.69, 7.24)
9V	0.71 (0.61, 0.83)	2.70 (2.35, 3.09)	0.35 (0.28, 0.42)	7.94 (6.83, 9.24)
14	1.53 (1.31, 1.79)	4.42 (3.82, 5.12)	0.66 (0.53, 0.81)	14.60 (12.44, 17.13)
18C	0.65 (0.55, 0.76)	2.69 (2.32, 3.12)	0.26 (0.21, 0.32)	7.07 (6.01, 8.32)
19A	0.47 (0.38, 0.58)	3.29 (2.89, 3.76)	0.52 (0.40, 0.68)	12.48 (10.76, 14.48)
19F	0.80 (0.67, 0.94)	4.16 (3.61, 4.79)	0.56 (0.44, 0.71)	12.50 (10.48, 14.91)
23F	0.96 (0.79, 1.18)	5.35 (4.55, 6.30)	0.90 (0.71, 1.15)	16.18 (13.75, 19.04)
Additional Serotypes				

Table 13: Pneumococcal IgG GMCs in Participants 15 Months to Less Than 5 Years of Age – Before and 1 Month After Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥15 to <24 Months N[b]=186-190		≥2 to <5 Years N[b]=179-183	
	Before Vaccination GMC[c] (95% CI[c])	After Vaccination GMC[c] (95% CI[c])	Before Vaccination GMC[c] (95% CI[c])	After Vaccination GMC[c] (95% CI[c])
8	0.04 (0.03, 0.05)	4.66 (4.17, 5.22)	0.05 (0.04, 0.06)	5.08 (4.45, 5.80)
10A	0.01 (0.01, 0.02)	1.23 (1.02, 1.48)	0.03 (0.02, 0.03)	2.76 (2.28, 3.34)
11A	0.03 (0.02, 0.03)	1.61 (1.40, 1.86)	0.06 (0.04, 0.08)	2.64 (2.25, 3.09)
12F	0.01 (0.01, 0.01)	0.22 (0.18, 0.27)	0.01 (0.01, 0.01)	0.38 (0.31, 0.46)
15B	0.02 (0.02, 0.03)	1.17 (0.97, 1.40)	0.05 (0.04, 0.07)	3.96 (3.12, 5.03)
22F	0.01 (0.00, 0.01)	9.57 (8.12, 11.29)	0.02 (0.01, 0.02)	12.46 (10.82, 14.35)
33F	0.02 (0.01, 0.02)	1.91 (1.60, 2.27)	0.04 (0.03, 0.05)	3.16 (2.63, 3.79)

Abbreviations: GMC=geometric mean concentration; IgG=immunoglobulin G; LLOQ= lower limit of quantitation.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
a. Study 1014 was conducted in the United States (NCT04642079).
b. N=Number of participants with valid IgG concentrations at the given sampling time point.
c. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

Children and adolescents 5 years to less than 18 years of age previously unvaccinated or vaccinated with 13vPnC or 7vPnC

In the study, age groups 5 years to less than 10 years and 10 years to less than 18 years, participants could be unvaccinated or previously vaccinated with 13vPnC or 7vPnC. PREVENAR 20 elicited robust IgG and OPA immune responses to the 20 vaccine serotypes after a single-dose in participants 5 to less than 18 years of age. OPA GMFRs ranged from 11.5 to 499.0 to the 7 additional serotypes and increases in OPA GMTs were observed for all 20 vaccine serotypes (Table 14).

In summary, a single-dose of PREVENAR 20 administered to children and adolescents 15 months to less than 18 years of age is expected to generate protective responses against pneumococcal disease due to the 7 additional serotypes, and to the 13 matched serotypes.

