ISHA'S GMP CONSULTANCY PVT. LTD.
Ensuring Global GMP Compliance™ ®

BRIMONIDINE API

STAGE-WISE MASS BALANCE | MANUFACTURING PROCESS

Source-based one-page technical illustration | All five Excel worksheets

TECHNICAL REVIEW | 2026

Material balance / FC / CC
Raw materials / Moles

GROSS STAGE INPUTS	GROSS STAGE OUTPUTS	FINAL PRODUCT REPORTED	REPORTED YIELD
148.218 kg	148.216 kg	1.000 kg	26%
MB reported total	MB reported total	Brimonidine tartarate [source]	Calculation requires review

PROCESS FLOW

STAGE A — Reaction / distillation / filtration / drying > STAGE B — Reaction / filtration / drying > STAGE C — Reaction / filtration / drying > FINAL — Reaction / filtration / drying

STAGE 01 — Stage A - initial synthesis

Reaction / distillation / filtration / drying

INPUTS / CHARGES	kg
6-amino 5 bromo quinoxaline	1.9519
Benzoyl Chloride	0.8916
Ammonium thio cyanate	0.524
Acetone	34.2041
DM water	34.2041
Sodium Hydroxide	1.1043
Conc HCl	2.3449

OUTPUTS / RECOVERY / LOSS	kg
Distillate -Recovery	30.13
Evaporation loss	3.93
Filterate -to ETP	31.44
Evaporation loss	5.24
Evaporation loss	2.62
Intermediate solid (stage output)	**2.0436**

IN 75.225 kg **OUT 75.404 kg**
Delta (out - in): +0.179 kg

STAGE 02 — Stage B - intermediate synthesis

Reaction / filtration / drying

INPUTS / CHARGES	kg
Stage-A	2.0436
Bromobenzene	19.519
Ethylene diamine	1.6506
Ethanol	13.6764

OUTPUTS / RECOVERY / LOSS	kg
Filtrate	30.13
Evaporation loss	2.62
Intermediate solid (stage output)	**1.124**

IN 36.890 kg **OUT 36.494 kg**
Delta (out - in): -0.396 kg

STAGE 03 — Stage C - intermediate isolation

Reaction / filtration / drying

INPUTS / CHARGES	kg
Stage-B	1.124
L(+) Tartaric acid	0.6602
Methanol	19.9382

OUTPUTS / RECOVERY / LOSS	kg
Filterate	15.72
Evaporation loss	2.61
Evaporation loss	3
Intermediate solid (stage output)	**1.5432**

IN 21.722 kg **OUT 22.873 kg**
Delta (out - in): +1.151 kg

STAGE 04 — Final API isolation

Reaction / filtration / drying

INPUTS / CHARGES	kg
Stage-C	1.5432
Water	3.668
IPA	9.17

OUTPUTS / RECOVERY / LOSS	kg
Filterate	9.825
Evaporation loss	1.31
Evaporation loss	1.31
Brimonidine tartarate - final	**1**

IN 14.381 kg **OUT 13.445 kg**
Delta (out - in): -0.936 kg

CHARGE SHEET + MOLAR / PROPOSED CONSUMPTION (CC + MOLES)

No.	Raw material	kg	Molar	MT/day
1	6-amino 5 bromo quinoxaline	1.95	1	0.6500
2	Benzoyl Chloride	0.89	0.728	0.2966
3	Ammonium thio cyanate	0.52	0.785	0.1733
4	Acetone	34.20	-	11.3999
5	Sodium Hydroxide	1.10	3.16	0.3666
6	Conc Hcl	2.34	-	0.7799

No.	Raw material	kg	Molar	MT/day
7	Bromobenzene	19.52	14.3	6.5066
8	Ethylene diamine	1.65	3.15	0.5499
9	Ethanol	13.68	-	4.5599
10	L(+) Tartaric acid	0.66	0.5	0.2199
11	Methanol	19.94	-	6.6466
12	IPA	9.17	-	3.0566

RECOVERY & WASTE SUMMARY

Acetone recovered	30.13 kg
Effluent to ETP	31.44 kg
Fugitive emissions (reported)	33.12 kg
Solid waste	Nil

DATA RECONCILIATION & GMP REVIEW POINTS

RECONCILIATION REQUIRED

01 Stage-by-stage imbalance
Out - in (kg): A +0.179; B -0.396; C +1.151; Final -0.936.

02 Gross total masks differences
MB records 148.218 kg in and 148.216 kg out; transfers recur.

03 Yield inconsistent
Source reports 26%; 1.00 / 1.97 theoretical = 50.76%.

04 Charges & waste need review
CC excludes water; evaporation rows total 25.26 kg vs 33.12 kg fugitive reported.

Source: 4-Brimonidine.xlsx (Material balance sheet, FC, CC, Raw materials, Moles). Gross stage totals include repeated intermediate transfers.

REFERENCE / TECHNICAL REVIEW ONLY - verify stage losses, reported yield, raw-material basis and waste data before approved GMP use.

ISHA'S GMP CONSULTANCY PVT. LTD. +91 86675 89984 info@ishasgmp.com www.ishasgmp.com
© 2026 ISHA'S GMP CONSULTANCY PRIVATE LIMITED. All rights reserved.
For illustration; not an approved manufacturing or mass-balance record.