Table 14: Pneumococcal OPA GMTs in Participants 5 to Less Than 18 Years of Age – Before and 1 Month After Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥5 to <10 Years N[b]=76-175		≥10 to <18 Years N[b]=86-187	
	Before Vaccination GMT[c] (95% CI[c])	After Vaccination GMT[c] (95% CI[c])	Before Vaccination GMT[c] (95% CI[c])	After Vaccination GMT[c] (95% CI[c])
Serotypes				
1	10 (9, 11)	548 (455, 660)	11 (9, 12)	396 (302, 519)
3	29 (22, 40)	155 (135, 178)	19 (14, 24)	105 (88, 124)
4	43 (27, 67)	2328 (1942, 2789)	34 (22, 51)	2290 (1822, 2878)
5	15 (15, 15)	385 (324, 458)	15 (15, 16)	216 (159, 294)
6A	74 (51, 106)	8268 (6617, 10331)	64 (44, 91)	9434 (7616, 11686)
6B	156 (99, 244)	6569 (5367, 8040)	237 (155, 363)	10085 (8263, 12309)
7F	541 (410, 713)	3981 (3446, 4598)	516 (381, 698)	3326 (2878, 3843)
9V	410 (289, 580)	11717 (9262, 14823)	469 (330, 667)	9627 (7492, 12369)
14	246 (172, 353)	4610 (3688, 5762)	97 (65, 145)	3925 (3153, 4885)
18C	152 (89, 261)	6766 (5585, 8197)	73 (45, 119)	3617 (2816, 4645)
19A	117 (76, 181)	2162 (1786, 2618)	66 (44, 100)	2212 (1801, 2717)
19F	91 (66, 125)	1095 (810, 1479)	57 (44, 73)	551 (401, 757)

Table 14: Pneumococcal OPA GMTs in Participants 5 to Less Than 18 Years of Age – Before and 1 Month After Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥5 to <10 Years N[b]=76-175		≥10 to <18 Years N[b]=86-187	
	Before Vaccination GMT[c] (95% CI[c])	After Vaccination GMT[c] (95% CI[c])	Before Vaccination GMT[c] (95% CI[c])	After Vaccination GMT[c] (95% CI[c])
23F	87 (53, 145)	2213 (1751, 2797)	46 (29, 73)	1842 (1391, 2439)
Additional Serotypes				
8	34 (28, 42)	3870 (3302, 4535)	35 (28, 43)	3125 (2680, 3642)
10A	745 (519, 1071)	21102 (17238, 25833)	554 (395, 777)	17417 (14301, 21214)
11A	1347 (962, 1887)	16882 (13650, 20880)	765 (543, 1076)	11677 (9751, 13982)
12F	48 (38, 60)	23860 (19002, 29959)	46 (36, 59)	20250 (16861, 24320)
15B	79 (54, 115)	25729 (19647, 33695)	45 (33, 61)	21496 (16697, 27672)
22F	259 (170, 394)	33615 (26198, 43130)	243 (161, 366)	27922 (22622, 34463)
33F	3334 (2847, 3905)	45921 (36768, 57353)	2895 (2448, 3424)	32363 (26219, 39946)

Abbreviations: GMT=geometric mean titer; LLOQ=lower limit of quantitation; OPA=opsonophagocytic activity.
Note: OPA titers for all serotypes were determined on serum from randomly selected subsets of participants except for the 7 additional serotypes among participants ≥5 to <18 years of age, which were determined from all available samples.
Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
a. Study 1014 was conducted in the United States (NCT04642079).
b. n=Number of participants with valid OPA titers at the given sampling time point.
c. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student's t distribution).

PREVENAR 20 clinical trials in adults

Three Phase 3 clinical trials, B7471006, B7471007 and B7471008 (Study 1006, Study 1007, and Study 1008, respectively), were conducted in the United States and Sweden evaluating the immunogenicity of PREVENAR 20 in different adult age groups and in individuals who were either pneumococcal vaccine-naïve or who were previously vaccinated with 13vPnC, PPSV23, or both.

Each study included healthy adults and immunocompetent adults with stable underlying conditions including chronic cardiovascular disease, chronic pulmonary disease, renal disorders, diabetes mellitus, chronic liver disease, and medical risk conditions and behaviors (e.g., smoking) that are known to increase the risk of serious pneumococcal pneumonia and IPD. A stable medical condition was defined as a medical condition not requiring significant change in therapy in the previous 6 weeks (i.e., change to new therapy category due to worsening disease) or any hospitalization for worsening disease within 12 weeks before receipt of the study vaccine.

In each study, immune responses elicited by PREVENAR 20 and the control pneumococcal vaccines were measured by an opsonophagocytic activity (OPA) assay. OPA assays measure functional antibodies to *S. pneumoniae*.

Comparison of immune responses of PREVENAR 20 to 13vPnC and PPSV23

In a randomized, active-controlled, double-blind noninferiority clinical trial (Study 1007) of PREVENAR 20 in the United States and Sweden, pneumococcal vaccine-naïve adults 18 years of age and older were enrolled into 1 of 3 cohorts based on their age at enrollment and randomized to receive either PREVENAR 20 or control.

Participants 60 years of age and older were randomly assigned (1:1 ratio) to PREVENAR 20 followed 1 month later with saline placebo or to 13vPnC followed 1 month later with PPSV23.

Serotype-specific OPA GMTs were measured before the first vaccination and 1 month after each vaccination. Noninferiority of immune responses, OPA GMTs 1 month after vaccination, with PREVENAR 20 to a control vaccine for a serotype was declared if the lower bound of the 2-sided 95% confidence interval (CI) for the GMT ratio (PREVENAR 20/13vPnC; PREVENAR 20/PPSV23) for that serotype was greater than 0.5.

In adults 60 years of age and older, immune responses to all 13 matched serotypes elicited by PREVENAR 20 were noninferior to the immune responses to the serotypes elicited by 13vPnC 1 month after vaccination. Immune responses to 6 out of the 7 additional serotypes induced by PREVENAR 20 were noninferior to the immune responses to these same serotypes induced by PPSV23 one month after vaccination. The response to serotype 8 missed the pre-specified statistical noninferiority criterion by a small margin (the lower bound of the 2-sided 95% CI for the GMT ratio being 0.49 versus >0.50) (Table 15).

The GMFR in OPA titers indicated that the response to serotype 8 (GMFR of 22.1) was within the range observed for the 13 serotypes in the 13vPnC group (GMFRs of 5.8 to 42.6). The same trend was also observed both in the percentage of participants with a ≥4-fold rise in OPA titers: 77.8% for serotype 8 in the PREVENAR 20 group, within the range of 54.0% to 84.0% across the 13 serotypes in the 13vPnC group and the percentage of participants with OPA titers ≥ lower limit of quantitation (LLOQ) at 1 month after vaccination: 92.9% for serotype 8 in the PREVENAR 20 group, within the range of 76.0% to 96.6% across the 13 serotypes in the 13vPnC group.

Table 15. OPA GMTs 1 Month After Vaccination in Adults 60 Years of Age and Older Given PREVENAR 20 Compared to 13vPnC for the 13 Matched Serotypes and PPSV23 for the 7 Additional Serotypes (Study 1007)[a,b,c,d]

	PREVENAR 20 (N=1157–1430)	13vPnC (N=1390–1419)	PPSV23 (N=1201–1319)	Vaccine Comparison
	GMT[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]
Serotype				
1	123	154		0.80 (0.71, 0.90)
3	41	48		0.85 (0.78, 0.93)
4	509	627		0.81 (0.71, 0.93)
5	92	110		0.83 (0.74, 0.94)
6A	889	1165		0.76 (0.66, 0.88)
6B	1115	1341		0.83 (0.73, 0.95)

Table 15. OPA GMTs 1 Month After Vaccination in Adults 60 Years of Age and Older Given PREVENAR 20 Compared to 13vPnC for the 13 Matched Serotypes and PPSV23 for the 7 Additional Serotypes (Study 1007)[a,b,c,d]

	PREVENAR 20 (N=1157–1430)	13vPnC (N=1390–1419)	PPSV23 (N=1201–1319)	Vaccine Comparison
	GMT[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]
7F	969	1129		0.86 (0.77, 0.96)
9V	1456	1568		0.93 (0.82, 1.05)
14	747	747		1.00 (0.89, 1.13)
18C	1253	1482		0.85 (0.74, 0.97)
19A	518	645		0.80 (0.71, 0.90)
19F	266	333		0.80 (0.70, 0.91)
23F	277	335		0.83 (0.70, 0.97)
Additional Serotypes				
8	466		848	0.55 (0.49, 0.62)
10A	2008		1080	1.86 (1.63, 2.12)
11A	4427		2535	1.75 (1.52, 2.01)
12F	2539		1717	1.48 (1.27, 1.72)
15B	2398		769	3.12 (2.62, 3.71)
22F	3666		1846	1.99 (1.70, 2.32)
33F	5126		3721	1.38 (1.21, 1.57)

Abbreviations: CI=confidence interval; GMT=geometric mean titer; LLOQ=lower limit of quantitation; N=number of participants; OPA=opsonophagocytic activity; 13vPnC=13-valent pneumococcal conjugate vaccine; PPSV23=pneumococcal polysaccharide vaccine (23-valent).

a. Study 1007 was conducted in the United States and in Sweden (NCT03760146).
b. Noninferiority for a serotype was met if the lower bound of the 2-sided 95% CI for the GMT ratio (ratio of PREVENAR 20/comparator) was greater than 0.5 (2-fold criterion for noninferiority).
c. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
d. Evaluable immunogenicity population.
e. GMTs and GMT ratios as well as the associated 2-sided CIs were based on analysis of log-transformed OPA titers using a regression model with vaccine group, sex, smoking status, age at vaccination in years, and baseline log transformed OPA titers.

Immunogenicity in adults 18 through 59 years of age

Two studies (Study 1007 and Study 1008) assessed immune responses in adults 18 through 59 years of age with no history of prior pneumococcal vaccination. In Study 1007, described above, participants 50 through 59 years of age and participants 18 through 49 years of age were randomly assigned (3:1 ratio) to receive 1 vaccination with PREVENAR 20 or 13vPnC. Serotype-specific OPA GMTs were measured before

vaccination and 1 month after vaccination. A noninferiority analysis of PREVENAR 20 in the younger age group versus PREVENAR 20 in adults 60 through 64 years of age for a serotype was performed to support the indication in adults 18 through 49 years of age and 50 through 59 years of age. Noninferiority was to be declared if the lower bound of the 2-sided 95% CI for the GMT ratio (PREVENAR 20 in participants 18 through 49 years of age/60 through 64 years of age and in 50 through 59 years of age/60 through 64 years of age) for the 20 serotypes was >0.5. PREVENAR 20 elicited immune responses to all 20 vaccine serotypes in both of the younger age groups that were noninferior to responses in adults 60 through 64 years of age 1 month after vaccination (Table 16).

Table 16. Comparisons of OPA GMTs 1 Month After PREVENAR 20 in Adults 18 Through 49 or 50 Through 59 Years of Age to Adults 60 Through 64 Years of Age (Study 1007)[a,b,c,d]

	18–49 Years (N=251–317)	60–64 Years (N=765–941)	18–49 Years Relative to 60–64 Years	50–59 Years (N=266–320)	60–64 Years (N=765–941)	50–59 Years Relative to 60–64 Years
	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]
Serotype						
1	163	132	1.23 (1.01, 1.50)	136	132	1.03 (0.84, 1.26)
3	42	42	1.00 (0.87, 1.16)	43	41	1.06 (0.92, 1.22)
4	1967	594	3.31 (2.65, 4.13)	633	578	1.10 (0.87, 1.38)
5	108	97	1.11 (0.91, 1.36)	85	97	0.88 (0.72, 1.07)
6A	3931	1023	3.84 (3.06, 4.83)	1204	997	1.21 (0.95, 1.53)
6B	4260	1250	3.41 (2.73, 4.26)	1503	1199	1.25 (1.00, 1.56)
7F	1873	1187	1.58 (1.30, 1.91)	1047	1173	0.89 (0.74, 1.07)
9V	6041	1727	3.50 (2.83, 4.33)	1726	1688	1.02 (0.83, 1.26)
14	1848	773	2.39 (1.93, 2.96)	926	742	1.25 (1.01, 1.54)
18C	4460	1395	3.20 (2.53, 4.04)	1805	1355	1.33 (1.06, 1.68)
19A	1415	611	2.31 (1.91, 2.81)	618	600	1.03 (0.85, 1.25)
19F	655	301	2.17 (1.76, 2.68)	287	290	0.99 (0.80, 1.22)
23F	1559	325	4.80 (3.65, 6.32)	549	328	1.68 (1.27, 2.22)
Additional Serotypes						
8	867	508	1.71 (1.38, 2.12)	487	502	0.97 (0.78, 1.20)
10A	4157	2570	1.62 (1.31, 2.00)	2520	2437	1.03 (0.84, 1.28)
11A	7169	5420	1.32 (1.04, 1.68)	6417	5249	1.22 (0.96, 1.56)

Table 16. Comparisons of OPA GMTs 1 Month After PREVENAR 20 in Adults 18 Through 49 or 50 Through 59 Years of Age to Adults 60 Through 64 Years of Age (Study 1007)[a,b,c,d]

	18–49 Years (N=251–317)	60–64 Years (N=765–941)	18–49 Years Relative to 60–64 Years	50–59 Years (N=266–320)	60–64 Years (N=765–941)	50–59 Years Relative to 60–64 Years
	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]
12F	5875	3075	1.91 (1.51, 2.41)	3445	3105	1.11 (0.88, 1.39)
15B	4601	3019	1.52 (1.13, 2.05)	3356	2874	1.17 (0.88, 1.56)
22F	7568	4482	1.69 (1.30, 2.20)	3808	4228	0.90 (0.69, 1.17)
33F	7977	5693	1.40 (1.10, 1.79)	5571	5445	1.02 (0.81, 1.30)

Abbreviations: CI=confidence interval; GMT=geometric mean titer; LLOQ=lower limit of quantitation; N=number of participants; OPA=opsonophagocytic activity; PPSV23=pneumococcal polysaccharide vaccine (23-valent).

a. Study 1007 was conducted in the United States and in Sweden (NCT03760146).
b. Noninferiority for a serotype was met if the lower bound of the 2-sided 95% CI for the GMT ratio (ratio of younger age group/60 through 64 years of age group) was greater than 0.5 (2-fold criterion for noninferiority).
c. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
d. Evaluable immunogenicity population.
e. GMTs, GMT ratios, and the associated 2-sided CIs were based on analysis of log-transformed OPA titers using a regression model with age group, sex, smoking status, and baseline log transformed OPA titers. The comparisons between adults 18 through 49 years of age and adults 60 through 64 years of age and between adults 50 through 59 years of age and adults 60 through 64 years of age were based on separate regression models.

Study 1008 was a randomized double-blind trial to evaluate immunogenicity of 3 separately manufactured lots of PREVENAR 20. It was conducted in the United States and enrolled adults 18 through 49 years of age. The 3 different lots of PREVENAR 20 elicited immune responses that met the objectives of the study.

Immunogenicity of PREVENAR 20 in adults previously vaccinated with pneumococcal vaccine

A Phase 3 randomized, open-label clinical trial (Study 1006) described immune responses to PREVENAR 20 in adults 65 years of age and older previously vaccinated with PPSV23 (≥1 to ≤5 years prior to enrollment), previously vaccinated with 13vPnC (≥6 months prior to enrollment), or previously vaccinated with 13vPnC followed by PPSV23 (with PPSV23 vaccination ≥1 year prior to enrollment). Participants in this study previously vaccinated with 13vPnC (13vPnC only or followed by PPSV23) were enrolled at sites in the United States and participants previously vaccinated with PPSV23 only were also enrolled from Swedish sites (35.5% in that category).

PREVENAR 20 elicited immune responses to all 20 vaccine serotypes in adults 65 years of age and older with prior pneumococcal vaccination (Table 17).

Table 17. Pneumococcal OPA GMTs Before and 1 Month After PREVENAR 20 in Adults 65 Years of Age and Older With Prior Pneumococcal Vaccination (Study 1006)[a,b,c,d]

	Prior PPSV23 Only		Prior 13vPnC Only		Prior 13vPnC and PPSV23	
	Before Vaccination (N=208–247)	After Vaccination (N=216–246)	Before Vaccination (N=210-243)	After Vaccination (N=201–243)	Before Vaccination (N=106–121)	After Vaccination (N=102-121)
	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]
Serotype						
1	24 (20, 28)	51 (42, 62)	34 (28, 41)	115 (96, 138)	42 (32, 56)	82 (61, 110)
3	13 (11, 15)	31 (27, 36)	15 (13, 18)	54 (47, 63)	20 (17, 25)	39 (32, 48)
4	29 (23, 35)	150 (118, 190)	67 (53, 84)	335 (274, 410)	73 (53, 101)	194 (143, 262)
5	27 (24, 31)	63 (53, 75)	38 (32, 44)	87 (73, 104)	47 (37, 59)	83 (65, 108)
6A	57 (46, 70)	749 (577, 972)	125 (99, 158)	1081 (880, 1327)	161 (116, 224)	1085 (797, 1478)
6B	107 (86, 133)	727 (574, 922)	174 (138, 219)	1159 (951, 1414)	259 (191, 352)	1033 (755, 1415)
7F	156 (132, 184)	378 (316, 452)	210 (175, 251)	555 (467, 661)	206 (164, 258)	346 (277, 432)
9V	203 (171, 241)	550 (454, 667)	339 (282, 408)	1085 (893, 1318)	352 (270, 459)	723 (558, 938)
14	212 (166, 270)	391 (315, 486)	282 (224, 356)	665 (554, 798)	336 (238, 473)	581 (434, 777)
18C	173 (137, 218)	552 (445, 684)	219 (177, 272)	846 (693, 1033)	278 (209, 369)	621 (470, 821)
19A	82 (66, 100)	239 (197, 288)	124 (100, 153)	365 (303, 440)	182 (141, 235)	341 (264, 439)
19F	61 (52, 71)	159 (131, 192)	89 (74, 107)	242 (199, 294)	120 (94, 154)	218 (168, 282)
23F	23 (18, 28)	152 (115, 199)	48 (37, 62)	450 (358, 566)	66 (46, 94)	293 (204, 420)
Additional Serotypes						
8	55 (45, 67)	212 (172, 261)	28 (24, 33)	603 (483, 753)	139 (99, 195)	294 (220, 392)
10A	212 (166, 269)	1012 (807, 1270)	141 (113, 177)	2005 (1586, 2536)	400 (281, 568)	1580 (1176, 2124)
11A	510 (396, 656)	1473 (1192, 1820)	269 (211, 343)	1908 (1541, 2362)	550 (386, 785)	1567 (1141, 2151)
12F	147 (112, 193)	1054 (822, 1353)	53 (43, 65)	1763 (1372, 2267)	368 (236, 573)	1401 (1002, 1960)
15B	140 (104, 189)	647 (491, 853)	74 (56, 98)	1480 (1093, 2003)	190 (124, 291)	1067 (721, 1578)
22F	167 (122, 230)	1773 (1355, 2320)	60 (45, 82)	4157 (3244, 5326)	286 (180, 456)	2718 (1978, 3733)
33F	1129 (936, 1362)	2026 (1684, 2437)	606 (507, 723)	3175 (2579, 3908)	1353 (1037, 1765)	2183 (1639, 2908)

Abbreviations: CI=confidence interval; GMT=geometric mean titer; LLOQ=lower limit of quantitation; N=number of participants; OPA=opsonophagocytic activity; 13vPnC=13-valent pneumococcal conjugate vaccine; PPSV23=pneumococcal polysaccharide vaccine (23-valent).

a. Study 1006 was conducted in the United States and in Sweden (NCT03835975).
b. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
c. Evaluable immunogenicity population.
d. Open-label administration of PREVENAR 20.
e. 2-sided CIs based on the Student's t distribution.

Concomitant vaccine administration

Infants and children

In Study 1012, the concomitant administration of Infanrix hexa (containing DTaP, HBV, IPV, and Hib antigens) with all 3 doses of PREVENAR 20 or 13vPnC and single doses of MMRVAXPRO and Varilrix vaccine (containing MMR and varicella antigens respectively) were also administered with the third dose and evaluated 1 month after the third (toddler) dose of PREVENAR 20 or 13vPnC. Noninferiority was demonstrated for immune responses to diphtheria, tetanus, acellular pertussis, hepatitis B, poliovirus, Hib, MMR, and varicella vaccine antigens co-administered with PREVENAR 20 compared with 13vPnC. The results from Study 1012 support co-administration of PREVENAR 20 with routine pediatric vaccines. No safety concerns were identified in this study.

In Study 1011, the concomitant administration of Pediarix (containing DTaP, HBV, IPV antigens) and Hiberix (Hib antigen) with each of the 3 infant doses of either PREVENAR 20 or 13vPnC were evaluated 1 month after the third dose. Concomitant administration of single doses of M-M-R II (MMR antigens) and VARIVAX (varicella antigens) with the fourth dose of either PREVENAR 20 or 13vPnC were evaluated 1 month following vaccination. Noninferiority was demonstrated for immune responses to the co-administered diphtheria, tetanus, acellular pertussis, hepatitis B virus, poliovirus, and Hib vaccine antigens 1 month after 3 infant doses and co-administered MMR, and varicella virus vaccine antigens after the fourth (toddler) dose of PREVENAR 20 compared with 13vPnC. The results from Study 1011 support co-administration of PREVENAR 20 with routine pediatric vaccines. No safety concerns were identified in this study.

Influenza and rotavirus vaccines were permitted to be administered concomitantly at any time during these studies according to local or national recommendations.

Clinical trial in adults to assess PREVENAR 20 given with influenza vaccine, adjuvanted (Fluad Quadrivalent, [QIV])

In a double-blind, randomized study B7471004 (Study 1004), adults 65 years of age and older were randomized in a 1:1 ratio to receive PREVENAR 20 concomitantly administered with an influenza vaccine, adjuvanted (Fluad Quadrivalent, [QIV]) (Group 1, N=898) or PREVENAR 20 administered 1 month after receiving QIV (Group 2, N=898). Pneumococcal serotype-specific OPA GMTs were evaluated 1 month after PREVENAR 20 and influenza vaccine strain hemagglutinin inhibition assay (HAI) GMTs were evaluated 1 month after QIV. The noninferiority criteria for the comparisons of OPA GMTs (lower limit of the 2-sided 95% CI of the GMT ratio [Group 1/Group 2] >0.5, 2-fold noninferiority criterion) were met for all 20 pneumococcal serotypes in PREVENAR 20. The noninferiority criteria for the comparisons of HAI GMTs (lower limit of the 2-sided 95% CI for the GMT ratio [Group 1/Group 2] >0.67, 1.5-fold noninferiority criterion) were also met for all 4 influenza vaccine strains.

Clinical trial in adults to assess PREVENAR 20 given with a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified)

In a double-blind, randomized descriptive study B7471026 (Study 1026), adults 65 years of age and older who had received 2 doses of COVID-19 mRNA vaccine (nucleoside modified) at least 6 months earlier, were randomized in a 1:1:1 ratio to receive PREVENAR 20 concomitantly administered with a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified) (N=190), PREVENAR 20 administered alone (N=191), or a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified) administered alone (N=189).

Immune responses to both vaccines were observed after co-administration of PREVENAR 20 and COVID-19 mRNA vaccine (nucleoside modified). OPA GMTs for the 20 pneumococcal serotypes were similar to PREVENAR 20 administered alone and IgG GMCs for the full-length S-binding protein were similar to COVID-19 mRNA vaccine (nucleoside modified) administered alone. A post-hoc analysis found the immune responses to all 20 serotypes elicited by PREVENAR 20 when co-administered with COVID-19 mRNA vaccine (nucleoside modified) would have met conventional 2-fold noninferiority criteria compared to PREVENAR 20 alone, and the full-length S-binding IgG GMC elicited by COVID-19 mRNA vaccine (nucleoside modified) would have met conventional 1.5-fold noninferiority criteria compared to COVID-19 mRNA vaccine (nucleoside modified) alone.

5.2. Pharmacokinetic properties

Not applicable.

5.3. Preclinical safety data

Nonclinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity and reproduction and developmental toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Aluminium phosphate
Succinic acid
Sodium chloride
Polysorbate 80
Water for injections

6.2. Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

6.3. Special precautions for storage

Store in a refrigerator 2°C to 8°C.

Syringes should be stored in the refrigerator horizontally to minimize the re-dispersion time.

Do not freeze. Discard if the vaccine has been frozen.

PREVENAR 20 should be administered as soon as possible after being removed from refrigeration.

PREVENAR 20 can be administered provided total (cumulative multiple excursions) time out of refrigeration (at temperatures between 8°C and 25°C) does not exceed 96 hours. Cumulative multiple excursions between 0°C and 2°C are also permitted as long as the total time between 0°C and 2°C does not exceed 72 hours. These are not, however, recommendations for storage.

6.4. Nature and contents of container

0.5 mL suspension for injection in pre-filled syringe (Type I glass) with a tip cap (synthetic isoprene/bromobutyl blend rubber) and a plunger stopper (chlorobutyl rubber).

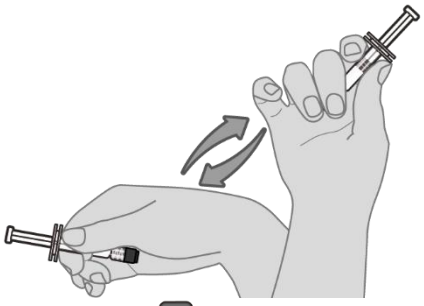
Pack size of 1 pre-filled syringe, with needle.

6.5. Special precautions for disposal and other handling

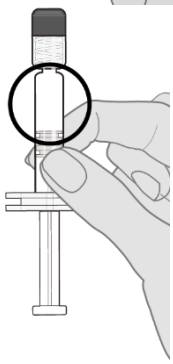
During storage, a white deposit and clear supernatant may be observed in the pre-filled syringe containing the suspension. Syringes should be stored horizontally to minimize the re-dispersion time.

Preparation for administration

Step 1. Vaccine resuspension
Hold the pre-filled syringe horizontally between the thumb and the forefinger and shake vigorously until the contents of the syringe are a homogeneous white suspension. Do not use the vaccine if it cannot be re-suspended.

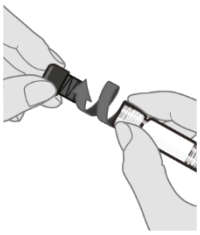


Step 2. Visual inspection
Visually inspect the vaccine for large particulate matter and discoloration prior to administration. Do not use if large particulate matter or discoloration is found. If the vaccine is not a homogeneous white suspension, repeat steps 1 and 2.



Step 3. Remove syringe cap
Remove the syringe cap from the Luer lock adapter by slowly turning the cap counter-clockwise while holding the Luer lock adapter.

Note: Care should be taken to ensure that the extended plunger rod is not depressed while removing the syringe cap.



Step 4. Attach a sterile needle
Attach a needle appropriate for intramuscular administration to the pre-filled syringe by holding the Luer lock adapter and turning the needle clockwise.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Manufactured and packed by:
Pfizer Ireland Pharmaceuticals Unlimited Company
Grange Castle Business Park
Nangor Road Dublin 22
Ireland

Released by:
Pfizer Manufacturing Belgium NV
Rijksweg 12

2870 Puurs-Sint-Amands
Belgium

Imported by:
PT. Pfizer Indonesia
Jakarta, Indonesia

8. MARKETING AUTHORISATION NUMBER(S)

PREVENAR 20® Box, 1 pre-filled syringe @ 0.5 mL (Reg. No.: DKI2486102143A1)

Obat Keras

HARUS DENGAN RESEP DOKTER

9. DATE OF REVISION OF THE TEXT

10. DATE OF FIRST APPROVAL

12 September 2024